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Pesticide residues in food 2007

Joint FAO/WHO Meeting on Pesticide Residues

REPORT 2007

World Health Organization

Food and Agriculture Organization of the United Nations

Pesticide residues in food 2007

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Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues
Geneva, Switzerland, 18–27 September 2007

WORLD HEALTH ORGANIZATION
FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS
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CONTENTS

T, toxicological evaluation; R, residue and analytical aspects; D, dietary risk assessment

* New compound

** Evaluated within the Periodic Re-evaluation Programme of the Code Committee on Pesticide Residues

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2007 Joint FAO/WHO Meeting on Pesticide Residues

GENEVA, 18–27 SEPTEMBER 2007

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ABBREVIATIONS

ADI	acceptable daily intake
ai	active ingredient
ARfD	acute reference dose
AST	aspartate aminotransferase
AUC	area under the curve for concentration–time
$BMDL_{10}$	benchmark-dose lower 95% confidence level
bw	body weight
CAS	Chemical Abstracts Service
CCFAC	Codex Committee on Food Additives and Contaminants
CCN	Codex classification number (for compounds or commodities)
CCPR	Codex Committee on Pesticide Residues
CSAF	chemical-specific assessment factor
C_{max}	maximum concentration
EC_{50}	the concentration of agonist that elicits a response that is 50% of the possible maximum
F_1	first filial generation
F_2	second filial generation
FAO	Food and Agricultural Organization of the United Nations
GAP	good agricultural practice
GC	gas chromatography
GGT	gamma-glutamyltransferase
GEMS/Food	Global Environment Monitoring System–Food Contamination Monitoring and Assessment Programme
GnRH	gonadotropin-releasing hormone
hCG	human chorionic gonadotrophin hormone
HPLC	High Performance Liquid Chromatography
HR	highest residue in the edible portion of a commodity found in trials used to estimate a maximum residue level in the commodity
HR-P	highest residue in a processed commodity calculated by multiplying the HR of the raw commodity by the corresponding processing factor
IC_{50}	concentration required to inhibit activity by 50%
IEDI	international estimated daily intake
IESTI	international estimate of short-term dietary intake
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry

JECFA	Joint FAO/WHO Expert Committee on Food Additives
JMPR	Joint Meeting on Pesticide Residues
JMPS	Joint FAO/WHO Meeting on Pesticide Specifications
LC	liquid chromatography
LC_{50}	median lethal concentration
LD_{50}	median lethal dose
LH	luteinising hormone
LOAEC	lowest-observed-adverse-effect concentration
LOAEL	lowest-observed-adverse-effect level
LOD	limit of detection
LOQ	limit of quantification
MTD	maximum tolerated dose
MCH	mean corpuscular haemoglobin
MCV	mean corpuscular volume
MEQ	methylethoxyquin
MIC	minimum inhibitory concentration
MRL	maximum residue limit
MS	mass spectrometry
MS/MS	tandem mass spectrometry
NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect level
OECD	Organization for Economic Co-operation and Development
PHI	pre-harvest interval
PPARα	peroxisome proliferator-induced receptor alpha
ppm	parts per million
STMR	supervised trials median residue
STMR-P	supervised trials median residue in a processed commodity calculated by multiplying the STMR of the raw commodity by the corresponding processing factor
TIPA	triisopropylammonium
TLC	thin-layer chromatography
THPI	1,2,3,6-tetrahydrophthalimide
TRR	total radiolabelled residue
TSH	thyroid stimulating hormone
TMDI	theoretical maximum daily intake
WHO	World Health Organization

USE OF JMPR REPORTS AND EVALUATIONS BY REGISTRATION AUTHORITIES

Most of the summaries and evaluations contained in this report are based on unpublished proprietary data submitted for use by JMPR in making its assessments. A registration authority should not grant a registration on the basis of an evaluation unless it has first received authorization for such use from the owner of the data submitted for the JMPR review or has received the data on which the summaries are based, either from the owner of the data or from a second party that has obtained permission from the owner of the data for this purpose.

PESTICIDE RESIDUES IN FOOD

REPORT OF THE 2007 JOINT FAO/WHO MEETING OF EXPERTS

1. INTRODUCTION

A Joint FAO/WHO Meeting on Pesticide Residues (JMPR) was held at the headquarters of the World Health Organization (WHO), Geneva, Switzerland, from 18 to 27 September 2007. The Meeting brought together the Food and Agriculture Organization of the United Nations (FAO) Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group.

The Meeting was opened by Dr Maria Neira, Director, WHO, on behalf of the Director-General of WHO and the Director-General of FAO. Dr Neira acknowledged the important role played by the work of the Meeting in the establishment of international food safety standards and its contribution to sustainable development. She informed the Meeting of the six-point agenda (promoting development, fostering health security, strengthening health systems, harnessing research, information and evidence, enhancing partnerships, and improving performance) that the new Director-General of WHO, Dr Margaret Chan, had proposed for the organization. That agenda also referred to using evidence to define strategies and measure results, and in that context the work of the Meeting was an important contribution to the goals of WHO. Dr Neira informed the Committee that the 50th World Health Assembly had approved an increased budget for food safety and nutrition and for public health and the environment, which illustrated the importance given by the Member States to these areas of work. She emphasized that FAO and WHO considered the provision of scientific advice in food safety an important and core activity.

The Meeting was held in pursuance of recommendations made by previous Meetings and accepted by the governing bodies of FAO and WHO that studies should be undertaken jointly by experts to evaluate possible hazards to humans arising from the occurrence of residues of pesticides in foods. The reports of previous Meetings (see Annex 5) contain information on acceptable daily intakes (ADIs), acute reference doses (ARfDs), maximum residue limits (MRLs), and the general principles that have been used for evaluating pesticides. The supporting documents (residue and toxicological evaluations) contain detailed monographs on these pesticides and include evaluations of analytical methods.

During the Meeting, the FAO Panel of Experts was responsible for reviewing residue and analytical aspects of the pesticides under consideration, including data on their metabolism, fate in the environment, and use patterns, and for estimating the maximum levels of residues that might occur as a result of use of the pesticides according to good agricultural practice. The estimation of MRLs and supervised trials median residue (STMR) values for commodities of animal origin was elaborated. The WHO Core Assessment Group was responsible for reviewing toxicological and related data in order to establish ADIs, and ARfDs, where necessary and possible.

The Meeting evaluated 31 pesticides, including 6 new compounds and 10 compounds that were reviewed within the Periodic Re-evaluation Programme of the Codex Committee on Pesticide Residues (CCPR) for toxicity or residues, or both. Toxicological evaluation and development of MRLs was also performed for 12 additional pesticides

The Meeting established ADIs and ARfDs, estimated MRLs and recommended them for use by the CCPR, and estimated STMR and highest residue (HR) levels as a basis for estimating dietary intakes.

The Meeting also estimated the dietary intakes (both short-term and long-term) of the pesticides reviewed and, on this basis, performed a dietary risk assessment in relation to their ADIs or ARfDs. Cases in which ADIs or ARfDs may be exceeded were clearly indicated in order to facilitate the decision-making process by the CCPR. The rationale for methodologies for long-term and short-term dietary risk assessment are described in detail in the reports of the 1997 JMPR (Annex 5,

reference *80*, section 2.3) and 1999 JMPR (Annex 5, reference *86*, section 2.2). Additional considerations are described in the report of the 2000 JMPR (Annex 5, reference *89*, sections 2.1–2.3).

The Meeting also considered a number of general issues addressing current issues related to the risk assessment of chemicals, the evaluation of pesticide residues and the procedures used to recommend maximum residue levels.

The Meeting responded to a number of specific concerns raised by CCPR.

The tentative agenda on the list of compounds for evaluation by the 2007 JMPR was amended as followings:

- Due to the lack of data in support of the residue evaluation of permethrin and the toxicological evaluation of vinclozolin, these compounds were removed from the agenda;
- In response to the 39th CCPR, residue evaluations of profenofos and dimethoate were rescheduled to the 2008 JMPR;
- The residue evaluation of tebuconazole was postponed to 2008 due to unforeseen circumstances.

1.1 DECLARATION OF INTEREST

The Secretariat informed the Committee that all experts participating in the 2007 JMPR had completed declaration-of-interest forms, and that no conflicts had been identified. The Meeting was informed of the following potentially relevant interests: Professor Boobis and Dr McGregor were or had been consulting on compounds not on the agenda of this meeting, but for companies that had submitted data for other compounds evaluated by this meeting; Professor Ray's research group had received funding from the pesticide industry for mechanistic studies on the toxicity of certain pyrethroids, none of which were on the agenda of the present Meeting.

2. GENERAL CONSIDERATIONS

2.1 SHORT-TERM DIETARY INTAKE ASSESSMENT: FURTHER CONSIDERATIONS

The 2006 Meeting had discussed the uncertainties in the calculation and interpretation of international estimated short-term intake (IESTI) (Annex 5, reference *107*, general item 2.4). In this context, the present Meeting welcomed the publication of an Opinion by the European Food Safety Authority (EFSA) on 'Acute dietary intake assessment of pesticide residues in fruit and vegetables'.[1]

The Meeting acknowledged the usefulness of the detailed analysis performed by EFSA, which was based on supervised field-trial data provided to the European Union, available national monitoring data and food-consumption databases from nine European countries covering the Global Environment Monitoring System—Food Contamination Monitoring and Assessment Programme (GEMS/Food) cluster diets F (Scandinavian), E (central European) and B (Mediterranean). Inter alia, the EFSA Opinion addressed the effect of choosing the default value of 3 for the variability factor and also the effect of replacing the highest residue (HR) in the IESTI equation by the maximum residue limit (MRL).

The MRL is the maximum concentration of a pesticide residue that the Codex Alimentarius Commission recommends should be legally permitted in a food.[2] MRLs are based on data on good agricultural practice (GAP) and foods derived from commodities that comply with the respective MRLs are intended to be safe for human consumption.[2] Whether a particular food commodity is safe for human consumption is assessed by comparing estimated extreme (high-end) intakes using the IESTI equation and comparing the estimated intake with the ARfD.

MRLs are based on maximum residue levels (a residue definition for enforcement purposes) estimated by JMPR as the maximum concentration of residue expected in food commodities when GAP is used. The HR is the highest residue value (a residue definition for risk-assessment purposes) in the edible portion of a food commodity and is estimated as the highest concentration of residue occurring in samples from valid supervised trials at maximum GAP. Maximum residue levels and HRs are derived from the same set of supervised field trials, in which residues have ideally been measured both in the whole commodity and in the edible portion. When no information is available on the residue in the edible portion, the residue in the whole commodity can be used as a worst-case estimate, provided that the residue definitions for enforcement and risk assessment are the same. When the residue definitions are the same and the whole food commodity is the edible portion, the maximum residue level is typically higher than the HR.

The Meeting noted that in the EFSA analysis, replacing the HR with the MRL in the IESTI equation had a slightly greater effect on the overall distribution of the percentage of person-days with intakes at or below the ARfD than did changing the variability factor from 7 or 5 to 3, the value used by JMPR since 2003. However, the Meeting noted that the intake on the vast majority of person-days would be less than the ARfD.

There is a public perception that small differences in estimated intake are real differences in terms of food safety (e.g., 120% ARfD is unacceptable, 80% ARfD is acceptable). Such differences could potentially arise from use of the HR versus the MRL in the IESTI equation. However, there is conservatism in the derivation of the ARfD and in the estimation of intake. For example, a safety

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[1] European Food Safety Authority (2007) *Opinion of the Scientific Committee on plant protection products and their residues on acute dietary intake of pesticide residues in fruit and vegetables*. Adopted on 19 April 2007 (http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178629328713.htm).

[2] Joint FAO/WHO Codex Alimentarius Commission (2006) *Codex Alimentarius Commission Procedural Manual*, 16th edition. FAO, Rome, (http://www.codexalimentarius.net/web/procedural_manual.jsp).

factor for inter-individual variation is included when the ARfD is established, and as such the ARfD is designed to protect those individuals at the upper-end of human susceptibility. The Meeting further noted that there is likely to be very limited overlap between the population with the greatest sensitivity to a particular pesticide and the population with estimated intake of residues greater than the ARfD. Therefore in cases where the ARfD is exceeded, additional considerations should be taken into account, e.g., the amount by which the ARfD is exceeded, the basis on which the ARfD has been established likely conservatism and possible consequences, and the uncertainties in the estimate of intake.

The Meeting concluded that, overall, IESTI using the HR as an input is a satisfactory indicator for assessing the acceptability of MRLs for the assessment of short-term dietary intake. However, from the perspective of public perception there may be benefits in estimating the IESTI from the MRL.

If using the MRL in the IESTI equation, adjustments and alternatives would be needed in situations where the edible portion is different from the commodity to which the MRL applies, where the risk-assessment definition is different from the enforcement definition and in situations where there are no detectable residues in the edible portions.

The Meeting reiterated its recommendation from 2006 that FAO and WHO should host a consultation to address the issues identified in the reports of the present Meeting and of the Meeting of the previous year, with the participation of relevant stakeholders. The main objectives would be the continued refinement of the estimation of the short-term dietary intake of pesticides and of the interpretation of the outcome of short-term dietary risk assessment conducted by JMPR. The Meeting recommended investigation of the practicalities of using the MRL in IESTI calculations, because allowance would be needed for residues in edible portions, for the risk-assessment residue definition and in situations where no residues are detectable in the edible portion. Furthermore, the issue of whether it is appropriate to use the IESTI equations for evaluating the safety of individual consignments should be further investigated. The discussion should include how to improve communication between JMPR and risk managers and the public on the output of the risk assessment conducted by the Meeting.

2.2 CODEX MAXIMUM RESIDUE LIMITS FOR COMPOUNDS NO LONGER SUPPORTED BY COMPANIES/SPONSORS

When a pesticide is scheduled under the Periodic Re-evaluation programme for review, the entire toxicology and residue chemistry data bases must be supplied to the JMPR by the sponsors, usually the manufacturer(s). Recently two scheduled periodic re-evaluations could not be conducted because companies declined to support the review or to supply the necessary studies to FAO and WHO. Vinclozolin and permethrin had to be removed from the JMPR schedules because toxicology or residue studies, respectively, were not provided. In other instances, only partial data packages were submitted, for example, support of only one isomeric mixture of a pesticide which is marketed as two or more different isomeric mixtures.

The JMPR recommendations are based only on the results of the scientific assessment of the data supplied. In the absence of sufficient toxicological and residue data the Meeting cannot make recommendations for maximum residue levels. The importance of complete data submissions was addressed by the 2006 JMPR (General Consideration 2.1, JMPR Report 2006). It is the prerogative of the CCPR to accept or reject those recommendations, including recommendations to withdraw previous maximum residue levels suitable for use as MRLs. The CCPR has the option to consider other factors that it deems appropriate in retaining MRLs.

2.3 TOXICOLOGICAL RELEVANCE OF TRIAZOLE FUNGICIDES AND THEIR COMMON METABOLITES

The following triazole fungicides have been evaluated by the Meeting:

- Bitertanol
- Difenoconazole
- Fenbuconazole
- Flusilazole
- Hexaconazole
- Myclobutanil
- Penconazole
- Propiconazole
- Tebuconazole
- Triadimefon + Triadimenol

Variable amounts of the common metabolites, 1,2,4-triazolyl acetic acid and 1,2,4-triazolyl alanine are formed in plants, and of 1,2,4-triazole in plants and animals. The amount of 1,2,4-triazole found in rat urine varies from approximately 1% to 65% of the dose administered, depending on the parent compound.

1,2,4-Triazolyl alanine was evaluated toxicologically by the 1989 JMPR. The Meeting at that time concluded from the available data that residues of triazole alanine arising from the use of triazole fungicides do not present a toxicological hazard.

There was less information available on 1,2,4-triazolyl acetic acid, but it is likely to have low toxicity similar to 1,2,4-triazolyl alanine.

1,2,4-Triazole exhibits a number of toxicological effects, but the no-observed-adverse-effect levels (NOAELs) for relevant end-points were higher than those for the respective parent compounds.

In 2004, the Meeting evaluated triadimenol and triadimefon. In this context the plant metabolites 1,2,4-triazole, 1,2,4-triazolyl acetic acid and 1,2,4-triazolyl alanine were also evaluated. The following conclusion was reached:

> Since 1,2,4-triazolyl alanine and 1,2,4-triazolyl acetic acid were of low systemic toxicity and developmental effects with 1,2,4-triazole occur at doses of ≥ 100 mg/kg bw per day, these metabolites were judged not to pose an additional risk to humans.

In a situation in which the metabolites arise from multiple triazole fungicides, they cannot be included in the residue definition. Since the metabolites cannot be linked to a specific triazole fungicide, they would have to be evaluated on their own. The Meeting did not have sufficient information to judge levels that would be without potential effect in consumers. However, the Meeting is aware that a number of studies of toxicity are available on the three common triazole metabolites. Therefore the Meeting recommended that a full evaluation of these metabolites should be performed.

In addition to the possibility of combined exposure to common triazole metabolites, the Meeting wished to draw attention to the possibility of combined exposures to more than one parent triazole. Some, but not all, of the triazole fungicides cause certain toxicological effects (e.g., developmental) that may share a common mode of action. Hence, this should ideally be taken into account when performing a refined intake assessment. The Meeting was aware of ongoing national and regional work on common mechanism groups for triazole fungicides and would welcome regular updates on this. The Meeting therefore recommended that work be undertaken to identify which triazole fungicides should be considered together in a cumulative risk assessment. This would most likely be undertaken at national or regional level, where adequate intake data would be available.

2.4 SETTING OF REFERENCE VALUES FOR ORGANOPHOSPHORUS PESTICIDES: RELEVANCE OF THE BIOCHEMICAL CHARACTERISTICS OF THE INDIVIDUAL COMPOUNDS

The present Meeting established ADIs and ARfDs for the organophosphorus insecticides azinphos-methyl (a di-methyl organophosphate) and profenofos (an ethyl-isopropyl organophosphate). The ADI was 0–0.03 mg/kg bw for both compounds, while the ARfDs were 0.1 and 1 mg/kg bw for azinphos-methyl and profenofos, respectively. The Meeting noted that the ARfD : ADI ratio is about 3.3 for azinphos-methyl and about 33 for profenofos. The Meeting also noted that the median (of results from available studies) oral median lethal doses (LD_{50}s) for azinphos-methyl and profenofos in rats were 13 mg/kg bw and 620 mg/kg bw, respectively, and hence the LD_{50} : ARfD ratio was about 130 for azinphos-methyl and about 620 for profenofos.

The likely explanation for these unexpectedly large differences between these compounds showing the same mode of action is given below.

General characteristics of inhibition of acetylcholinesterase activity by organophosphorus compounds

The molecular target of organophosphorus insecticides is acetylcholinesterase present in the nervous system. Typical clinical signs appear when acetylcholinesterase activity in the nervous system is inhibited by more than about 50% and, in the absence of treatment with antidote, death occurs when acetylcholinesterase activity is inhibited by more than 90%. Inhibition of brain acetylcholinesterase activity (or of its surrogate, erythrocyte acetylcholinesterase activity) by 20% or more is the relevant end-point with which to identify the NOAEL to be used for establishing the ADI or the ARfD.

The inhibited (organophosphorylated) acetylcholinesterase enzyme may either age (i.e., lose a side-chain of the phosphoryl residue), becoming resistant to spontaneous and pharmacologically-mediated reactivation, or may spontaneously reactivate.

Dimethyl-phosphorylated acetylcholinesterase reactivates with a half-life of about 1 h and ages relatively slowly (with a half-life of about 4 h). Hence most of the inhibited acetylcholinesterase will reactivate within a few hours after peak effect and only a relatively small fraction will age (i.e., will be irreversibly inhibited).

Reactivation of di-ethyl phosphorylated acetylcholinesterase is very slow (with a half-life of about 2 days) and there is no measurable reactivation of di-isopropyl phosphorylated acetylcholinesterase. Hence, essentially all acetylcholinesterase inhibited in this way will age.

Given these differences, it is expected that to reach the same level of effect via accumulation of inhibited acetylcholinesterase will require higher and possibly more doses of a di-methyl organophosphate than of a di-ethyl or di-isopropyl organophosphate.

Azinphos-methyl and profenofos

Table 1 shows the oral LD_{50}s in rats and NOAELs in animals given a single dose or repeated doses of azinphos-methyl or profenofos.

From the table it can be seen that, as expected, the dose of azinphos-methyl that was without significant effect on acetylcholinesterase activity after repeated daily doses was only about three times lower (2 versus 0.7) than the single dose that was without significant effect. On the other hand, the daily non-effective dose of profenofos was about 30 times (100 versus 3) lower than the single non-effective dose. This difference is consistent with the biochemical characteristics of inhibited

acetylcholinesterase as described above. However, differences in toxicokinetic parameters, not discussed here, might also play a role in this difference.

The present Meeting used a safety factor of 10 to set the ADI and the ARfD for azinphos-methyl in the light of the availability of reliable data from humans. Based on these data, the Meeting established an ARfD of 0.1 mg/kg bw and an ADI of 0–0.03 mg/kg bw. No relevant data from humans were available for profenofos and the standard safety factor of 100 was therefore applied to the data from animals.

However, while there is an approximately 130-fold difference between the ARfD and the oral LD_{50} in rats for azinphos-methyl and about a 620-fold difference for profenofos, it should be noted that the ARfD for azinphos-methyl is less uncertain since it is based on data from humans.

The Meeting concluded that due attention should be given to the structure of the organophosphorus compound under evaluation in order to properly understand the results of studies with single or repeated doses. Such understanding, together with the availability of adequate toxicokinetics data, might help in defining the chemical-specific assessment factor and in judging the adequacy of the available toxicological data.

Table 1. Oral LD_{50}s in rats and NOAELs for azinphos-methyl and profenofos

Substance	Median oral LD_{50} in rats[a] (mg/kg bw)	NOAEL in animals		Ratio of NOAEL for single dose versus NOAEL for repeated doses
		Single dose (mg/kg bw)	Repeated doses (mg/kg bw per day)	
Azinphos-methyl	13	2	0.7	2.9
Profenofos	620	100	3	33
Ratio for profenofos : azinphos-methyl	48	50	4.3	—

[a] Median of results for available studies.

2.5 CONSIDERATION OF SELECTION OF RESIDUE DATA FROM SUPERVISED TRIALS

The objective in evaluating residue trial data is to select residue values representing the GAP so as to estimate the maximum, median and high residues occurring in commodities treated according to the maximum GAP.

The estimation of STMR and HR values relies on the selection of residue data from trials within GAP. No more than one data point for each value is selected from each trial. A sufficient number of trials approximating GAP are needed to represent field and cultural practice variability (*FAO Manual* 2nd ed. 71).

When considering residue data from trials any one of the following may apply when several residue values are described as “replicates”:

1. replicate laboratory samples taken from a field sample
2. replicate field samples (each sample is taken randomly through a whole sprayed plot)
3. samples from replicate plots or sub or split-plots (the whole trial is subject to the same spraying operation, but it is divided into 2 or more areas that are sampled separately)
4. samples from replicate trials (trials from the same site that are not independent may be considered as replicate trials)

By definition, the Codex MRLs refer to the average residue in the bulk sample taken according to the Codex sampling procedure (Recommended method of sampling for the determination

of pesticide residues for compliance with MRLs
(www.codexalimentarius.net/download/standards/379/cxs_229.pdf).

Consequently, those results which best represent the average residue in independent trials single samples should be selected.

It can be assumed that the normally large samples taken in supervised trials correspond to the size of bulk samples specified by the Codex procedure. Accordingly the maximum residue level for plant commodities can be estimated from the residues measured in composite samples, having a standard deviation of s_i.

Where the average residue measured in replicate random samples taken from one field would be used as a single residue value the true distribution of the residues would be apparently reduced proportional to the square root of the number of replicate field samples.

According to the sampling theory the standard deviation (also called 'standard error') of mean residue in n samples taken from the populations of "i" samples is:

$$S_{\bar{n}} = \frac{S_i}{\sqrt{n}}$$

Consequently if we use the average of two randomly selected replicate field samples taken from a plot, we reduce the standard deviation of the residues by 1.41.

Based on the above considerations, the Meeting decided to use the highest residues measured in replicate field samples taken from one experimental plot in future evaluations.

The Meeting will continue to apply the procedures described in the FAO Manual for the other situations. The Meeting will calculate the average of the analysis results of replicate test portions (replicate laboratory sample), and will select the highest residue value from the various definitions of replicates as the single value for purpose of identifying the STMR or HR value or recommending the maximum residue level.

2.6 RECONSIDERATION OF ALTERNATIVE GAPS

At the 37th Session of the CCPR in 2005 it was proposed that when an estimated exposure for a particular GAP and pesticide/commodity combination exceeds the ARfD, the JMPR should consider alternative GAPs with adequate supporting field trials (ALINORM 05/28/24; para. 67, 68 and 81). The procedures for examining alternative GAPs are identified by the JMPR as either a retrospective or a prospective approach. These were discussed in 2005 and 2006 by the JMPR and CCPR at its 38th Session (ALINORM 06/29/24; para 29).

At the 39th Session of CCPR in 2007 the delegation of the USA presented a paper which summarizes the suggestions made by the CCPR and JMPR from 2005 to 2006 and proposes an explicit process to be used in future (ALINORM 07/30/24; para.21, 22, 41, 42). The Committee noted that the proposed procedure included a number of activities involving JMPR, and agreed that the document would be forwarded to the 2007 JMPR for consideration and advice. The Committee would also consider the alternative GAP procedure at its next session in the light of the advice received from JMPR (ALINORM 07/30/24, para. 43).

The 2007 JMPR welcomed the document which summarizes the lessons learned from the past and gives guidance on the way to proceed. Since the Meeting noted that it had already used a similar procedure for the retrospective and prospective approach in its residue evaluations in 2006 and 2007, the Meeting agreed with the proposals in general.

However, the Meeting was cautious about the proposal to derive an "acceptable highest residue" for the situation, where an alternative GAP is not available. Prospective approach, #2: "*The JMPR should also indicate an approximate acceptable Highest Residue (HR) as one of the*

conclusions of their analysis, i.e., a value that would yield an acceptable IESTI calculation. This information should be in the JMPR Report. This would provide a benchmark for interested parties and would help to alleviate the submission of non-relevant data to JMPR".

The JMPR's concern is that an "acceptable highest residue" would only consider the ARfD and consumption data. Such a value is not based on an existing GAP and on appropriate supervised residue trials. Residues arising from the use of pesticides in agriculture should generally not be present in food unless there is a GAP and then the estimation of maximum residue levels should be based on supervised residue trials data that support the GAP. Therefore an evaluation of pesticide residue data for exposure estimation and trade purposes has to be made on a scientific basis. A theoretical calculated value cannot be used to estimate a maximum residue level. There is an ethical obligation for data submitters to provide a full data set including all the supervised residue trials data related to the relevant GAPs (General Item 2.1, JMPR Report 2006).

The Meeting emphasized that the work of the JMPR is based on the best available scientific information. JMPR considers for its residue evaluations all aspects of the use and the fate of the pesticide and its residues, which implies that all studies that provide such information are necessary.

2.7 MRLS FOR PROCESSED FOODS (ESTABLISHMENT OF MRLS AND/OR PROCESSING FACTORS FOR PROCESSED AND READY-TO-EAT FOODS)

The 39th CCPR (2007) agreed to refer agenda paper CX/PR 07/39/8 (and other relevant documents such as CRD 22) to the 2007 JMPR on the understanding that the JMPR comments would be considered at the 2008 session of CCPR where it would be decided whether to develop guidelines on the application of processing factors (ALINORM 07/30/24 - Rev. 1).

The current policy of the JMPR is that MRLs for raw agricultural commodities should also apply to all processed foods and feeds derived from them (without adjustment), and that separate MRLs are not recommended for processed commodities unless residues are shown to concentrate during processing.

The Meeting reiterated its support for the existing policy and confirmed that it is impractical to establish maximum residue limits for all processed commodities. However, in light of the discussions of the CCPR it is clear that guidance is required to clarify when processing studies may be required, when maximum residue levels should be recommended for processed commodities and the appropriate use of default processing factors.

The Meeting considered there are two main uses of processing studies:

- determining whether or not residues concentrate during processing to the extent that residues legitimately present in the processed commodity occur at levels that may disrupt trade if a maximum residue limit is not established. In this situation processing studies are used in the estimation of a maximum residue level.
- refining dietary intake estimates used by the Meeting in assessing safety to consumers.

It was recalled by some members that the protocol for the superseded Theoretical Maximum Daily Intake (TMDI) calculations required the use of MRLs as estimates of residues. To facilitate refinement of TMDI calculations, maximum residue levels were recommended for a variety of processed commodities with lower residues than the raw agricultural commodity (RAC). International recognition of more realistic long-term exposure estimates such as the International Estimated Dietary Intake (IEDI) which uses high residues (HRs and HR-Ps) and Supervised Trial Median Residues (STMRs and STMR-Ps), negates the need for recommendations where concentration does not occur.

Internationally, refinement of dietary intake estimates is often constrained by a lack of information on consumption of processed commodities. The ability of JMPR to utilise processing factors to refine dietary intake calculations is hampered by an understandable lack of precise

consumption figures. This has been compounded by the recent changes from using 5 regional diets to the use of the 13 cluster diets developed by GEMS/Food. The food balance and other information available in developing 13 cluster diets has led to a smaller number of processed commodities for which consumption figures are available.

Despite the current constraints on the effective use of processing studies by the Meeting when considering dietary intake, it was felt that processing studies should continue to be documented.

Identification of metabolites/degradation products that might form upon processing is an important aspect of an evaluation. Unless processing involves fermentation where the residue may be exposed to metabolism by organisms different from that observed in crop, animal and soil metabolism studies, studies on the pH and temperature dependent hydrolysis and photolysis of the residues should be sufficient to indicate if different degradation products need to be considered in processed commodities.

Specific comments on each of the four recommendations of CCPR agenda paper CX/PR 07/39/8 are provided below:

(1) Processing studies should be mandatory for a relatively short list of commodities (e.g., the 16 commodities proposed by the US). Draft CXLs for the RACs do not advance to Step 8 without the submission to and acceptance by JMPR of the requisite processing studies.

The potential to disrupt trade is likely to be the major driver for processing studies, e.g., concentration of residues in wheat bran. The use of processing studies in dietary risk assessment is typically to enable refinement of the intake estimate (reduction) to obtain more realistic values. While highly desirable, the provision of processing studies is generally not essential for performing risk assessment at the international level. In some cases processing studies allow the refinement of intake estimates to acceptable levels.

The Meeting reviewed processing factors reported in a German database (http://www.bfr.bund.de/cd/579 [3]) obtained from JMPR reports 1995–2006, selected EU-Draft Assessment Reports 2003–2005, BVL: Food monitoring data 2002 and ATLANTA: Citrus fruit data 2007. The review, supported by the experience of panel members, indicates that few processes result in concentration of residues in the processed commodity. These generally involve the separation of the RAC into different components such as bran, hulls and husks from grains, skins and pulp from flesh after juicing, extraction of the oil component from oilseeds and olives and removal of water by dehydration.

Additional factors such as significance in trade and the diet, when combined with likelihood of concentration in the processed commodity, are suitable criteria for establishing a list of commodities requiring processing studies to enable CCPR as risk managers to make appropriate decisions on maximum residue recommendations. The JMPR currently relies on the Codex Alimentarius Classification as its guide to identify major internationally traded processed commodities.

The Meeting observed that many regulators currently require processing studies for commercial processing of RAC that are known to give rise to concentration of residues for some pesticides. JMPR will evaluate the data provided.

If residue levels are low or not detected in the RAC there would be no value in requiring a processing study (see JMPR 1999, page 13).

To assist the CCPR in their discussions the Meeting developed a list of commodities for which processing studies should routinely be submitted as experience suggests residues may concentrate in processed commodities that are in trade (Table 2). The Meeting recognized that it is a CCPR decision whether to advance maximum residue limits for commodities listed in Table 2

[3] At present, the BfR processing factor database contains 1042 processing factors for foods for 116 pesticides and 433 processing factors for feedstuffs for 91 pesticides.

depending on the availability of suitable processing studies. As there are a potentially large number of commodities for which processing studies might be required, the Meeting explored the potential for extrapolation of processing of commodities within a commodity group.

The number of processing studies conducted with a single pesticide on different members of a commodity group is generally small and inadequate to provide guidance on extrapolation of processing studies. However, for a limited number of commodities, the Meeting considered that the available data together with the nature of the related commodities and the similarity of the process would allow pragmatic decisions on extrapolation to be made. These proposals are also indicated in Table 2.

(2) CXLs or processing factors should be established or recommended for those processed commodities where a significant increase (more than 1.3 times) of residue of concern occurs from RAC to processed commodity. It should be decided in advance for which commodities CXLs and for which processing factors will be established.

The Meeting considered that processing studies should only routinely be provided for commodities listed in Table 2. Table 2 also indicates the Meetings suggestions on commodities for which maximum residue levels should be recommended if concentration occurs upon processing.

The JMPR's experience suggests that the accuracy and precision of processing studies is such that a PF of 1.3 cannot be adequately distinguished from a value of 0.7. Concentration of 1.3× is considered not to represent "significant increase" in residues. Where application of the PF to residues from trials leads to estimates in the processed commodity that are less than the proposed maximum residue level for the unprocessed commodity, the JMPR would not normally recommend a separate maximum residue level for the processed commodity.

(3) CXLs or processing factors should be established or recommended for those processed commodities where a significant decrease in residue occurs from RAC to processed commodity, and this should be decided in advance. The processing factor must be considered in order to achieve a satisfactory dietary exposure assessment.

The Meeting was of the opinion that maximum residue levels are not required for processed commodities where residues do not concentrate. In these cases it should be sufficient to document the processing factors used in decision making and in dietary intake (e.g., estimation of STMR-P and HR-P values) in line with current JMPR practice. Table 3 lists types of processing procedures that the Meeting considered would be useful for refining dietary intake calculations but not essential for estimating maximum residue levels. Suggested extrapolations for the use of processing data in dietary intake calculations are also listed.

An exception to not recommending a maximum residue level would be if the acute intake estimate for consumption of the processed commodity was close to the acute reference dose in which case a maximum residue level would be recommended to CCPR. This is considered to be an unlikely event.

(4) A limited number of default (generic) processing factors should be established or recommended for some predefined common processes, starting with dehydration (e.g., dried vegetables, spices, fruits herbal infusions, milk powder). These can be used nationally and internationally for risk assessment purposes.

The Meeting agreed that default dehydration factors are of use in dietary intake assessment (where processing study results are not available) and is aware of a range of default factors employed by the US EPA that would be suitable. Table 4 details a range of default factors that are considered reliable and could be used by the JMPR. Use of default factors would be restricted to situations where there was no other form of processing involved and would not apply to situations such as whole milk → skim milk powder (change in fat content prior to dehydration) or sugar beet → beet pulp, dry (juice extracted prior to dehydration).

Default values assume that no loss of pesticide occurs during drying. For some pesticides, losses by volatilization and decomposition may occur. Defaults would always be superseded by factors based on data. Defaults are not applicable where the process generates a relevant compound e.g., dithiocarbamates → ETU.

Table 2. Industrial processes involving well-defined procedures typically practised on a large scale for major commodities. Most regulatory authorities consider studies for these processes essential for estimation of maximum residue levels.

Raw Agricultural Commodity	Processing	Processed commodity	Required	Extrapolations	Purpose		
					MRL	Diet	Animal feed
Cereal grain – oats, rye, triticale, wheat	Milling	Bran	Y	Wheat → small grains (oats, rye, triticale) except rice	✓	✓	✓
		Flour	Y			✓	
		Germ	Y			✓	
		Wholemeal	O			✓	✓
		Bread	O			✓	
Cereal grain - Rice	Milling	Husked rice	Y	None	✓		✓
		Bran	Y		✓		✓
		Hulls	Y				✓
		Polished rice	O			✓	
Cereal grain – maize	Milling wet/dry	Oil	Y	Maize (dry milling only) → grain sorghum	✓	✓	
		Flour	Y			✓	
		Meal	Y			✓	✓
Citrus fruit[1]	Juicing	Juice	Y	Orange → all citrus		✓	
		Pulp	Y				✓
		Peel	O			✓	
		Molasses	O		✓		
Pome fruit	Juicing	Juice	Y	Apple → pome fruit		✓	
		Pomace, wet or dry	Y		✓		✓
		Sauce	O			✓	
Grapes	Juicing/ Dehydration	Juice	Y	None		✓	
		Pomace, wet or dry	Y		✓		✓
		Raisins	Y		✓	✓	
		Wine (fermentation)	Y			✓	
Plums	Dehydration	Prunes	Y	None	✓	✓	
Tomato	Juicing	Juice	Y	None		✓	
		Paste	O			✓	
		Purée	O			✓	
Sweet corn		Kernels	Y	None		✓	
		Cannery waste	Y				✓
Oilseeds	Solvent extraction/ crushing	Oil refined	Y	Soy bean ↔ rape (canola) ↔ cottonseed ↔ sunflower ↔ sesame ↔ linseed (flax) ↔ peanut ↔	✓	✓	

Raw Agricultural Commodity	Processing	Processed commodity	Required	Extrapolations	Purpose		
					MRL	Diet	Animal feed
				safflower			
		Hulls	Y				✓
		Meal	Y		✓		✓
	Cold press	Oil	Y	Soy bean ↔ rape (canola) ↔ cottonseed ↔ sunflower ↔ sesame ↔ linseed (flax) ↔ peanut ↔ safflower	✓	✓	
		Hulls	Y				✓
		Meal	Y		✓		✓
Olives	Pressing/ extraction	Oil	Y	None	✓	✓	
Potato		Peel /processing waste	Y	None			✓
		Granules	O			✓	
		Chips	O			✓	
		Crisps	O			✓	
Sugar beet, Sugarcane	Press	Sugar	Y	Sugar beet ↔ sugarcane		✓	
		Molasses	Y		✓		✓
		Beet pulp, dry	Y		✓		✓
		Cane bagasse	O				✓

Y=yes; O=optional

[1] The Meeting noted that processing of citrus fruit to produce citrus oil often results in concentration of residues, however citrus oil was not included in the table as there is no Codex Commodity Classification. Citrus oil is used as flavouring and is an extremely minor component in the diet.

Table 3. Additional household preparation, processing procedures and possible extrapolations for refinement of dietary intake (all studies optional, i.e., not essential for estimation of maximum residue levels)

Processing procedure	Explanations	Examples of major crop[1]	Extrapolations[6]
Distribution in the edible / non edible portion	Normally covered by the residue trials	Citrus Tropical fruits (with inedible peel) e.g. Banana Winter squash, Melon	Orange ↔ grapefruit ↔ lime ↔ lemon ↔ tangerine (clementine, mandarin) Banana ↔ plantains Melons → all inedible peel cucurbits
Preparation of vegetable juice other than tomato		Carrot	
Infusions and extractions	Infusions, including green and black tea. Roasting and extraction (including instant coffee)	Tea Cacao Coffee	
Preparation of canned and frozen fruit		*Canned:* Apple/Pear Peach Pineapple *Frozen:* Strawberry Apple Peach Blueberry	Any one canned fruit ↔ all canned fruits Any one frozen fruit ↔all frozen fruits
Preparation of other fruit	Includes production of	Pome fruit	Any one fruit ↔ other major fruits

Processing procedure	Explanations	Examples of major crop[1]	Extrapolations[6]
products (primary processes only)	marmalade, jam, jelly, sauce/puree	Stone fruit Grape Citrus (orange)	
Preparation of alcoholic beverages	Fermentation Brewing/distillation	Rice Barley Other Cereals (wheat, maize, rye) Sugar [for grapes see table 2]	Grapes[4] → all wine-producing RACs except rice Rice (beer, wine) → None Barley ↔ all beer-producing RACs (except rice, including hops) Barley ↔ all whiskey-type producing RACs
Cooking vegetables, pulses and cereals in water		Carrots Beans Peas (succulent and dry) Potatoes Spinach	
Preparation of canned and/or frozen vegetables	Both commercial-type canning and freezing procedures should be demonstrated.	Common (green or snap) bean Corn (sweet) Pea (garden, succulent) Potato Spinach Beet (garden, table) Broccoli (frozen) Tomato	Common bean, corn, pea, or spinach → all vegetables Potato → sweet potato
Miscellaneous preparations of other vegetable products	Frying Microwaving	Potatoes	Potatoes ↔ all vegetables
Processing of products of animal origin including preparation of meat and fish[2]	Boiling Pasteurisation Baking Smoking Frying Fermentation Poaching	Milk, eggs Milk Eggs Meat, fish Meat Milk Eggs, fish	
Dehydration[3]	Removal of water	Fruits (other than grapes, plums) Vegetables Grasses	None
Fermentation of soya beans, rice and others (except alcoholic beverages)	Fermentation	Cabbage Soya (soy bean) Rice	
Pickling	Brining or corning, the process of preserving food by anaerobic fermentation in salt solution	Cucumber	

[1] The crops mentioned are only examples giving some important crops for this kind of study. The selection of crop depends on the use pattern of the pesticide.

[2] Conducted only if a veterinary use is requested

[3] Default processing factors may be used in lieu of processing studies for some dehydration processes (see Table 2). No extrapolations are possible as each commodity contains a different percentage of water.

[4] Processing studies are necessary for both red and white wine grapes.

[5] Processing need to be similar e.g., Canning of peeled fruit

[6] Wider extrapolation may be possible depending on the pesticide, e.g., thermal or hydrolytic degradation of the pesticide to give no residues

Table 4. Products with known dehydration factors.

Raw agricultural commodity	Processed product	Dry matter content in RAC	Dry matter in dried product	Theoretical processing factor
FT 0297 Figs	Fruit, dried	22%	74%	3.4
FB 0269 Grapes	Fruit, dried	18%	85%	4.7
Grass	Hay	20%	86%	4.3
FS 0014 Plums	Prunes	20%	70%	3.5
FP 226 Apple	Fruit, dried	17%	68%	4.0
FS 0240 Apricot	Fruit, dried	14%	69%	4.9
FP 0230 Pear	Fruit, dried	16%	73%	4.6
VO 0448 Tomato	Tomato, sun dried	6.1%	85%	14
VO 0445 Peppers Sweet	Sweet pepper, dry	9%	92.9%	10
VO 0444 Peppers chilli	Chilli pepper, dry	13%	92.9%	7

2.8 CROP GROUPS AND COMMODITY GROUP MRLS

The FAO Manual explains that the establishment of commodity group MRLs as opposed to MRLs for individual commodities has long been considered an acceptable procedure at both the national and international levels.

The Meeting was aware of the progress being made by the CCPR on the Revision of the Codex Classification of Foods and Animal Feeds.[4]

In November 2005, an FAO/WHO consultation[5] was held in The Netherlands to update the principles and methods of risk assessment relating to the establishment of MRLs for pesticides and veterinary drugs. The Consultation encouraged the wider use of group MRLs.

The 2006 JMPR report [6] explained the uses of MRLs and suggested a more liberal extrapolation to group MRLs.

JMPR recommended to CCPR:

After dietary intake assessment, commodity group MRLs may be proposed on the following minimum conditions:

(1) The pesticide is registered or authorized for use on the crop group; and

(2) Relevant and adequate residue data are available for at least one major commodity of the group. (However, all relevant data for the commodities of the group should be taken into account.)

At its 39th Session, CCPR agreed to the revised procedure[7].

Commodity group MRLs are the most practical way of introducing MRLs for commodities of minor crops. For full implementation, the directions for use on pesticide product labels will need close attention and changes to the Codex Commodity Classification will be needed.

We should note the distinction between the crop group and the commodity group. The distinction is not always clear because we use the same words to describe the crop and the

[4] CCPR. 2007. *Report of the 39th Session of the Codex Committee on Pesticide Residues, Beijing, China, 7 - 12 May 2007.* ALINORM 07/30/24 - Rev. 1. Para 151-154.

[5] FAO/WHO. 2006. Updating the Principles and Methods of Risk Assessment: MRLs for Pesticides and Veterinary Drugs. http://www.fao.org/ag/AGP/AGPP/Pesticid/JMPR/DOWNLOAD/bilthoven_2005.pdf

[6] Annex 5, reference 107.

[7] CCPR. 2007. *Report of the 39th Session of the Codex Committee on Pesticide Residues, Beijing, China, 7 - 12 May 2007.* ALINORM 07/30/24 - Rev. 1. Paragraph 34.

commodity, e.g., in one context, "pineapples" can mean the crop in the field and in another context "pineapples" can mean the fruit itself.

This ambiguity sometimes suggests that “crop” and “commodity” are the same, e.g., a sentence in a recent circular letter[8] states: “By adding minor commodities in the crop groups, minor crops could be more easily added on the plant protection products labels”. The intention is probably to add commodities (produced by minor crops) to commodity groups, so that the minor crops could be added to suitable corresponding crop groups.

For field uses, pesticides are applied to the crop, so it is the crop or crop group that should appear on pesticide product labels.

MRLs and residues are expressed on commodities, so commodities and commodity groups appear in MRL tables.

To be useful on pesticide labels, crops within a crop group should have similar growth pattern and production characteristics, similar cultural practices and similar pests that require the same pesticide treatment. Such a crop group then needs a corresponding commodity group so that a group MRL can be established.

Examples of crop groups on labels and corresponding commodity groups suitable for group MRLs.

Crop group	Commodity group
Cereals	GC 0080 Cereal grains
Citrus	FC 0001 Citrus fruits
Grain legumes	VD 0070 Pulses
Pome fruit	FP 0009 Pome fruits
Vegetables - leafy	VL 0053 Leafy vegetables

Some crop groups on labels do not readily translate to corresponding commodity groups, e.g.:

Field crops	Very broad – no corresponding commodity group.
Crucifers	Does not match a Codex commodity group.
Legumes	Commodity groups could be pulses, legume vegetables or legume animal feeds
Nuts	Commodities could be peanuts and various tree nuts.
Asian fruiting vegetables	No clear commodity group.

Some of the current Codex Commodity Groups do not relate to practical crop groups for label instructions. For example, the crops relating to "Assorted tropical and sub-tropical fruits inedible peel" have diverse characteristics and possibly different pests; similarly for "Fruiting vegetables other than cucurbits".

“Tree nuts” is a somewhat artificial crop group, because the various crops within the group do not have similar characteristics and are not expected to be susceptible to the same pests and diseases requiring the same pesticide treatment.

In practice, residues in tree nuts (expressed on edible portion) from field use are often low or not detectable irrespective of the pesticide use, so a tree nut group MRL can be achieved.

The situation is more straightforward for post-harvest uses, where the product label directions refer to commodities. For example, “tree nuts” and “cereal grains” are suitable commodity groups for post-harvest uses and related group MRLs.

[8] CAC. 2007. Request for comments on the proposals for ‘Bulb vegetables’ and ‘fruiting vegetables’. Circular letter CL 2007/36 – PR. Paragraph 3.

Examples of commodity group MRLs from the 2006 JMPR

Recommendations from the 2006 JMPR were examined for MRL grouping and MRL mutual support without grouping.

When the data from a number of commodities are put together for mutual support, it suggests that the use pattern on the crops was similar and the residues on the commodities were similar, but extrapolation to the wider commodity group could not be justified.

'Commodity group except xxx' MRLs suggest that, at least in the specific case, there was some problem that prevented the inclusion of those excepted commodities.

Examination of 'mutual support' decisions may provide starting points for practical smaller groups or sub-groups of crops and corresponding commodities that would be useful on product labels and in MRL tables respectively.

The following commodity groups readily lend themselves to group MRLs:

- citrus fruits;
- pome fruits;
- stone fruits;
- cucurbit fruiting vegetables; and
- Brassica vegetables.

The following are notable difficulties, mostly because the use patterns are not the same on the crops producing the commodities:

- Grapes do not group well with berries and other small fruits.
- Rice does not group well with other cereal grains.
- Sweet corn and mushrooms do not group well with fruiting vegetables other than cucurbits.
- 'Tropical-fruits-inedible-peel' is too broad – smaller sub-groups are needed.

Commodity group and mutual support groupings from 2006 JMPR

Compound	Commodities with data supporting MRL	Group or commodities with MRL recommendation	Code
Pirimicarb	mandarin, orange	citrus fruits	FC
Thiabendazole	mandarin, orange	citrus fruits	FC
Bifenazate	apple, pear	pome fruits	FP
Fludioxonil	apple, pear	pome fruits	FP
Pirimicarb	apple	pome fruits	FP
Thiacloprid	apple, pear	pome fruits	FP
Bifenazate	apricot, cherry, peach	stone fruits	FS
Pirimicarb	cherry, nectarine, peach, plum	stone fruits	FS
Pyraclostrobin	cherry, peach, plum	stone fruits	FS
Thiacloprid	peach, sweet cherry	stone fruits	FS
Pirimicarb	currant, gooseberry, raspberry	berries and other small fruits (except grapes and strawberries)	FB
Thiacloprid	currant, raspberry, strawberry	berries and other small fruits (except grapes)	FB
Endosulfan	avocado, custard apple, mango, papaya	mutual support: avocado, custard apple, mango, papaya	FI
Endosulfan	litchi, persimmon	mutual support: litchi, persimmon	FI
Pirimicarb	broccoli, Brussels sprouts, cauliflower, cabbage	Brassica vegetables	VB
Bifenazate	cantaloupe, cucumber, summer squash	cucurbit fruiting vegetables	VC
Propamocarb	cucumber, melon, summer squash	cucurbit fruiting vegetables	VC
Pirimicarb	cucumber, summer squash	cucurbit fruiting vegetables (except melons and watermelons	VC

Compound	Commodities with data supporting MRL	Group or commodities with MRL recommendation	Code
Thiacloprid	melon, watermelon	mutual support: melon, watermelon	VC
Pirimicarb	sweet peppers, tomato	fruiting vegetables other than cucurbits (except mushrooms, fungi, sweet corn)	VO
Pirimicarb	beans, peas	legume vegetables (except soya beans)	VP
Propargite	dry beans, dry broad-bean, dry chick-pea, dry lupin	mutual support: dry beans, dry broad-bean, dry chick-pea, dry lupin	VD
Pirimicarb	dry beans, dry peas	pulses (except soya beans)	VD
Endosulfan	potato, sweet potato	mutual support: potato, sweet potato	VR
Pirimicarb	carrot, potato, sugar beet	root and tuber vegetables	VR
Endosulfan	hazel nuts, Macadamia nuts	mutual support: hazel nuts, Macadamia nuts	TN
Bifenazate	almond, pecan	tree nuts	TN
Thiacloprid	almond, pecan, walnut	tree nuts	TN
Aminopyralid	barley, oats, wheat	barley, oats, wheat, triticale	GC
Pirimicarb	barley, maize, wheat	cereal grains (except rice)	GC
Pirimicarb	barley straw, maize fodder, wheat straw	straw and fodder of cereal grains except rice	AS
Aminopyralid	barley straw, oats straw, wheat straw	straw of barley, oats, wheat, triticale	AS

Recommendations

CCPR should note the different purposes for crop groups (directions for use on pesticide product labels) and commodity groups (MRLs) and should aim for an integrated system that will, in practice, produce more crop group registrations and corresponding commodity group MRLs.

Ideally, there should be crop groups

1. that have similar pesticide product label directions within each crop group,

AND

2. that produces commodity groups with similar residue characteristics within each commodity group.

Registration authorities, industry and researchers should give careful consideration to using crop groups and commodity groups that meet the above criteria.

2.9 STATISTICAL METHODS FOR THE ESTIMATION OF MRL

The JMPR estimates maximum residue levels that it recommends for use as Codex MRLs. The recommendation is accompanied by an evaluation of the pesticide's toxicity and a determination of the human dietary exposure. The recommendations may become Codex MRLs only where the exposure does not exceed established ADIs or ARfDs. The maximum residue levels are derived from the a set of values composed of the highest result, usually in mg/kg, for residues found in a series of supervised field trials conducted under maximum GAP conditions. The set will contain a variable number of data points (field trials), typically from 3 to 50 or more. Additionally, sets of data from trials conducted in different countries or regions may be combined where the GAPs are similar and the sets are deemed not to be from different populations. This is ascertained by use of the Mann-Whitney U Test, which compares the medians. Sets are combined to provide more data points upon which to estimate the maximum residue level or to allow estimation of a maximum residue level for a commodity group, e.g., combining pear and apple data to estimate pome fruit.

The maximum residue level must be estimated "somewhat" above the highest residue value (HR). The issue is defining "somewhat." Until recently, the Meeting relied upon professional judgment only. The maximum residue level tended to be estimated near the high residue where there

were many data points (≥ 12) and more distant from the HR where there were few data point (n=3 to 8) and/or those points were clustered near the HR. The maximum residue level needs to be set such that it represents the residue level not likely to be exceeded when the pesticide is applied according to the relevant GAP. Setting it too low risks disrupting trade where the pesticide has been used according to GAPs reviewed by the JMPR; setting it too high may encourage misuse of the pesticide.

Some national regulatory authorities utilize statistical methods to assist in the determination of the appropriate maximum residue level. The JMPR has been investigating this approach and most recently considered the NAFTA statistical calculation (General Item 2.5, JMPR Report 2005; General Item 2.10, JMPR Report 2006) and the binomial calculation (General Item 2.10, JMPR Report 2006). Following these considerations the JMPR adopted the NAFTA method as a tool, to be used in determining MRL estimates. The Meeting previously agreed that where this statistical tool is used, class rounding (scaling) is not appropriate. Rather the result should be rounded up to one significant figure.

The Meeting welcomed the availability of the NAFTA paper *Statistical Basis of the NAFTA Method for Calculating Pesticide maximum Residue Limits from Field Trial Data*[9]. The document details the development and testing of the NAFTA Method and also gives some explanation of and comparison to other available methods for calculating MRL estimates from a residue data set.

The 2006 JMPR also considered the binominal procedure for MRL calculation and found that it generally gave results comparable to those from the NAFTA method. However, the NAFTA paper details both theoretical and practical problems with the binomial procedure. Because of these concerns, simulations with normal and log normal data sets were conducted. It was found that the binominal method does not give unbiased estimates of the 95th percentile.

The 2007 Meeting performed a simple analysis of the maximum residue level estimations obtained from the NAFTA spreadsheet, using the default value provided by the logic tree of the spreadsheet (rounded up to one significant figure), and the estimate made independently by the entire FAO panel expert group.

There were a total of 94 plant commodity data sets considered. Excluded were data sets for livestock commodities (meat, milk, poultry, eggs), as these are not generally amenable to statistical calculation. Also excluded were plant commodity data sets with more than 60% < LOQ values (censored data, n=36). Of those considered, 44% resulted in the same estimate by the NAFTA spreadsheet and the Panel judgment. An additional 16% differed by 20% or less (difference/Panel judgment × 100). The Panel judgment was less than and more than the spreadsheet rounded estimate in about equal amounts of 28%.

There were no clear trends with which to correlate the differences in spreadsheet and professional judgment. One disagreement was a spreadsheet estimate below the HR. The Meeting previously agreed that a maximum residue estimate would not be made below the HR where the HR is judged to be scientifically valid. For difenoconazole on celery there were nine trial points with a high residue of 2 mg/kg. The spreadsheet suggested 1.18 mg/kg (log normal), but the Meeting considered a value somewhat above the high residue appropriate, or 3 mg/kg. This situation was repeated more dramatically for cyromazine on cabbage, where there were six trial points with a high residue of 6.1 mg/kg. The NAFTA spreadsheet recommended 3 mg/kg (log normal), i.e., considerably below the HR. The Meeting considered that given only 6 data points, the estimate should be substantially above the high residue and estimated 10 mg/kg.

There were other cases where the spreadsheet seemed to overestimate the maximum residue level. For example, for dimethomorph on corn salad (lambs lettuce) there were 6 residue values with

[9] Statistical Basis of the NAFTA Method for Calculating Pesticide maximum Residue Limits from Field Trial Data 1 (US EPA and Canada PMRA, May, 2007: http://www.pmra- arla.gc.ca/english/pdf/nafta/docs/nafta_mrls-e.pdf)

an HR of 7.1 mg/kg. The NAFTA spreadsheet recommended (log normal) 24 mg/kg. The Meeting recommended 10 mg/kg.

A particular continuing concern is the estimation of MRLs for very small data sets. The general JMPR policy is to require at least six independent trials (n=6), but often recommendations are made on a case-by-case basis for as few as three trials (n=3). The latter typically occurs for minor commodities which show a small spread (low RSD) in residue values. It may also occur for commodities where all results are at or near the LOQ and which have other supporting information, such as the results of metabolism studies and residue levels from exaggerated rate treatments. The NAFTA Paper states for apparent log normal data sets, the minimum acceptable value for n is 6. Below 6 values the estimate of the 95th percentile is extremely unreliable. An analysis paper on the NAFTA model from Australia [10] suggests an underestimation of the 95th percentile happens somewhere between 20 and 10 samples. Clearly extra caution must be taken in interpreting statistically generated MRL estimates with small data sets (n=3 to 15).

Another special case is the situation where many of the data points in the supervised field trial data set are < LOQ, or censored data. The NAFTA Paper recommends assigning values to the < LOQs by using a maximum likelihood estimate (MLE) procedure, but only up to about 60% censored data. The MLE approach assumes a log normal distribution. The Meeting questions if there are other procedures for handling the censored data that do not require assumptions on the distribution.

The Meeting also noted that currently available statistical spreadsheets/methods for the estimation of MRLs do not address the issue of application of such tools to data sets that are the composite of two or more subsets. The NAFTA model is exactly suited to NAFTA field trial data, where the data are from a *single population* and *proportional to production as distributed among zones and represent one GAP*. Such is often not the case with the data voluntarily submitted to JMPR. Data from various countries or regions may be *combined* for a given crop where the GAPs are comparable and apparently not from different populations.

The Meeting considered that expert judgment must be the primary factor in estimating maximum residue levels. No statistical approach can accommodate the scientific and technical aspects of residue data sets that go beyond mathematical distributions. Consider the hypothetical data set (n=12): 1, 1.1, 1.3, 3.1, 3.9, 5.0, 5.6, 5.8, 7.6, 8.2, 8.5, 9.6 mg/kg. The NAFTA spreadsheet estimates 30 mg/kg for the maximum residue level based on the 99th percentile log normal. Additional information available indicates that the three highest values were from sampling 1 day less than the PHI of 4 days, but within the variability in GAP allowed by JMPR. Thus, the residues might be somewhat overstated in the three samples with highest residues. Also, several trials conducted at exaggerated application rates (1.6 ×) and not included in the set gave residues of 8–11 mg/kg. These additional facts lead the evaluators to consider 30 mg/kg excessive and to estimate the maximum residue level at 20 mg/kg. This illustrates the importance of professional judgment.

The Meeting affirmed that reviewers will continue the practice of preparing summary calculation sheets for each compound and its commodities under review. This will include the various estimations from the NAFTA spreadsheet (EU normal, EU nonparametric, NAFTA log normal (3 types), mean plus 3 standard deviations). The Meeting will routinely consider these values as a part of its deliberations in making maximum residue level estimates.

The Meeting concluded that:

I. Any statistical method of maximum residue level (MRL) estimation from a data set is a tool and not the controlling factor in making the estimate. Professional judgment of the JMPR FAO Panel and transparent evaluation of the data set must be performed.

II. The binominal procedure should not be used at this time, pending resolution of apparent deficiencies.

[10] Stern, S. (2007) Comparing Two Methodologies for Setting MRLs for Field Trial Data, DSI Consulting, Australia.

III. Regulatory authorities and other interested parties are encouraged to give additional consideration to:

a. Appropriate techniques for handling data sets with substantial censored data (< LOQ values).

b. Combination of multiple data sets into one set for MRL estimation and the appropriateness of statistical MRL estimation in such situations.

2.10 OECD LIVESTOCK FEED TABLES - JMPR CALCULATION OF LIVESTOCK DIETARY BURDEN

In 2006, JMPR was advised of the development of OECD livestock feed tables intended as guidelines for manufacturers to determine livestock dietary burdens during the planning of livestock feeding or transfer studies[11]. The tables of OECD feedstuffs were included as Annex 6 to the JMPR Report. Subsequently, the full OECD report[12] was issued.

The OECD tables include data for beef cattle, dairy cattle, sheep, lambs, swine, broilers, layers and turkeys. Data are available from three different geographic regions: US-Canada, EU and Australia. Feedstuff categories in the OECD tables were chosen to ensure that the highest residue levels are estimated and a realistic although not nutritionally optimal livestock diet is composed. The primary purpose of the tables was to estimate a highest livestock dietary burden from the geographic regions which would then be used to set appropriate dosing for a livestock feeding study. JMPR is using the livestock diets in the tables to estimate livestock dietary burdens from available residue data.

Information is included on typical dry matter content for each commodity, allowing calculation of residues on a dry weight basis when measured dry matter or moisture content is not available. The tables also suggest, for each feed commodity, whether to use the highest residue or STMR for calculation of the maximum dietary burden.

The Meeting agreed to use the OECD tables as a replacement for those previously used – originating from the USA and published in the *FAO Manual*[13].

Feeding studies are normally available for lactating dairy cattle and laying hens. For this situation, livestock dietary burdens will be calculated for beef and dairy cattle, broiler and layer hens.

Essentially the same process is followed as described in the *FAO Manual*.

The aim is to calculate the dietary burden from the livestock feed tables and available residue data in such a way as to estimate the highest dietary burden. Starting with the feed item with the largest residue concentration on a dry weight basis, the percentage of livestock diet for each feed is allocated using the OECD Table. One feed commodity from each Codex Commodity Group is used or, if more than one, only up to the highest percentage % feed allocation for a commodity of that Group. Feeds are allocated a percentage of the livestock diet for each animal until no more than 100% of the diet is used. The residue contribution of each feed (mg/kg) is then calculated using the residue on a dry weight basis and the corresponding percentage of the diet. All residue contributions for each animal are then summed to determine the total dietary burden (see worked example).

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[11] Annex 5, reference 107.

[12] OECD. 10-Oct-2006. Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology. Series on Testing and Assessment. Number 64. Series on Pesticides. Number 32. Guidance Document on Overview of Residue Chemistry Studies. Document ENV/JM/MONO(2006)32.

[13] FAO. 2002. Submission and evaluation of pesticide residues data for the estimation of maximum residue levels in food and feed. Appendix IX. Maximum proportion of agricultural commodities in animal feed. *FAO Plant Production and Protection Paper*, 170.

Highest residue, STMR and STMR-P values are chosen as indicated in the OECD table for the maximum burden calculation. STMR and STMR-P values are chosen for the mean dietary burden.[14] [15] In the maximum burden calculation for some raw agricultural commodities (RACs), e.g., cereal grains, STMR values are used for residues from pre-harvest pesticide uses because of bulking and blending of the RAC, but highest residue values are used for post-harvest uses (could occur after bulking and blending).

Calculations are made for the maximum and mean dietary burdens for the 3 geographic regions for beef and dairy cattle, layers and broiler chickens, i.e., 24 calculated values. Highest values among the regions are chosen from the mean and maximum calculations to represent the dietary burdens. One proviso is that the dietary burdens related to residues in milk and eggs must come from dairy cattle (not beef cattle) and laying hens (not broilers) respectively.

The Meeting noted differences in consumption of specific feed items between the previously used tables and the new OECD tables. For example, the new tables assign 5% of the diet of beef cattle in US-Canada to cotton gin by-products, whereas the previous value was 20% of the diet of beef and dairy cattle assigned to cotton gin by-products.

The meeting also noted some new commodities in the tables that were not previously designated as feed items for the purpose of calculating livestock dietary burdens: e.g., cabbage, kale, bean seed, grape pomace and sugarcane bagasse.

JMPR 2006 agreed to use the new data tables for livestock dietary burden estimation beginning in 2007. Estimations from previous years would not be revised unless a new evaluation was required for some reason such as a new data submission.

Livestock dietary burden calculations for 2007 will be included as an annex to the JMPR Report.

Worked example (difenoconazole)

First, dietary burdens are calculated from commodity percent of diet and residues expressed on dry weight.

Estimated maximum dietary burden of livestock

BEEF CATTLE MAX

Commodity	Commod group	Residue mg/kg	Basis	% Dry matter	Residue dw mg/kg	*Diet content (%)*			Residue contribution (ppm)		
						US-CAN	*EU*	*AU*	US-CAN	EU	AU
Sugar beet leaves or tops	AM AV	0.95	highest residue	23	4.130		*20*			0.83	
Apple pomace, dry	AB	1.65	STMR-P	100	1.650	*20*	*20*	*20*	0.33	0.33	0.33
Wheat straw and fodder	AS	1.2	highest residue	88	1.364	*10*	*20*	*80*	0.14	0.27	1.09
Cabbage heads, leaves	VC	0.19	HR	15	1.267		*20*			0.25	
Carrot culls	VR	0.13	HR	12	1.083	*10*	*15*		0.11	0.16	
Oilseed rape fodder	AM AV	0.14	highest residue	100	0.140	*20*			0.03		
Potato culls	VR	0.01	HR	20	0.050	*20*	*5*		0.01	0.00	
Rape seed (for meal)	SO	0.02	STMR	88	0.023	*15*			0.00		
Soya bean seed	VD	0.02	STMR	89	0.022	*5*			0.00		
Total						*100*	*100*	*100*	0.62	1.85	1.42

[14] Annex 5, reference 92.

[15] Annex 5, reference 101.

DAIRY CATTLE MAX

Commodity	Commod group	Residue mg/kg	Basis	% Dry matter	Residue dw mg/kg	*Diet content (%)* *US-CAN*	*EU*	*AU*	Residue contribution (ppm) US-CAN	EU	AU
Sugar beet leaves or tops	AM AV	0.95	highest residue	23	4.130		*30*			1.24	
Apple pomace, dry	AB	1.65	STMR-P	100	1.650	*10*	*10*	*10*	0.17	0.17	0.17
Wheat straw and fodder	AS	1.2	highest residue	88	1.364	*10*	*20*	*20*	0.14	0.27	0.27
Cabbage heads, leaves	VC	0.19	HR	15	1.267		*20*			0.25	
Carrot culls	VR	0.13	HR	12	1.083	*10*	*15*	*5*	0.11	0.16	0.05
Grape pomace, dry	AB	0.36	STMR-P	100	0.360			*10*			0.04
Oilseed rape fodder	AM AV	0.14	highest residue	100	0.140	*20*		*40*	0.03		0.06
Potato culls	VR	0.01	HR	20	0.050		*5*	*5*		0.00	0.00
Rape seed (for meal)	SO	0.02	STMR	88	0.023	*15*		*10*	0.00		0.00
Soya bean seed	VD	0.02	STMR	89	0.022	*15*			0.00		
Total						*80 (note)*	*100*	*100*	0.44	2.10	0.59

Note: Insufficient feed items with residues from the use of the pesticide are available to reach 100% of this diet.

Estimated mean dietary burden of livestock

BEEF CATTLE MEAN

Commodity	Commod group	Residue mg/kg	Basis	% Dry matter	Residue dw mg/kg	*Diet content (%)* *US-CAN*	*EU*	*AU*	Residue contribution (ppm) US-CAN	EU	AU
Apple pomace, dry	AB	1.65	STMR-P	100	1.650	*20*	*20*	*20*	0.33	0.33	0.33
Sugar beet leaves or tops	AM AV	0.25	STMR	23	1.087		*20*			0.22	
Wheat straw and fodder	AS	0.685	STMR	88	0.778	*10*	*20*	*80*	0.08	0.16	0.62
Carrot culls	VR	0.05	STMR	12	0.417	*10*	*15*		0.04	0.06	
Grape pomace	AB	0.36	STMR-P	100	0.360						
Cabbage heads, leaves	VC	0.035	STMR	15	0.233		*20*			0.05	
Oilseed rape fodder	AM AV	0.06	STMR	100	0.060	*20*			0.01		
Potato culls	VR	0.01	STMR	20	0.050	*20*	*5*		0.01	0.00	
Rape seed (for meal)	SO	0.02	STMR	88	0.023	*15*			0.00		
Soya bean seed	VD	0.02	STMR	89	0.022	*5*			0.00		
Total						*100*	*100*	*100*	0.48	0.81	0.95

DAIRY CATTLE MEAN

Commodity	Commod group	Residue mg/kg	Basis	% Dry matter	Residue dw mg/kg	*Diet content (%)* *US-CAN*	*EU*	*AU*	Residue contribution (ppm) US-CAN	EU	AU
Apple pomace, dry	AB	1.65	STMR-P	100	1.650	*10*	*10*	*10*	0.17	0.17	0.17
Sugar beet leaves or tops	AM AV	0.25	STMR	23	1.087		*30*			0.33	
Wheat straw and fodder	AS	0.685	STMR	88	0.778	*10*	*20*	*20*	0.08	0.16	0.16
Carrot culls	VR	0.05	STMR	12	0.417	*10*	*15*	*5*	0.04	0.06	0.02
Grape pomace	AB	0.36	STMR-P	100	0.360			*20*			0.07
Cabbage heads, leaves	VC	0.035	STMR	15	0.233		*20*			0.05	
Oilseed rape fodder	AM AV	0.06	STMR	100	0.060	*20*		*40*	0.01		0.02
Potato culls	VR	0.01	STMR	20	0.050		*5*	*5*		0.00	0.00
Rape seed (for meal)	SO	0.02	STMR	88	0.023	*15*			0.00		
Soya bean seed	VD	0.02	STMR	89	0.022	*15*			0.00		
Total						*80*	*100*	*100*	0.30	0.76	0.44

The calculations for poultry follow the same approach, but are not shown here.

The calculations are then summarized and the highest dietary burdens (underlined) are selected for MRL and STMR estimates on animal commodities.

	Livestock dietary burden, difenoconazole, ppm of dry matter diet					
	US-Canada		EU		Australia	
	max	mean	max	mean	max	mean
Beef cattle	0.62	0.48	1.85	0.81	1.42	<u>0.95</u>
Dairy cattle	0.44	0.30	<u>2.10</u>	<u>0.76</u>	0.59	0.44
Poultry - broiler	0.01	0.01	0.12	0.05	0.01	0.01
Poultry - layer	0.01	0.01	<u>0.54</u>	<u>0.20</u>	0.01	0.01

Select the highest maximum and highest mean dietary burdens for estimating animal commodity MRLs and STMRs respectively.

	Dietary burden, ppm or mg/kg dry matter	
	for estimating MRLs	for estimating STMRs
Mammalian meat	2.10	0.95
Milk	2.10	0.76
Poultry meat	0.54	0.20
Eggs	0.54	0.20

These values are then used in combination with data from livestock feeding studies to estimate the MRLs and STMRs for meat, milk and eggs. The procedure is described on pages 80–81 of the *FAO Manual*.

2.11 STATUS REPORT FROM THE OECD EXPERT GROUP ON RESIDUE CHEMISTRY GUIDELINES

The purpose of the OECD Expert Writing Group (EG) and its implications for JMPR were explained in the 2006 JMPR Report (General Consideration 2.11). The Meeting was presented with an update of the EG efforts in 2007.

Guidelines on (1) the nature of the residue in processed commodities and (2) storage stability and a guidance document on analytical methods have been completed and approved. Additionally, an advanced draft of the magnitude of the residue in processing guideline, provided to the Meeting, is under EG comment/revision and will most likely be submitted for OECD approval before the end of 2007.

The magnitude of the residue in field trials guideline drafting group is now starting work. The initial (2007–2008) activities will centre on details of conducting a residue trial. A critical aspect will be a delineation of the variables that enter into a specific GAP and the degree of variation in these variables that will be allowed in designating different GAPs among OECD countries as equivalent. The group will also address methods for deriving an MRL estimate from a data set and procedures for combining equivalent data sets. This will include consideration of the possible applicability of the proportionality concept, that is, that the residue concentration on the crop is proportional to the rate of application. Upon completion of the core document, attention will be given (2008) to zoning and its implications on the geographic location of field trials. New work by the US EPA and reanalysis of the FAO/OECD zoning project results will be considered.

The Meeting was presented with draft versions of templates for crop field trials, nature of the residue in processing, magnitude of the residue in processing, analytical methods, and storage stability. These are designed to be used by sponsors/manufacturers in summarizing studies for submission.

The JMPR reiterated that the OECD documents will be utilized in the preparation of future versions of the *FAO Manual*. Such utilization will promote maximum harmonization and will facilitate work share. It was noted that the OECD livestock feeding tables were adopted in 2006 and utilized by the 2007 Meeting.

2.12 RESIDUES IN DRIED CHILLI PEPPERS

The 2004 JMPR, taking into account the water content of fresh peppers and the estimated water content of dried chilli peppers, as well as the decision of CCPR, applied a generic factor of 10 for conversion of residues in fresh peppers to dried chilli peppers. For the estimation of maximum residue

levels, in or on dried chilli peppers, the Codex MRLs established primarily for fresh sweet peppers were used.

The delegation of the Republic of Korea opposed the proposed Codex MRLs (Step 8) for dried chilli peppers at the 38th Session of the CCPR and offered to submit compound- specific processing factors which were much lower than the default factor (10) used by the JMPR.

The effects of the drying of chilli peppers on the residues of azinphos-methyl, chlorfenapyr, clothianidin, diazinon, diethofencarb, EPN, folpet, imidacloprid, indoxacarb, metalaxyl, methomyl, methoxyfenozide, tetraconazole, and vinclozolin were reported by the Republic of Korea. The results were evaluated by the present Meeting.

Methods of residue analysis

The pesticide residues were extracted with acetone, partitioned with dichloromethane, except diethofencarb for which hexane was used. Following the liquid-liquid partitioning, the concentrated extracts were cleaned up on Florisil columns with various elution mixtures.

Methomyl was determined with a different procedure based on extraction with acetonitrile and cleanup on solid phase microextraction cartridges. The cleaned extracts were analysed with GC-ECD or HPLC DAD or FLD.

Recovery tests were performed at 0.2 and 1 mg/kg levels in three replicates. The LOQs claimed were 0.02 mg/kg for all pesticides in fresh red peppers and 0.04 mg/kg in dried red peppers. The recovery tests were performed at 10 and 50 times higher concentrations than the corresponding LODs. On the other hand, the spike levels were much lower than the actual residues measured in fresh and dried peppers, which were between 1–6.5 mg/kg and 1.7–20.6 mg/kg, respectively. The report on the validation of the method was not submitted.

The processing of the samples started between 9 and 30 days after the sampling. Test portions of fresh and dried chilli peppers were fortified at 0.5 mg/kg residue levels at the time of receiving the samples, and the residues were determined, together with the analysis of the samples. No analytical recovery tests were performed at the time of analysis of samples. The results available indicate that the residue levels did not change during the storage of the samples.

The fresh red chilli peppers were processed as per the conventional method used in Korea, which is also specified by the Korean Food Code. A 4 kg portion of a sample was dried for 35 h at 60 °C. The seeds were removed and the dried flesh was ground to powder. The water content of powdered red chilli peppers was determined by drying 5 g of material at 105 °C for 5 h. The water content of fresh and dried peppers was determined in triplicate.

The average water contents of fresh red chilli peppers and powdered red chilli peppers were 84.04 ± 0.55 and 31.25 ± 0.47%, respectively.

Residues in fresh and dried chilli peppers

Field trials were performed at two sites in a major cultivation area of red peppers in Korea, where the peppers were cultivated according to widely used conventional methods.

The last two pesticide applications were performed with backpack-type sprayers fitted with standard nozzles, 10 days apart at site 1, and 4 days apart at site 2, with double the authorised rates to obtain sufficient residue levels for the processing studies.

The residues were determined in fresh peppers and in the dried powder with three replicate analyses. The processing factors (pf=residue in dried/residue in fresh) obtained from the crops treated at the two sites were azinphos-methyl (1.9, 2.9), chlorfenapyr (5.1, 4.2), clothianidin (2.6, 3.1), diazinon (4.6, 3.0), diethofencarb (2.5, 2.5), EPN (1.8, 3.5), folpet (2.5, 4.6), imidacloprid (2.5, 1.7),

indoxacarb (2.4, 3.2), metalaxyl (3.1, 3.3), methomyl (3.4, 2.9), methoxyfenozide (3.1, 3.2), tetraconazole (2.8, 2.3), and vinclozolin (2.3, 1.7).

The processing factors derived from the Korean trials ranged from 1.7 to 5.1. The repeatability of the procedures, expressed as relative differences, varied between 2% (diethofencarb) and 61% (EPN) with a repeatability relative standard deviation of 23%.

The theoretical concentration factor (cf) calculated from the reported water content of fresh and dried peppers is 4.31. If all residues remained in the sample then the pf/cf should be 1. However, the experimental pf/pc values ranged from 0.39 to 1.2 indicating that a pesticide residue will disappear in a compound-specific way under the same drying processes. It should be noted that the experimental values are affected by the combined uncertainty of all the procedures.

Interpretation of the results

As the trials were performed at exaggerated rates, the residues obtained cannot be used for the estimation of maximum residue levels, however they are suitable for the calculation of processing factors.

In addition to the results of drying chilli peppers, as per the Korean Food Code procedure, information was collected on the water content of fresh chilli peppers, sweet peppers and dried peppers from Australia, New Zealand, Germany, Japan and the USA to provide the best estimate of concentration factors, resulting from the drying process.

The water content of fresh bell peppers is higher (91–94%) than in the chilli peppers (75–93%), depending upon the species. The dried ground powder made from chilli peppers shows a relatively larger variation (1.7–31%) in water content than in fresh peppers.

The ground red peppers obtained in the Korean trials contained much higher percentages of water (31%), than the levels found in other countries (1.7 to < 12%).

Taking into account all available information on the water content of the fresh chilli peppers and the dried chilli peppers prepared from them, the concentration factors are: 3.9, 4.3, 6.3, 6.5, 7.5, 7.7, 7.7, and 14. The median and average concentration factors are 7.0 and 7.2.

The concentration factors calculated from the national standards for situations where dry peppers are prepared from sweet peppers are: 10, 11, 12, 13, 14 and 15.

The 2004 JMPR took note of the similarity in distribution of concentration factors, and the results of an inter-comparison study performed by the Spice Industry indicating an average water content of 7.06% in ground chilli pepper samples taken from commercial commodities. The 2004 JMPR concluded that a rounded figure of 10 for dehydration/concentration factors, based on the average water content (7.06%)(determined from a large number of commercial products), would be an appropriate basis for estimating pesticide residue levels in dried chilli peppers, from MRLs established for peppers (2004 JMPR Evaluation p.1152). The present Meeting supports that conclusion.

The variations of compound specific processing factors provided by the Korean trials (1.7–5.1) indicate that ideally, processing studies representing the world-wide practices for drying chilli peppers would be needed for each pesticide as is the case for any major commodities. In view of the fact that chilli peppers are a very minor crop in most countries, the provision of sufficient representative processing studies, for the estimation of compound specific maximum residue levels for dried chilli peppers, cannot generally be expected. Consequently the decision of the CCPR allows the application of default concentration factors to be used in such cases.

Recommendation

Based on the available information, the Meeting recommends continuing the use of the concentration factor of 10 for the estimation of maximum residue levels of pesticides in dried chilli peppers from the HR values estimated for residues in or on sweet peppers.

Where the residues on fresh chilli peppers are available, the Meeting recommends that in the future a concentration factor of 7 should be used for the estimation of maximum residue levels in dried chilli peppers from maximum residue levels in or on fresh chilli peppers. The concentration factor should be applied to multiply the actual measured residue values in fresh chilli peppers, and estimate the maximum residue and median residue levels from the converted data set.

Where residue data, reflecting the GAP and representative processing studies on residues in or on chilli peppers are available, the maximum residue levels for dried chilli peppers shall be estimated based on the actual experimental data.

The present Meeting applied this principle, and the estimated residue levels are listed under the specific pesticides.

3. RESPONSE TO SPECIFIC CONCERNS RAISED BY THE CODEX COMMITTEE ON PESTICIDE RESIDUES

3.1 CARBENDAZIM (072)

Background

At the 38th Session of the CCPR,[16] the delegation of the European Community (EC) raised concerns regarding the ARfD established by the JMPR in 2005 on the basis of developmental effects (Annex 5, reference *104*). The ARfD established by the EC is different to that established by JMPR and the EC thus has requested harmonization.

Evaluation of carbendazim by the JMPR

In 2005, the Meeting established an ARfD of 0.1 mg/kg bw based on an overall NOAEL of 10 mg/kg bw per day for developmental toxicity from three studies in rats and a NOAEL of 10 mg/kg bw per day in one study in rabbits, and a safety factor of 100. The Meeting concluded that this ARfD applies only to women of childbearing age.

For the general population including children, the Meeting established an ARfD of 0.5 mg/kg bw based on the NOAEL of 50 mg/kg bw in the study of toxicity to the male reproductive system in rats and supported by the studies on micronucleus or aneuploidy induction in vivo, using a safety factor of 100.

An additional safety factor for the severity of the effects was considered to be unnecessary because the underlying mechanism is well understood and there is a clear threshold identified for these effects, both mechanistically and biologically.

Evaluation of carbendazim by the EC

In the EC, an ARfD of 0.02 mg/kg bw had been proposed for carbendazim based on the NOAEL of 10 mg/kg bw per day for developmental effects from studies in rats and rabbits, and using a safety factor of 500. An increased safety factor was used since carbendazim is classified for mutagenic and reproductive effects as “Category 2” (presumed human mutagenic and reproductive toxicants).

Comment by JMPR

JMPR and the EC identified the same overall NOAEL for development effects as the basis for the ARfD. The primary difference in the JMPR and EC assessments was that the EC applied an additional safety factor to address the hazard classifications. JMPR uses an overall weight-of-evidence approach that considers the severity of the effect, mode of action, and dose–response relationship in its assessment of the need for additional safety factors. As clearly stated in the JMPR report, an additional safety factor was not considered necessary because the mechanism causing reproductive toxicity and genotoxicity (aneuploidy) is well understood and has a clear threshold mechanism for which a NOAEL was identified.

3.2 BIFENAZATE (219)

Bifenazate was evaluated for the first time by JMPR in 2006 and an ADI of 0–0.01 mg/kg was established. An ARfD was determined to be unnecessary. MRLs were recommended for a number of crop and animal commodities.

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[16] Codex Alimentarius Commission. *Report of the 38th Session of the Codex Committee on Pesticide Residues, 3–8 April 2006, Fortaleza*, Brazil (ALINORM06/29/24).

CCPR at its 39th Session (2007) requested JMPR to address the USA concern relating to the animal dietary burden (ALINORM 07/30/24 – Rev 1, para 129).

The concern relates to the bifenazate high residue value of 18 mg/kg for cotton fodder, which was the main contributor to the cattle dietary burden. It was noted that bifenazate residues were not particularly stable in cotton commodities during frozen storage and that the cotton gin by-product samples were stored for a long interval prior to analysis, so it might be appropriate to adjust for residue loss during sample storage. With a high residue value above 18 mg/kg in cotton gin by-products, the increased animal dietary burden might necessitate an MRL of 0.1 mg/kg in place of the current recommendation of 0.05 mg/kg for mammalian meat (fat).

Clarification was also sought if 'cotton fodder' means 'cotton gin byproducts.'

In the Codex Commodity Classification, 'Cotton fodder, dry' is the only feed commodity listed for cotton. It has been taken to mean cotton gin by-products and cotton stubble.

JMPR compares the freezer-storage intervals for samples from supervised trials with the intervals demonstrating storage stability in the freezer-storage tests. If the storage interval in a supervised trial exceeds the interval for demonstrated stability (i.e. no more than approx 30% loss) the data from that trial are rejected. Residue data are not adjusted for estimated storage losses.

In the freezer storage tests on cotton gin trash approximately 50% of the residue had disappeared in 44 days. The interval between ginning and analysis for the trial with the highest residue (18 mg/kg) was 17 days (theoretically < 30% loss) and so the trial data were accepted as valid.

In 2007, JMPR adopted the OECD Harmonized Table of Livestock Feed Commodities[17] for animal dietary burden calculation.

In the revised tables, cotton gin byproducts now contribute a maximum of 5% to the diet of beef cattle (US–Canada) as compared with a maximum 20% listed in the previous tables from the US[18]. The revised tables also specify that the STMR should be used for calculation of dietary burden for residues in cotton gin byproducts.

In view of these developments, a recalculated dietary burden for bifenazate is unlikely to exceed the one calculated in 2006.

The Meeting recommended no change to the animal commodity MRLs proposed in 2006.

3.3 METHIOCARB (132)

At the 38th Session of the CCPR in April 2006, the German Delegation raised concerns regarding the MRL proposed by the JMPR in 2005 for Peppers, sweet. The EU submitted a concern form in June 2006 which indicated that the short-term dietary intake calculated using the German model for children (between the ages of 2 and 5 years old) for Peppers, sweet was 470% (with a variability factor of 7) or 200% (with a variability factor of 3) of the ARfD established by 2005 JMPR.

The CCPR noted that no intake concerns were identified by JMPR for this compound and advanced all proposed draft MRLs to Step 5/8 (ALINORM 06/29/24, para. 104). The 29th Session of Codex Alimentarius Commission in July 2006 adopted all the MRLs for methiocarb as proposed by the 38th CCPR as Codex MRLs.

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[17] OECD. 10-Oct-2006. Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology. Series on Testing and Assessment. Number 64. Series on Pesticides. Number 32. Guidance Document on Overview of Residue Chemistry Studies. Document ENV/JM/MONO(2006)32.

[18] FAO. 2002. Submission and evaluation of pesticide residues data for the estimation of maximum residue levels in food and feed. Appendix IX. Maximum proportion of agricultural commodities in animal feed. FAO Plant Production and Protection Paper, 170.

No additional data became available for consideration by the current Meeting. The Meeting therefore confirmed its previous recommendation for Peppers, sweet.

3.4 QUINOXYFEN (223)

Livestock Dietary Burden Aspects

Quinoxyfen was reviewed for the first time by the 2006 JMPR. An ADI of 0–0.2 mg/kg bw was established, and it was determined that an ARfD was not necessary. Several MRL recommendations were made at the time.

The 39th CCPR requested JMPR to reconsider the dietary burden for cattle and its impact upon the proposed MRL for meat (ALINORM 07/30/24, Par. 133). It was noted that the dietary burden of beef cattle was utilized, whereas it might be appropriate to utilize the higher dietary burden of dairy cattle for the determination of the MRL for meat.

The maximum dietary burdens of quinoxyfen for beef cattle and dairy cattle are 0.66 ppm and 2.14 ppm, respectively. The STMR dietary burdens for beef cattle and dairy cattle are 0.25 ppm and 0.40 ppm, respectively. The Meeting confirmed that it is appropriate to use the higher dietary burden value for estimations involving cattle tissues. In this case, the values for dairy cattle would be used.

The augmented total residue calculations are summarized as follows, with new entries in bold:

Quinoxyfen total residues, mg/kg

Dietary burden (ppm) Feeding level [ppm]		Cream	Milk	Muscle		Liver		Kidney		Fat	
		Mean	Mean	Highest	Mean	Highest	Mean	Highest	Mean	Highest	Mean
MRL, beef cattle	(0.66) [0.6]			(< 0.01) [< 0.002]		(< 0.01) [< 0.01]		(< 0.01) [< 0.01]		(0.02) [0.02]	
MRL, dairy cattle	(2.1) [2]	(0.068) [0.068]	(0.0088) [0.0088]	**(< 0.01) [< 0.01]**		**(< 0.01) [< 0.01]**		**(< 0.01) [< 0.01]**		**(0.11) [0.10]**	
STMR beef cattle	(0.25) [0.2]				(0.002) [< 0.002]		(0.002) [< 0.002]		(< 0.01) [< 0.01]		(0.01) [0.01]
STMR dairy cattle	(0.40) [0.2/0.6]	(0.01) [0.003/ 0.016]	(0.002) [< 0.001/ 0.002]		**(0.002) [< 0.002/ < 0.002]**		**(0.006)[1] [< 002/ < 0.01]**		**(< 0.01) [< 0.01/ < 0.01]**		**(0.011) [0.01/ 0.012]**

[1] The kidney value (0.01 mg/kg) is used as the STMR for offal. Thus, 0.006 vs. 0.002 mg/kg had no effect.

The Meeting noted that the use of the dairy cattle diet as opposed to the beef cattle diet leads to an increase in the estimate of the maximum residue level for meat from "0.02 fat" mg/kg to "0.2 fat" mg/kg. No other cattle commodity MRLs are impacted and the STMR values as used in the human dietary risk assessment calculation are unchanged.

Definition of the residue

Plants and Animals

Definition of the residue (for compliance with MRL and estimation of dietary intake): quinoxyfen

The residue is fat soluble.

The Meeting estimated the maximum residue level of 0.2 (fat) mg/kg and STMR values of 0.011 (fat) and 0.002 muscle mg/kg to replace the previous recommendations. The maximum residue level is recommended for use as an MRL.

3.5 THIABENDAZOLE (065)

Thiabendazole is authorized as a post-harvest fungicide on citrus in many countries. It was evaluated for residues several times by the JMPR from 1970 to 2006. The 1997 JMPR reviewed the compound under the CCPR Periodic Re-evaluation Programme and proposed withdrawal of the existing CXL for citrus fruits of 10 mg/kg. The 2000 JMPR reviewed residue data from Spain on the basis of which an MRL of 3 mg/kg was proposed. At the CCPR Meeting in 2004, the MRL of citrus fruits was returned to Step 6 pending receipt of new residue data. The 2006 JMPR received new residue data on oranges and mandarins from Morocco and proposed for thiabendazole a maximum residue level of 5 mg/kg Po for citrus fruits.

At the 39th Session of the CCPR in 2007, the Committee noted the concerns expressed by Australia and the USA regarding the proposed MRL of 5 mg/kg Po of thiabendazole for citrus fruits. The delegations suggested, based on the reported HR of 5.2 mg/kg and statistical analysis, a more appropriate MRL would be 7 mg/kg. The Committee decided to advance the proposed draft MRL for citrus fruits of 5 mg/kg for adoption at Step 5 and to request JMPR to reconsider the statistical calculation used to derive the MRL.

Results of supervised trials on crops

Citrus fruits

The 2006 JMPR received information on supervised field trials on citrus fruits from trials conducted in Morocco during 2003 and 2004. Thiabendazole, formulated as a 500 SC, was applied to oranges (15 trials) and mandarins (eight trials) according to Moroccan GAP (post-harvest use, spray application mixed with wax, 0.375 kg ai/hL).

The residue levels in whole oranges treated according to the GAP were: 1.6, 1.6, 1.8, 1.8, 2.1, 2.2, 2.5, 3.3, 3.3, 3.4, 3.4, 3.8, 4.0, 4.2 and 5.2 mg/kg. The residue levels in whole mandarins treated according to the GAP were: 1.3, 2.4, 2.7, 2.7, 2.7, 2.8, 3.5 and 3.5 mg/kg. The 2006 JMPR decided to combine the data for whole oranges and mandarins to give a data set for whole citrus fruits (n=23): 1.3, 1.6, 1.6, 1.8, 1.8, 2.1, 2.2, 2.4, 2.5, 2.7, 2.7, 2.7, 2.8, 3.3, 3.3, 3.4, 3.4, 3.5, 3.5, 3.8, 4.0, 4.2 and 5.2 mg/kg.

The 2007 JMPR did not receive additional new information or data, but reconsidered the data reported by the 2006 JMPR because the proposed maximum residue level of 5 mg/kg for thiabendazole in citrus fruits fails to account for the value above 5 mg/kg.

The Meeting estimated a maximum residue level of 7 mg/kg Po for thiabendazole in citrus fruits to replace the previous recommendation of 5 mg/kg.

The HR value of 0.84 mg/kg and the STMR value of 0.045 mg/kg were derived by the 2006 JMPR from thiabendazole residues in the edible portion of the fruits from the same data set.

Dietary risk assessment

The MRL recommendation of 7 mg/kg Po for thiabendazole in citrus fruits will not alter the dietary intake estimates provided by the 2006 JMPR as these were based on the HR and the STMR values in the edible portion of the fruits from the same dataset. For long- and short-term intake estimations see the JMPR report 2006.

4. DIETARY RISK ASSESSMENT FOR PESTICIDE RESIDUES IN FOODS

Assessment of risk from long-term dietary intake

At the present Meeting risks associated with long-term dietary intake were assessed for compounds for which MRLs were recommended and STMRs estimated. International estimated daily intakes (IEDIs) were calculated by multiplying the concentrations of residues (STMRs and STMR-Ps) by the average daily per capita consumption estimated for each commodity on the basis of the 13 GEMS/Food Consumption cluster diets, available at http://www.who.int/foodsafety/chem/gems/en/index1.html. IEDIs are expressed as a percentage of the ADI for a 55 kg or 60 kg person, depending on the cluster diet.

The toxicological evaluation of atrazine was recommended by the WHO Drinking-water Guidelines programme and an ADI established. As the residues of this compound in food have not been considered by the JMPR, the long-term dietary risk assessment was not conducted by the Meeting.

The evaluation of bifenazate, captan, carbaryl, carbendazim, fenpyroximate, folpet, indoxacarb, methiocarb, thiabendazole and quinoxyfen performed at this Meeting do not affect the long-term dietary assessment conducted by the previous JMPR for these compounds.

Azinphos-methyl, lambda-cyhalothrin, procymidone, and profenofos were evaluated toxicologically at this Meeting under the Periodic Re-evaluation Programme and new ADIs were allocated. The long-term dietary risk assessment for these compounds will be considered during the periodic re-evaluation for residues at subsequent Meetings.

A summary of the long-term dietary risk assessments conducted by the present meeting is shown on Table 6. The detailed calculations of long-term dietary intakes are given in Annex 3. The percentages are rounded to one whole number up to 9 and to the nearest 10 above that. Percentages above 100 should not necessarily be interpreted as giving rise to a health concern because of the conservative assumptions used in the assessments. Calculations of dietary intake can be further refined at the national level by taking into account more detailed information, as described in the Guidelines for predicting intake of pesticide residues.[19]

Table 6. Summary of long-term dietary risk assessments conducted by the 2007 JMPR.

CCPR code	Compound Name	ADI (mg/kg bw)	Range of IEDI as % of maximum ADI
220	*Aminopyralid*	*0 - 0.9*	*0*
156	*Clofentezine*	*0 - 0.02*	*0 - 3*
157/228	*Cyfluthrin/Beta Cyfluthrin*	*0 - 0.04*	*0 - 2*
169	*Cyromazine*	*0 - 0.06*	*0 – 2*
224	*Difenoconazole*	*0 - 0.01*	*0 – 10*
225	*Dimethomorph*	*0 - 0.2*	*0 – 1*
037	*Fenitrothion*	*0 - 0.006*	*30 – 80*
165	*Flusilazole*	*0 - 0.007*	*2 – 10*
103	*Phosmet*	*0 - 0.01*	*2 – 90*
160	*Propiconazole*	*0 - 0.07*	*0 – 2*
226	*Pyrimethanil*	*0 - 0.2*	*0 – 5*
133/168	*Triadimefon/ Triadimenol*	*0 - 0.03*	*1– 4*
143	*Triazophos*	*0 - 0.001*	*0 – 20*
227	*Zoxamide*	*0 - 0.5*	*0*

[19] WHO (1997) Guidelines for predicting dietary intake of pesticide residues. 2nd revised edition, GEMS/Food Document WHO/FSF/FOS/97.7, Geneva

Assessment of risk from short-term dietary intake

Available consumption data was reviewed at the present Meeting to assess the risks associated with short term dietary intake for compounds with STMR and HR estimated values and established acute reference doses (ARfDs). The procedures for calculating the short-term intake were defined primarily in 1997 at an FAO/WHO Geneva Consultation,[20] refined at the International Conference on Pesticide Residues Variability and Acute Dietary Risk Assessment sponsored by the Pesticide Safety Directorate and at subsequent JMPR Meetings.

Data on the consumption of large portions were provided by the governments of Australia, France, The Netherlands, Japan, South Africa, Thailand, the UK and the USA. Data on unit weights and per cent edible portions were provided by the governments of France, Sweden, the UK and the USA. The body weights of adults and children aged ≤ 6 years were provided by the governments of Australia, France, the Netherlands, South Africa, the UK and the USA. The consumption, unit weight and body weight data used for the short-term intake calculation were compiled by GEMS/FOOD and are available at http://www.who.int/foodsafety/chem/acute_data/en/. The documents are dated May, 2007 (large portions and body weights) and May, 2003 (unit weights).

The procedures used for calculating the International estimated short-term intake (IESTI) are described in detail in Chapter 3 of the 2003 JMPR report. Detailed guidance on setting ARfD is described in Section 2.1 of the 2004 JMPR report.[21]

The toxicological evaluation of atrazine was recommended by the WHO Drinking-water Guidelines programme and an ARfD was established. As the residues of this compound in food have not been considered by the JMPR, the short-term dietary risk assessment was not conducted by the Meeting.

The evaluation of captan, carbendazim, folpet, methiocarb and thiabendazole performed at this Meeting do not affect the short-term dietary assessment conducted by the previous JMPR for these compounds.

Azinphos-methyl, lambda-cyhalothrin, procymidone, and profenofos were evaluated toxicologically at this Meeting under the Periodic Re-evaluation Programme, and new ARfDs allocated. The short-term dietary risk assessment for these compounds will be considered during the periodic re-evaluation for residues at subsequent Meetings.

On the basis of data received by the present or previous Meeting, the establishment of an ARfD for aminopyralid, bifenazate, clofentezine, pyrimethanil, quinoxyfen and zoxamide was considered to be unnecessary. The short-term intakes of these compounds were not estimated.

The short-term intakes as percentages of the ARfDs for the general population and for children are summarized in Table 7. The percentages are rounded to one whole number up to 9 and to nearest 10 above that. Percentages above 100 should not necessarily be interpreted as giving rise to a health concern because of the conservative assumptions used in the assessments.

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[20] WHO (1997) Food consumption and exposure assessment of chemicals. Report of a FAO/WHO Consultation. Geneva, Switzerland, 10-14 February 1997, Geneva

[21] Annex 5, reference 98.

Table 7. Summary of short-term dietary risk assessments conducted by the 2007 JMPR.

CCPR code	Compound Name	ARfD (mg/kg bw)	Commodity	Percentage of ARf D	
				General population	Children aged ≤ 6 years
008	*Carbaryl*	*0.2*	*Cranberry and dried chilli pepper*	*0*	*0 – 1*
157/ 228	*Cyfluthrin/ Beta Cyfluthrin*	*0.04*	*Broccoli*	*70*	*120*
			Cabbage, head	*100*	*240*
			Other commodities	*0 – 60*	*0 – 80*
169	*Cyromazine*	*0.1*	*Cabbage, head*	*120*	*280*
			Spinach	*130*	*390*
			Other commodities	*0 – 20*	*0 – 40*
224	*Difenoconazole*	*0.3*	*All commodities*	*0 – 7*	*0 – 10*
225	*Dimethomorph*	*0.6*	*All commodities*	*0 – 10*	*0 – 20*
037	*Fenitrothion**	*0.04*	*Wheat bran, unprocessed*	*70*	*110*
			Other commodities	*0 – 80*	*0 – 70*
193	*Fenpyroximate*	*0.02*	*Apple*	*20*	*60*
			Grape	*60*	*150*
165	*Flusilazole*	*0.02*	*All commodities*	*0 – 40*	*0 – 100*
216	*Indoxacarb*	*0.1*	*Cabbage, head*	*40*	*90*
103	*Phosmet*	*0.2*	*All commodities*	*1 – 50*	*0 – 100*
160	*Propiconazole*	*0.3*	*All commodities*	*0 – 1*	*0 – 3*
133/ 168	*Triadimefon/ Triadimenol*	*0.08*	*Grapes (excluding wine)*	*80*	*220*
			Other commodities	*0 – 20*	*0 – 60*
143	*Triazophos*	*0.001*	*Soya bean (immature)*	*140*	*230*
			Cotton seed oil	*2*	*5*

* Since unprocessed wheat bran is not an edible commodity and further processing is likely to reduce the level of residues, the Meeting assumed that the intake of fenitrothion from processed wheat bran would be below the ARfD. The Meeting concluded that the short-term intake of residues of fenitrothion from uses considered by the Meeting was unlikely to present a public health concern.

5. EVALUATION OF DATA FOR ACCEPTABLE DAILY INTAKE AND ACUTE DIETARY INTAKE FOR HUMANS, MAXIMUM RESIDUE LEVELS AND SUPERVISED TRIAL MEDIAN RESIDUE VALUES

5.1 AMINOPYRALID (220)

Toxicology

Aminopyralid is the International Organization for Standardization (ISO) approved name for 4-amino-3,6-dichloropyridine-2-carboxylic acid (Chemical Abstracts Service, CAS No. 150114-71-9). It is a post-emergent auxin-type herbicide for the control of a wide variety of broadleaf weed species. Most of the toxicological studies evaluated were performed with the aminopyralid acid. However, some studies were performed with the commercially available aqueous solution of aminopyralid triisopropylammonium (TIPA) salt, called GF-871, since products are also marketed in this form. Throughout the current evaluation, aminopyralid acid is termed aminopyralid and its TIPA salt is termed aminopyralid TIPA. GF-871 is a 41.3–41.9% aqueous solution of aminopyralid TIPA corresponding to approximately 21.7% aminopyralid. If not otherwise stated, doses are given as aminopyralid equivalents.

Aminopyralid has not been evaluated previously by the Meeting. The evaluation of aminopyralid was scheduled for the 2006 JMPR but, owing to incomplete submission of data, was postponed to the present Meeting. Aminopyralid was reviewed at the request of CCPR. All pivotal studies with aminopyralid and aminopyralid TIPA were certified as complying with GLP.

Biochemical aspects

In a study of the absorption, distribution, metabolism and excretion of radiolabelled aminopyralid administered by oral gavage, male rats were given single doses at 50 or 1000 mg/kg bw, or a single dose at 50 mg/kg bw after 14 days pre-treatment with unlabelled aminopyralid at a dose of 50 mg/kg bw per day. Male rats also received radiolabelled aminopyralid TIPA salt as a single oral gavage dose at 96 mg/kg bw (equal to aminopyralid at 50 mg/kg bw). The pharmacokinetic behaviour of aminopyralid and its TIPA salt was very similar. Of the administered dose, 42–59% was absorbed and rapidly excreted in the urine, most within the first 24 h. Excretion was biphasic, with half-lives of 3.0–3.8 h and 10.2–12.3 h. Biliary excretion was assumed to be negligible. After a depletion period of 168 h, virtually all tissue samples showed concentrations of radiolabel of less than 0.01% of the administered dose. Aminopyralid was not metabolized in rats; more than 95% of the radiolabel was accounted for. On the basis of lack of coordination in gait after exposure to aminopyralid and aminopyralid TIPA in rabbits but not in rats, an extensive study of the absorption, distribution, metabolism and excretion of aminopyralid in rabbits was performed. A group of non-pregnant rabbits received radiolabelled aminopyralid as a single dose at 280–370 mg/kg bw. A group of pregnant rabbits (“late-stage”) received non-labelled aminopyralid on days 7–21 of gestation and then radiolabelled aminopyralid as a single dose at 280–370 mg/kg bw on day 22 of gestation. An additional group of pregnant rabbits (“early-stage”) received radiolabelled aminopyralid as a single dose at 280–370 mg/kg bw on day 7 of gestation, without pre-treatment with unlabelled aminopyralid. Using plasma from animals in these three groups and from a group of non-pregnant rats given radiolabelled aminopyralid as a single dose at 280–370 mg/kg bw, a study of plasma-protein binding was performed. In late-stage pregnant rabbits pre-treated with repeated doses of unlabelled aminopyralid, the absorption of aminopyralid (based on lower T_{max}, higher area under the curve for concentration–time [AUC] and increased renal excretion) was somewhat more rapid and greater than in non-pregnant and early-stage pregnant rabbits. Plasma-protein binding was lower (43–58%) in late-stage pregnant rabbits pre-treated with repeated doses of unlabelled aminopyralid than in non-

pregnant and early-stage pregnant rabbits (47–68%). The difference in bioavailability (expressed as unbound compound) of aminopyralid was at most twofold. However, interpretation of these results remains ambiguous because of the different dosing regimens used (single dose without pre-treatment in non-pregnant and early-stage pregnant rabbits and single dose after pre-treatment in late-stage pregnant rabbits). Based on renal excretion of radiolabel, absorption of aminopyralid in rabbits was close to 80% or greater, being 20–40% higher than in rats.

Toxicological data

Aminopyralid and aminopyralid TIPA have low acute toxicity in rats when administered orally, dermally or by inhalation. The oral and the dermal LD50s are both > 5000 mg/kg bw, and by inhalation, the LC50 is > 5.5 mg/L, the highest dose tested. Aminopyralid is clearly irritating to the eye, while aminopyralid TIPA is only slightly irritating. Aminopyralid is not a dermal irritant, while aminopyralid TIPA is a slightly irritant. In guinea-pigs, aminopyralid and aminopyralid TIPA produced no signs of skin-sensitizing potential, as tested by the Magnusson & Kligman method.

In short-term feeding studies in mice, rats and dogs and in a study of dermal exposure studying rats, animals received aminopyralid at doses of up to 1000 mg/kg bw per day. Body weight was reduced only in female dogs receiving aminopyralid at 967 mg/kg bw per day, the highest dose tested in a 1-year study. Males and females at this dose also showed a slight increase in relative liver weights accompanied by hepatocyte hypertrophy in two out of four animals per sex. In male and female rats at doses of 500 mg/kg bw per day and greater, reversibly increased absolute and relative weights of full and empty caeca were observed and slight mucosal hyperplasia of the caecum and the ileum was found in males at the highest dose. These changes were considered to be a consequence of physiological adaptation. Mucosal hyperplasia of the stomach was observed in all dogs at 967 mg/kg bw per day. Treatment-related clinical chemistry changes were restricted to the urine of rats at 500 mg/kg bw per day and greater, where decreased pH values and decreased concentrations of protein and ketone were found. Changes in the pH of the urine were most likely due to urinary excretion of the unchanged, acid parent compound. Generally, aminopyralid was well tolerated by mice, rats and dogs in short-term studies. The NOAEL for aminopyralid in mice was 1000 mg/kg bw per day (the highest dose tested), 1000 mg/kg bw per day in rats (the highest dose tested) and 93.2 mg/kg bw per day in dogs, on the basis of histopathological changes in the gastric mucosa at the highest dose tested. In a 13-week feeding study in rats with aminopyralid TIPA, the same effects on caecal weights and urine chemistry were observed as with aminopyralid. Based on the lack of other effects, the NOAEL for aminopyralid TIPA in rats was 2421 mg/kg bw per day as GF-871, equal to aminopyralid at 525 mg/kg bw per day, the highest dose tested.

In an 18-month study in mice and a 24-month feeding study in rats, diets adjusted to provide aminopyralid at maximal doses of 1000 mg/kg bw per day did not induce any increases in the incidence of neoplastic findings.

Mortality was increased in all groups of female mice receiving aminopyralid, but appeared to be compound-related only in animals at the highest dose. Animals that died showed an increased incidence of age-related nephropathy. Although the overall incidence of nephropathy was not increased in this or any treated group, exacerbation of the effects of age-related nephropathy in these animals may have been responsible for the increase in mortality. Other treatment-related signs of toxicity in this group e.g., pale kidneys, reduced body fat, haemolysed blood in the gastrointestinal tract, atelectasis of the lung and perineal soiling, were most likely a reflection of the moribund state of the animals. The NOAEL was 250 mg/kg bw per day on the basis of increased mortality in females at 1000 mg/kg bw per day. Although the final cumulative mortality in rats was comparable at all doses, the onset of mortality in males at 1000 mg/kg bw per day appeared earlier. As statistical significance and clear treatment-related causes for death were lacking, the Meeting did not consider this finding as being related to treatment.

Slightly reduced body-weight gain was observed in male rats at 500 mg/kg bw per day and above. Increased absolute and relative weights of full and empty caeca were observed in males and females at 500 mg/kg bw per day and above, accompanied by very slight mucosal hyperplasia of the caeca, which was statistically significant only in males at the highest dose. This finding is common to many substances and, due to the lack of further histological changes, was not considered to be an adverse finding. In males and females at 500 and 1000 mg/kg bw per day, increased urine volumes, decreased specific gravity and protein and ketone contents and reduced pH values were observed without any renal histopathological correlate. These changes were not considered to be toxicologically significant, the change in pH most likely reflecting urinary excretion of the acidic parent compound. The NOAEL in this feeding study in rats was 500 mg/kg bw per day on the basis of slight but statistically significant body-weight decreases in males at 1000 mg/kg bw per day.

Aminopyralid was not carcinogenic in mice or rats.

Aminopyralid and its TIPA salt were tested for genotoxicity in an adequate range of tests, including an assay for reverse mutation in *Salmonella typhimurium* and *E. coli*, an assay for forward mutation in HGPRT with Chinese hamster ovary cells, an assay for chromosomal aberration in rat lymphocytes in vitro and an assay for micronucleus formation in mouse bone marrow in vivo. In the assay for chromosomal aberration in rat lymphocytes in vitro, an increased frequency of chromosomal aberration was seen only after 24 h of treatment at clearly cytotoxic concentrations of aminopyralid and in the absence of metabolic activation. The results of all other assays showed no evidence for genotoxicity.

The Meeting concluded that aminopyralid and aminopyralid TIPA are unlikely to be genotoxic.

In view of the lack of genotoxicity and the absence of carcinogenicity in rats and mice, the Meeting concluded that aminopyralid is unlikely to pose a carcinogenic risk to humans.

In a two-generation study of reproduction in rats given diets containing aminopyralid, only increases in the weight of full and empty caeca in parental animals treated with aminopyralid were observed and no changes in reproductive parameters were observed. The caecal changes were not considered to be toxicologically significant. The NOAEL for general toxicity and reproductive toxicity was 1000 mg/kg bw per day, the highest dose tested. In pregnant rats and rabbits treated with aminopyralid by gavage, even the highest doses tested, 1000 and 500 mg/kg bw per day, respectively, did not induce any treatment-related malformations in the offspring. When rats and rabbits were treated with aminopyralid TIPA, no treatment-related malformations occurred, but foetal body-weight reduction was observed in only in rabbits at high doses (aminopyralid equivalents, 526 mg/kg bw per day).

In rabbits treated with aminopyralid at doses of 500 mg/kg bw per day and greater, body-weight gain was reduced, and uncoordinated gait was evident immediately after dosing, lasting for approximately 2 h. Neither the severity nor the duration of uncoordinated gait increased as the study progressed. Additionally, two rabbits treated with aminopyralid at the highest dose were killed in a moribund condition on day 17 of gestation, being found to have pale kidneys, watery and dark caecal contents and erosions/ulcers in the glandular mucosa of the stomach. Owing to severe clinical signs observed at 750 mg/kg bw per day, all remaining animals in this study were killed at day 20 of gestation and were not available for evaluation of reproductive performance. Therefore, the NOAEL for maternal toxicity was 250 mg/kg bw per day. In pregnant rabbits treated with aminopyralid TIPA, maternal toxicity was evident as uncoordinated gait at a dose of 78 mg/kg bw per day as aminopyralid equivalents and greater. At higher doses, the clinical effects observed were similar to those seen with aminopyralid. The NOAEL for maternal toxicity was 26 mg/kg bw per day as aminopyralid equivalents.

In a study of acute toxicity and a 1-year study of neurotoxicity in rats treated with aminopyralid, no signs of behavioural changes and no histopathological findings suggesting neurotoxic potential were observed. Faecal and urine soiling at 2000 mg/kg bw in the study of acute

toxicity were most likely due to general toxicity rather than indicative of specific neurotoxicity. The NOAELs for neurotoxicity in these two studies were 2000 and 1000 mg/kg bw per day as aminopyralid, respectively, the highest doses tested.

To obtain further insight into the possible mode of action leading to uncoordinated gait in rabbits, pregnant and non-pregnant animals were treated with aminopyralid and aminopyralid TIPA. Again, uncoordinated gait was observed but without any histopathological correlate in the central or peripheral nervous system. Additionally, no changes in consciousness, muscle strength or autonomic and somatic control were observed. For the acute dietary risk assessment, the occurrence of unco-ordination after one or two doses in pregnant rabbits treated with aminopyralid may be the only relevant end-point. The NOAEL for aminopyralid for this effect was 250 mg/kg bw per day. In one study with aminopyralid TIPA, slight unco-ordination was seen in one animal after 1 day of treatment at a dose of 173.6 mg/kg bw per day as aminopyralid equivalents. In another two studies of developmental toxicity in rabbits receiving aminopyralid TIPA, a dose-related increase in the incidence of unco-ordination was found. However, at doses at which unco-ordination was observed, i.e., 78, 105, 263 and 525 mg/kg bw per day as aminopyralid equivalents, the effect occurred only after at least six exposures. The NOAEL was 26 mg/kg bw per day as aminopyralid equivalents. The Meeting concluded that the weight of evidence indicated that the NOAEL for acute unco-ordination was 250 mg/kg bw as aminopyralid. Effects observed in short-term studies in dogs were not considered relevant for establishing an acute reference dose.

The Meeting concluded that the existing data were adequate to characterize the potential hazard to foetuses, infants and children.

Toxicological evaluation

The Meeting established an ADI of 0–0.9 mg/kg bw based on a NOAEL of 93.2 mg/kg bw per day identified on the basis of histological changes in the gastric mucosa at higher doses in a 1-year study in dogs, and a safety factor of 100.

The Meeting concluded that it was not necessary to establish an ARfD for aminopyralid. The only end-point that might be suitable as a basis for establishing an ARfD for aminopyralid was uncoordinated gait in the studies of developmental toxicity in rabbits. Although this effect was observed after repeated exposure at 78 mg/kg bw with a NOAEL of 26 mg/kg bw, it was observed after one or two exposures only at higher doses, with a NOAEL of 250 mg/kg bw. As this effect was dependent on C_{max} and in view of the kinetics of aminopyralid and the dynamics of this response, the Meeting considered it appropriate to adjust the safety factor. Applying a safety factor of 25 to the NOAEL of 250 mg/kg bw would result in a putative ARfD of 10 mg/kg bw which is greater than the JMPR-recommended cut-off value for an ARfD of 5 mg/kg bw.

A toxicological monograph was prepared.

Levels relevant to risk assessment

Species	Test material	Study	Effect	NOAEL[b]	LOAEL[b]
Mouse	Aminopyralid	Eighty-week study of toxicity and carcinogenicity[a]	Toxicity	250 mg/kg bw per day	1000 mg/kg bw per day
			Carcinogenicity	1000 mg/kg bw per day[c]	—
Rat	Aminopyralid	Two-year study of toxicity and carcinogenicity[a]	Toxicity	500 mg/kg bw per day	1000 mg/kg bw per day
			Carcinogenicity	1000 mg/kg bw per day[c]	—

	Aminopyralid	Two-generation study of reproductive toxicity[a]	Parental toxicity/	1000 mg/kg bw per day[c]	—
			Offspring toxicity	1000 mg/kg bw per day[c]	—
	Aminopyralid	Developmental toxicity[b]	Maternal toxicity	1000 mg/kg bw per day[c]	—
			Embryo/fetotoxicity	1000 mg/kg bw per day[c]	—
	Aminopyralid TIPA	Developmental toxicity[d]	Maternal toxicity	525 mg/kg bw per day[c]	—
			Embryo/fetotoxicity	525 mg/kg bw per day[c]	—
	Aminopyralid	Long-term study of neurotoxicity	Neurotoxicity	1000 mg/kg bw per day[c]	—
Rabbit	Aminopyralid	Developmental toxicity[d]	Maternal toxicity	250 mg/kg bw per day	500 mg/kg bw per day
			Embryo/fetotoxicity	500 mg/kg bw per day[c]	—
	Aminopyralid TIPA	Developmental toxicity[d]	Maternal toxicity	26 mg/kg bw per day	78 mg/kg bw per day
			Embryo/fetotoxicity	263 mg/kg bw per day	526 mg/kg bw per day
Dog	Aminopyralid	One-year study of toxicity[a]	Toxicity	93.2 mg/kg bw per day	967 mg/kg bw per day

TIPA, triisopropylammonium.

[a] Dietary administration.

[b] Values for aminopyralid TIPA are given as aminopyralid equivalents.

[c] Highest dose tested.

[d] Gavage administration.

Estimate of acceptable daily intake for humans

0–0.9 mg/kg bw

Estimate of acute reference dose

Unnecessary

Information that would be useful for the continued evaluation of the compound

Results from epidemiological, occupational health and other such observational studies of human exposures

Critical end-points for setting guidance values for exposure to aminopyralid

Absorption, distribution, excretion and metabolism in mammals	
Rate and extent of oral absorption	Rapid, 42–59%

Dermal absorption	No data
Distribution	Extensive
Potential for accumulation	No evidence of accumulation
Rate and extent of excretion	Rapid
Metabolism in animals	Minimal. No metabolites identified.
Toxicologically significant compounds in animals, plants and the environment	Aminopyralid
Acute toxicity	
Rat, LD_{50}, oral	> 5000 mg/kg bw
Rat, LD_{50}, dermal	> 5000 mg/kg bw
Rat, LC_{50}, inhalation	> 5.5 mg/L
Rabbit, dermal irritation	Aminopyralid is not an irritant, aminopyralid TIPA is a slight irritant.
Rabbit, ocular irritation	Aminopyralid is an irritant, aminopyralid TIPA is not an irritant.
Skin sensitization (test method used)	Not a sensitizer (Magnusson & Kligman test)
Short-term studies of toxicity	
Target/critical effect	Histopathological changes in stomach
Lowest relevant oral NOAEL	93.2 mg/kg bw per day (1-year study in dogs)
Lowest relevant dermal NOAEL	1000 mg/kg bw per day, the highest dose tested (4-week study in rats)
Lowest relevant inhalation NOAEC	No studies available
Genotoxicity	
	No genotoxic potential
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	Increased mortality in female mice
Lowest relevant NOAEL	250 mg/kg bw per day (18-month study in mice)
Carcinogenicity	Not carcinogenic
Reproductive toxicity	
Reproduction target/critical effect	No reproductive effects in rats
Lowest relevant reproductive NOAEL	1000 mg/kg bw per day, the highest dose tested
Developmental target/critical effect	No developmental effects in rats and rabbits with aminopyralid; foetal body-weight changes with aminopyralid TIPA.
Lowest relevant developmental NOAEL	263 mg/kg bw per day (rabbit)
Neurotoxicity/delayed neurotoxicity	
	No neurotoxic effects in rats with aminopyralid and aminopyralid TIPA; uncoordinated gait in pregnant rabbits, with both aminopyralid and aminopyralid TIPA.
Lowest relevant NOAEL	26 mg/kg bw per day (repeated doses), 250 mg/kg bw (single dose)

Medical data

No data available

Summary

	Value	Study	Safety factor
ADI	0–0.9 mg/kg bw	Dog, 1-year study	100
ARfD	Unnecessary	—	—

TIPA, triisopropylammonium

RESIDUE AND ANALYTICAL ASPECTS

Aminopyralid was evaluated for residues and toxicology by the 2006 JMPR and a discussion of residue aspects included in the report of the 2006 JMPR. As the toxicological evaluation was not completed in 2006 a dietary risk assessment could not be conducted and recommendations for maximum residue levels were not made. The current Meeting has completed the evaluation of the toxicological data and, based on the evaluation of the 2006 JMPR, recommendations are now made for maximum residue levels in various commodities.

Recommendations

On the basis of the data from supervised trials and farm animal feeding studies reported by the 2006 JMPR, the Meeting concluded that the residue levels as listed in Annex 1 are appropriate for establishing maximum residue limits and for IEDI assessment.

Definition of the residue for plants and animals (for compliance with MRLs and estimation of dietary intake): aminopyralid and its conjugates that can be hydrolysed, expressed as aminopyralid.

DIETARY RISK ASSESSMENT

Long-term intake

The evaluation of aminopyralid resulted in recommendations for MRLs and STMR values for raw and processed commodities. The International Estimated Daily Intakes (IEDI) of aminopyralid in the 13 GEMS/Food cluster diets, based on estimated STMRs were all < 1% of the maximum ADI of 0.9 mg/kg bw. The Meeting concluded that the long-term intake of residues of aminopyralid from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The 2007 JMPR decided that an ARfD is unnecessary. The Meeting therefore concluded that the short-term intake of aminopyralid residues is unlikely to present a public health concern.

5.2 ATRAZINE

TOXICOLOGY

Atrazine, 6-chloro-N^2-ethyl-N^4-isopropyl-1,3,5-triazine-2,4-diamine (International Union of Pure and Applied Chemistry, IUPAC) (CAS No. 1912-24-9), is a selective systemic herbicide of the

chlorotriazine class, used for the control of annual broadleaf and grassy weeds. It acts as a photosynthetic electron transport inhibitor at the photosystem II receptor site. Atrazine and its chloro-*s*-triazine metabolites deethyl-atrazine (DEA), deisopropyl-atrazine (DIA) and diaminochlorotriazine (DACT) have been found in surface and ground water as a result of the use of atrazine as a pre-emergent or early post-emergent herbicide. Hydroxyatrazine is more commonly detected in ground than in surface water. The relative order of concentrations in rural wells in the USA was generally as follows: atrazine ~DEA ~DACT > DIA > hydroxyatrazine. However, concentrations of DEA that are several-fold higher than those of the parent compound have been reported.

Atrazine was evaluated previously by WHO, a tolerable daily intake (TDI) of 0.0005 mg/kg bw being established in the 1993 Guidelines for Drinking-water Quality based on a NOAEL of 0.5 mg/kg bw per day in a study of carcinogenicity in rats and using a safety factor of 1000 (100 for inter- and intraspecies variation and 10 to reflect potential carcinogenic risk to humans).

Atrazine had not been previously evaluated by JMPR, and no ADI had been established. For that reason, the WHO Drinking-water Guidelines programme recommended that atrazine should be evaluated toxicologically by JMPR.

The database on atrazine was extensive, consisting of a comprehensive set of GLP-compliant guideline studies with atrazine and its four key metabolites, as well as a large number of published studies. The present Meeting did not aim to perform a review of the database de novo, but to summarize the key studies focusing on the issues of carcinogenicity, endocrine disruption (especially its neuroendocrine mode of action) and immunotoxicity. Reference was made to a number of reviews made by national and international agencies and organizations in recent years.

Biochemical aspects

After oral administration to rats, [^{14}C] labelled atrazine was rapidly and almost completely absorbed, independent of dose and sex. Radioactivity was widely distributed throughout the body. Excretion was more than 93% of the administered dose within 7 days, primarily via the urine (approximately 73%) and to a lesser extent via the faeces (approximately 20%; approximately 7% via bile), with more than 50% being excreted within the first 24 h. The elimination half-life of radiolabel from the whole body was 31.3 h in rats; this prolonged half-life was caused by covalent binding of atrazine to cysteine sulfhydryl groups in the β-chain of rodent haemoglobin. Seven days after administration of a single low dose (1 mg/kg bw), tissue residues represented 6.5–7.5% of the dose, with the highest concentrations in erythrocytes (≤ 0.63 ppm), liver (≤ 0.50 ppm) and kidneys (≤ 0.26 ppm). Atrazine was extensively metabolized; more than 25 metabolites have been identified in rats. The major metabolic pathways were stepwise dealkylation via either deisopropyl-atrazine (DIA) or deethyl-atrazine (DEA) to diaminochlorotriazine (DACT), the major metabolite. Dechlorination involving conjugation with glutathione was a minor pathway. The biotransformation of atrazine in rats and humans was qualitatively similar.

Toxicological data

Atrazine was of low acute toxicity in rats exposed orally (LD_{50}, 1870–3090 mg/kg bw), dermally (LD_{50}, > 2000 mg/kg bw) or by inhalation (LC_{50}, > 5.8 mg/L). Atrazine was not a skin irritant or an eye irritant in rabbits. Although spray dilutions of atrazine did not appear to be sensitizing in humans, atrazine was a skin sensitizer in tests in guinea-pigs (Magnusson & Kligman, Maurer optimization test).

In short-term studies of toxicity in rats, dogs and rabbits, the consistent toxic effects noted across species included reduced body-weight gain and food intake and a slight decrease in erythrocyte parameters. Also in rats, liver weights and splenic haemosiderin deposition were increased, while in dogs there was marked cardiac toxicity.

In a 90-day study of toxicity in rats, the NOAEL was 50 ppm, equal to 3.3 mg/kg bw per day, on the basis of decreased body-weight gain and increased splenic haemosiderin deposition at 500 ppm.

In a 52-week study of toxicity in dogs, the NOAEL was 150 ppm, equal to 5 mg/kg bw per day, on the basis of decreased body-weight gain and marked cardiac toxicity at 1000 ppm, equal to 33.7 mg/kg bw per day.

In a 25-day study in rabbits treated dermally, the NOAEL for systemic toxicity was 100 mg/kg bw per day on the basis of decreased body-weight gain and food intake, a slight reduction in erythrocyte parameters and increased spleen weight at 1000 mg/kg bw per day.

Atrazine was tested for genotoxicity in a large number of studies covering an adequate range of end-points, including assays for gene mutation in bacteria and eukaryotic cells in vitro, for DNA damage and repair in bacteria and mammalian cells (rat hepatocytes, human fibroblasts) in vitro, and for chromosomal aberration in vitro and in somatic and germ cells in vivo. Mostly negative results were obtained in standard assays. In a few published studies, positive responses were reported. However, a number of reviews by national and international agencies (United States Environmental Protection Agency, European Union, International Agency for Research on Cancer) have concluded that, based on the weight of evidence, atrazine is not genotoxic.

The Meeting agreed that it is unlikely that atrazine is genotoxic.

Long-term studies of toxicity and carcinogenicity were conducted in mice and rats. As in short-term studies, reduced body weight gain and food intake and a decrease in erythrocyte parameters were noted consistently. Additionally, reduced survival of females and cardiovascular effects (atrial thrombi) in both sexes were observed in mice at high doses.

In three studies of carcinogenicity in mice, no treatment-related carcinogenic effects were observed at dietary concentrations of up to 3000 ppm, equal to about 386 and 483 mg/kg bw per day in males and females, respectively. Overall, the NOAEL was 10 ppm, equal to 1.2 mg/kg bw per day, on the basis of lower body weight/body-weight gain at 300 ppm, equal to 38.4 mg/kg bw per day, and greater.

In two studies of carcinogenicity in Fischer-344 (F344) rats fed diets containing atrazine at concentrations of up to 400 ppm, equivalent to about 20 mg/kg bw per day, there was no effect at any dose on the onset or incidence of tumours. The NOAEL was 70 ppm, equivalent to about 3.5 mg/kg bw per day, on the basis of decreased body weight at concentrations of 200 ppm and greater. In a non-guideline study of carcinogenicity in F344 rats, there was a significant increase in the incidence of benign mammary tumours in males and in uterine adenocarcinomas in females at the highest dose of 750 ppm, equivalent to about 38 mg/kg bw per day; however, interpretation of the result was limited by increased survival at the highest dose, and a survival-adjusted analysis of tumour prevalence did not indicate any significant increase in the incidence of benign, malignant or combined mammary tumours.

In seven studies of carcinogenicity in Sprague-Dawley rats fed diets containing atrazine at concentrations of up to 1000 ppm (equal to about 42 and 65 mg/kg bw per day in males and females, respectively), an increased incidence of mammary tumours (adenomas, carcinomas, fibroadenomas) with or without an earlier onset (relative to controls) was observed in four studies, while in two studies there was an earlier onset of mammary tumours without any increase in their overall lifetime incidence. An earlier onset of pituitary tumours was also observed in one study, with no increase in incidence at term. Overall, the NOAEL for mammary carcinogenicity was 25 ppm, equal to 1.5 mg/kg bw per day, on the basis of a statistically significant increased incidence in mammary tumours at 50 ppm, equal to 3.1 mg/kg bw per day.

In a study of carcinogenicity in ovariectomized Sprague-Dawley rats, neither increases in mammary-gland proliferative changes nor mammary tumours were seen at dietary concentrations of

up to 400 ppm (equal to about 21 mg/kg bw per day), suggesting that the carcinogenic mode of action of atrazine in Sprague-Dawley rats is related to ovarian function.

In a mechanistic 6-month study in Sprague-Dawley rats, attenuation of the luteinizing hormone (LH) surge and subsequent disruption of the oestrous cycle (characterized by an increase in days in oestrous) were observed at ≥ 50 ppm (equal to 3.65 mg/kg bw per day), with a NOAEL of 25 ppm (equal to 1.8 mg/kg bw per day). The NOAEL and LOAEL for these effects were comparable to those found in the studies of carcinogenicity. The effects on the LH surge and disruption of the oestrous cycle were further supported by a number of short-term mechanistic studies. Additional experiments suggested that the effects of atrazine on LH and prolactin secretion are mediated via a hypothalamic site of action.

The postulated mode of action for atrazine-induced mammary tumours in female Sprague-Dawley rats involved disruption of the hypothalamic–pituitary–ovary axis. Atrazine modifies catecholamine function and the regulation of gonadotropin-releasing hormone (GnRH) pulsatility in the rat hypothalamus, with the consequence that the pulse of LH released from the pituitary gland is of insufficient amplitude or duration to trigger the ovulation. The failure to ovulate results in persistent secretion of oestrogen, which provides a feedback to the pituitary leading to increased secretion of prolactin. As a result, atrazine accelerates the normal reproductive ageing process in female Sprague-Dawley rats whereby reproductive senescence is characterized by persistent exposure to oestrogen and prolactin. In contrast, women respond to reduced levels of LH by reductions in levels of oestrogen. Thus, the Meeting considered that the mode of carcinogenic action in certain susceptible rat strains is not relevant for human risk assessment.

Investigations of other modes of action did not provide any evidence that atrazine had intrinsic estrogenic activity or that it increased aromatase activity in vivo.

The Meeting concluded that atrazine is not likely to pose a carcinogenic risk to humans.

Although carcinogenicity in humans was not a concern owing to the rat-specific mode of action, alterations in neurotransmitter and neuropeptide function regulating LH and secretion of prolactin may potentially induce adverse effects during critical periods of development (as found in special studies showing pregnancy loss, delayed puberty in males and females, and decreased suckling-induced prolactin release in lactating dams). Unlike the carcinogenic effects, the developmental effects do not appear to be specific to certain strains of rats and the Meeting therefore considered these effects to be relevant for risk assessment in humans.

In special studies of reproductive toxicity, exposure of rats during early pregnancy (i.e., the LH-dependent period) caused increased pre- or post-implantation losses, including full-litter resorptions. Effects were seen at doses of ≥ 50 mg/kg bw per day after treatment on days 6–10 of gestation, with a NOAEL of 25 mg/kg bw per day. In contrast, exposure on days 11–15 of gestation (after the LH-dependent period of pregnancy) at a dose of 200 mg/kg bw per day did not induce full-litter resorptions.

Suppression of the suckling-induced prolactin release in lactating rats was seen with atrazine at doses of ≥ 25 mg/kg bw per day, with a NOAEL of 12.5 mg/kg bw per day. Treatment of lactating rats on postnatal days 1–4 affected the development of tuberoinfundibular dopaminergic neurons in the pups (presumably due to the lack of prolactin derived from the dam’s milk), with the consequence of impaired regulation of prolactin secretion, hyperprolactinaemia prior to puberty and prostatitis in the adult male offspring.

A delay in sexual development was observed in female rats after exposure on postnatal days 21–46 at doses ≥ 30 mg/kg bw per day, with a NOAEL of 10 mg/kg bw per day, and in male rats after exposure on postnatal days 23–53 at doses ≥ 12.5 mg/kg bw per day, with a NOAEL of 6.25 mg/kg bw per day.

In a standard two-generation study of reproduction (conducted according to earlier guidelines, which did not include end-points such as oestrous cyclicity and sexual development) in rats, there was

no effect on fertility at 500 ppm, the highest dose tested. The NOAEL for parental toxicity was 50 ppm, equal to 3.6 mg/kg bw per day, on the basis of decreased body-weight gains and food consumption at 500 ppm, equal to 36.1 mg/kg bw per day. The NOAEL for reproductive toxicity was 50 ppm on the basis of decreased body weights of male pups at postnatal day 21 at 500 ppm.

In two studies of prenatal developmental toxicity in rats given atrazine on days 6–15 of gestation, the NOAELs for maternal toxicity were 10 or 25 mg/kg bw per day on the basis of decreased body-weight gain and food intake at 70 or 100 mg/kg bw per day, respectively. The NOAELs for developmental toxicity were 10 or 25 mg/kg bw per day on the basis of incomplete ossification at several sites at 70 or 100 mg/kg bw per day, respectively. In a study of prenatal developmental toxicity in rabbits given atrazine on days 7–19 gestation, the NOAEL for maternal toxicity was 5 mg/kg bw per day on the basis of clinical signs, abortion and decreased food intake and body-weight gain at 75 mg/kg bw per day. The NOAEL for developmental toxicity was 5 mg/kg bw per day on the basis of increased resorptions, reduced litter size and incomplete ossification at 75 mg/kg bw per day. In rats and rabbits, the developmental effects were observed only at maternally toxic doses.

The Meeting concluded that atrazine was not teratogenic.

Studies using a variety of test systems in vitro and in vivo indicated that modulation of the immune system occurs after exposure to atrazine. However, effects suggestive of impaired function of the immune system were only observed at doses greater than those shown to affect neuroendocrine function, leading to disruption of the oestrous cycle or developmental effects.

A range of epidemiological studies (including cohort studies, case–control studies, and ecological or correlational studies) assessed possible relationships between atrazine or other triazine herbicides and cancer in humans. For some cancer types, such as prostate or ovarian cancer and non-Hodgkin lymphoma, the increased risks reported in single studies could either be explained by the methodology used or had not been confirmed in more reliable studies. Thus, the weight of evidence from the epidemiological studies did not support a causal association between exposure to atrazine and the occurrence of cancer in humans.

The Meeting concluded that the existing database on atrazine is adequate to characterize the potential hazards to foetuses, infants and children.

Metabolites of atrazine

The toxicity profiles and mode of action of the chloro-*s*-triazine metabolites were similar to those of atrazine; the potency of these metabolites appeared to be similar to that of the parent compound with regard to their neuroendocrine-disrupting properties.

Like atrazine, the chloro-*s*-triazine metabolites were of moderate or low acute oral toxicity in rats; LD_{50}s were 1110, 1240 and 2310–5460 mg/kg bw for DEA, DIA and DACT, respectively.

Like atrazine, its chloro-*s*-triazine metabolites delayed sexual development of male rats exposed on postnatal days 23–53 at atrazine molar equivalent doses of ≥ 25 (DEA, DIA) and ≥ 12.5 mg/kg bw per day (DACT), with NOAELs of 12.5 and 6.25 mg/kg bw per day, respectively. Exposure of female rats to DACT on postnatal days 22–41 delayed sexual development at atrazine molar equivalent doses of ≥ 50 mg/kg bw per day, and the NOAEL was 25 mg/kg bw per day. Doses at which these effects occurred were similar to those observed for parent atrazine.

In short-term feeding studies in rats, the main effects of the chlorinated metabolites were similar to those of atrazine and included reduced body-weight gain and decreased erythrocyte parameters, and also for DACT-induced disruption of the oestrous cycle. The NOAELs were 50 ppm (equal to 3.2 mg/kg bw per day) for DEA and DIA, and 100 ppm (equal to 7.6 mg/kg bw per day) for DACT.

In a 29/52-week study with DACT in Sprague-Dawley rats, effects comparable to those observed with atrazine (attenuation of the LH surge, increased incidences of mammary tumours) were

seen at 270 ppm; the NOAEL was 48 ppm, equal to 3.4 mg/kg bw per day. No long-term studies were performed with DEA or DIA.

In short-term feeding studies in dogs, the main effects of the chlorinated metabolites were similar to those of atrazine and included reduced body-weight gain and decreased erythrocyte parameters, while DEA and DACT showed cardiac toxicity. The NOAELs were 100 ppm, equal to 3.7, 3.8 and 3.5 mg/kg bw per day, for DEA, DIA and DACT, respectively.

DEA, DIA and DACT did not show genotoxicity in an adequate range of tests in vitro and in vivo.

In studies of prenatal developmental toxicity in rats, the chlorinated metabolites induced increased incidences of fused sternebrae and/or incomplete ossification at doses of 25 to 100 mg/kg bw per day; the NOAELs for developmental toxicity were 25, 5 and 2.5 mg/kg bw per day for DEA, DIA and DACT, respectively. The effects were seen only at doses that also produced maternal toxicity.

The metabolite hydroxyatrazine does not have the same mode of action or toxicity profile as atrazine and its chlorometabolites. The main effect of hydroxyatrazine was kidney toxicity (owing to its low solubility in water, resulting in crystal formation and a subsequent inflammatory response), and there was no evidence that hydroxyatrazine has neuroendocrine-disrupting properties. Also, the acute oral toxicity of hydroxyatrazine in rats (LD_{50}, > 5050 mg/kg bw) was lower than that of atrazine or its chlorometabolites.

In short-term feeding studies, the main effects of hydroxyatrazine in rats included reduced body-weight gain, increased water consumption, changes in clinical chemistry and urine analysis parameters, and kidney lesions. The overall NOAEL was 100 ppm, equal to 6.3 mg/kg bw per day. In dogs, effects included reduced body-weight gain and food consumption, changes in clinical chemistry and urine analysis parameters, and kidney lesions; the NOAEL was 150 ppm, equal to 5.8 mg/kg bw per day.

In a 2-year study of toxicity and carcinogenicity in rats, the effects of hydroxyatrazine included clinical signs and increased mortality, reduced body-weight gain and food consumption, increased water consumption, changes in haematological, clinical chemistry and urine analysis parameters, and kidney lesions. The NOAEL was 25 ppm, equal to 1.0 mg/kg bw per day. There was no evidence of carcinogenicity.

Hydroxyatrazine did not show genotoxicity in an adequate range of tests in vitro and in vivo.

In a study of prenatal developmental toxicity in rats, the effects of hydroxyatrazine consisted of reduced food consumption and body-weight gain in dams and increased incidences of incomplete and absent ossification in foetuses at 125 mg/kg bw per day; the NOAEL was 25 mg/kg bw per day for maternal and developmental toxicity. Exposure of female rats on postnatal days 22–41 at atrazine molar equivalent doses of up to 200 mg/kg bw per day did not delay sexual development.

Toxicological evaluation

Drinking-water may contain metabolites of atrazine as well as atrazine itself. The chloro-*s*-triazine metabolites DEA, DIA and DACT share the same mode of action as atrazine and have a similar toxicological profile and hence the Meeting decided to establish a group ADI and ARfD. Hydroxyatrazine, the plant and soil degradate, was not included because its mode of action and toxicological profile are different to those of atrazine and its chloro-*s*-triazine metabolites.

The Meeting established a group ADI of 0–0.02 mg/kg bw based on the NOAEL for atrazine of 1.8 mg/kg bw per day identified on the basis of LH surge suppression and subsequent disruption of the oestrous cycle seen at 3.6 mg/kg bw per day in a 6-month study in rats, and using a safety factor of 100. The Meeting considered that this NOAEL is protective for the consequences of

neuroendocrine and other adverse effects caused by prolonged exposure to atrazine and its chloro-*s*-triazine metabolites.

The Meeting established a group ARfD of 0.1 mg/kg bw based on the NOAEL for atrazine of 12.5 mg/kg bw per day identified on the basis of impaired suckling-induced prolactin secretion in dams and subsequent alterations in development of the central nervous system and prolactin regulation in male offspring in a special 4-day study in rats, and using a safety factor of 100. This ARfD was supported by the results of other studies of developmental toxicity with atrazine and its chlorometabolites, from which overall NOAELs/LOAELs of 25/50 mg/kg bw per day in rats and 5/75 mg/kg bw per day in rabbits were identified on the basis of effects that might occur after a single exposure (i.e., post-implantation loss, fused sternebrae). The study in rabbits (in which there was a 15-fold difference between NOAEL and LOAEL) was not selected as the basis for the ARfD, because examination of the studies in rats indicated that the dose selected for the ARfD would be adequately protective for these end-points in rabbits.

For hydroxyatrazine, the Meeting established an ADI of 0–0.04 mg/kg bw based on the NOAEL of 1.0 mg/kg bw per day identified on the basis of kidney toxicity (caused by low solubility in water resulting in crystal formation and a subsequent inflammatory response) at 7.8 mg/kg bw per day in a 24-month study in rats, and using safety factor of 25. A modified safety factor based on kinetic considerations was deemed appropriate since the critical effect of hydroxyatrazine is dependent on its physicochemical properties and the interspecies variability for such effects is lower than for AUC-dependent effects.

The Meeting concluded that it was not necessary to establish an ARfD for hydroxyatrazine in view of its low acute toxicity, the absence of relevant developmental toxicity that could be a consequence of acute exposure, and the absence of any other toxicological effects that would be likely to be elicited by a single dose.

A toxicological monograph was prepared.

Levels relevant to risk assessment

(a) Atrazine

Species	Study	Effect	NOAEL	LOAEL
Mouse	Long-term studies of carcinogenicity[a,d]	Toxicity	10 ppm, equal to 1.2 mg/kg bw per day	300 ppm, equal to 38.4 mg/kg bw per day
		Carcinogenicity	3000 ppm, equal to 385.7 mg/kg bw per day[c]	—
Rat	Thirteen-week study of toxicity[a]	Toxicity	50 ppm, equal to 3.3 mg/kg bw per day	500 ppm, equal to 34.0 mg/kg bw per day
	Two-year studies of toxicity and carcinogenicity[a,d] (Sprague-Dawley rats)	Toxicity	70 ppm, equal to 2.6 mg/kg bw per day	500 ppm, equal to 19.9 mg/kg bw per day
		Carcinogenicity	25 ppm, equal to 1.5 mg/kg bw per day	50 ppm, equal to 3.1 mg/kg bw per day[e]
	Two-year studies of toxicity and carcinogenicity[a,d] (Fischer 344 rats)	Toxicity	70 ppm, equal to 3.5 mg/kg bw per day	200 ppm, equal to 10 mg/kg bw per day
		Carcinogenicity	400 ppm, equal to 20 mg/kg bw per day[c]	—
	Multigeneration study of reproductive toxicity[a]	Fertility	500 ppm, equal to 36.1 mg/kg bw per day[c]	—

Species	Study	Effect	NOAEL	LOAEL
		Parental toxicity	50 ppm, equal to 3.6 mg/kg bw per day	500 ppm, equal to 36.1 mg/kg bw per day
		Offspring toxicity	50 ppm, equal to 3.6 mg/kg bw per day	500 ppm, equal to 36.1 mg/kg bw per day
	Developmental toxicity[b,d]	Maternal toxicity	10 mg/kg bw per day	70 mg/kg bw per day
		Embryo/fetotoxicity	10 mg/kg bw per day	70 mg/kg bw per day
	Special 6-month study[a]	Endocrine disruption (luteinizing hormone surge)	25 ppm, equal to 1.8 mg/kg bw per day	50 ppm, equal to 3.65 mg/kg bw per day
	Special 4-day study[b]	Endocrine disruption (prolactin release)	12.5 mg/kg bw per day	25 mg/kg bw per day
	Special 5-day study[b]	Post-implantation loss	25 mg/kg bw per day	50 mg/kg bw per day
	Special 25-day study[b]	Female pubertal delay	10 mg/kg bw per day	30 mg/kg bw per day
	Special 30-day study[b]	Male pubertal delay	6.25 mg/kg bw per day	12.5 mg/kg bw per day
Rabbit	Developmental toxicity[b]	Maternal toxicity	5 mg/kg bw per day	75 mg/kg bw per day
		Embryo/fetotoxicity	5 mg/kg bw per day	75 mg/kg bw per day
Dog	One-year study of toxicity[a]	Toxicity	150 ppm, equal to 5 mg/kg bw per day	1000 ppm, equal to 33.7 mg/kg bw per day

[a] Dietary administration.

[b] Gavage administration.

[c] Highest dose tested.

[d] Results of two or more studies combined.

[e] Mammary gland tumours—not relevant to humans.

(b) Deethyl-atrazine (DEA)

Species	Study	Effect	NOAEL	LOAEL
Rat	Thirteen-week study of toxicity[a]	Toxicity	50 ppm, equal to 3.2 mg/kg bw per day	500 ppm, equal to 35.2 mg/kg bw per day
	Developmental toxicity[b]	Maternal toxicity	5 mg/kg bw per day	25 mg/kg bw per day
		Embryo- and fetotoxicity	25 mg/kg bw per day	100 mg/kg bw per day
	Special 30-day study[b]	Male pubertal delay	12.5 mg/kg bw per day[c]	25 mg/kg bw per day[c]
Dog	Thirteen-week study of toxicity[a]	Toxicity	100 ppm, equal to 3.7 mg/kg bw per day	1000 ppm, equal to 28.9 mg/kg bw per day

[a] Dietary administration.

[b] Gavage administration.

[c] Atrazine molar equivalent dose.

(c) Deisopropyl-atrazine (DIA)

Species	Study	Effect	NOAEL	LOAEL
Rat	Thirteen-week study of toxicity[a]	Toxicity	50 ppm, equal to 3.2 mg/kg bw per day	500 ppm, equal to 34.9 mg/kg bw per day
	Developmental toxicity[b]	Maternal toxicity	5 mg/kg bw per day	25 mg/kg bw per day

		Embryo/fetotoxicity	5 mg/kg bw per day	25 mg/kg bw per day
	Special 30-day study[b]	Male pubertal delay	12.5 mg/kg bw per day[c]	25 mg/kg bw per day[c]
Dog	Thirteen-week study of toxicity[a]	Toxicity	100 ppm, equal to 3.8 mg/kg bw per day	500 ppm, equal to 18.0 mg/kg bw per day

[a] Dietary administration.

[b] Gavage administration.

[c] Atrazine molar equivalent dose.

(d) Diaminochlorotriazine (DACT)

Species	Study	Effect	NOAEL	LOAEL
Rat	Thirteen-week study of toxicity[a]	Endocrine disruption (oestrous cycle)	100 ppm, equal to 7.6 mg/kg bw per day	250 ppm, equal to 19.7 mg/kg bw per day
	Developmental toxicity[b]	Maternal toxicity	2.5 mg/kg bw per day	25 mg/kg bw per day
		Embryo/fetotoxicity	2.5 mg/kg bw per day	25 mg/kg bw per day
	Special study, 29/52-weeks[a]	Endocrine disruption (LH surge)	48 ppm, equal to 3.4 mg/kg bw per day	270 ppm, equal to 18.8 mg/kg bw per day
	Special 19-day study[b]	Female pubertal delay	25 mg/kg bw per day[c]	50 mg/kg bw per day[c]
	Special 30-day study[b]	Male pubertal delay	6.25 mg/kg bw per day[c]	12.5 mg/kg bw per day[c]
Dog	Thirteen-/52-week study of toxicity[a]	Toxicity	100 ppm, equal to 3.5 mg/kg bw per day	1500/750 ppm, equal to 23.8 mg/kg bw per day

[a] Dietary administration.

[b] Gavage administration.

[c] Atrazine molar equivalent dose.

(e) Hydroxyatrazine

Species	Study	Effect	NOAEL	LOAEL
Rat	Thirteen-week study of toxicity[a]	Toxicity	100 ppm, equal to 6.3 mg/kg bw per day	300 ppm, equal to 18.9 mg/kg bw per day
	Two-year study of toxicity and carcinogenicity[a] (Sprague-Dawley rats)	Toxicity	25 ppm, equal to 1.0 mg/kg bw per day	200 ppm, equal to 7.8 mg/kg bw per day
		Carcinogenicity	400 ppm, equal to 17.4 mg/kg bw per day[c]	—
	Developmental toxicity[b]	Maternal toxicity	25 mg/kg bw per day	125 mg/kg bw per day
		Embryo/fetotoxicity	25 mg/kg bw per day	125 mg/kg bw per day
	Special 19-day study[b]	Female pubertal delay	200 mg/kg bw per day[c,d]	—
Dog	Thirteen-/52-week study of toxicity[a]	Toxicity	150 ppm, equal to 5.8 mg/kg bw per day	1500 ppm, equal to 59.6 mg/kg bw per day

[a] Dietary administration.

[b] Gavage administration.

[c] Highest dose tested.

[d] Atrazine molar equivalent dose.

Estimate of acceptable daily intake for humans

Group ADI for atrazine, deethyl-atrazine, deisopropyl-atrazine and diaminochlorotriazine
0–0.02 mg/kg bw
Hydroxyatrazine
0–0.04 mg/kg bw

Estimate of acute reference dose

Group ARfD for atrazine, deethyl-atrazine, deisopropyl-atrazine and diaminochlorotriazine

0.1 mg/kg bw

Hydroxyatrazine

Unnecessary

Information that would be useful for the continued evaluation of the compound

Results from epidemiological, occupational health and other such observational studies of human exposures

Critical end-points for setting guidance values for exposure to atrazine

Absorption, distribution, excretion and metabolism in animals	
Rate and extent of oral absorption	Rapid, > 80% in rats
Distribution	Widely distributed
Rate and extent of excretion	> 50% in 24 h and > 93% within 7 days; approximately 73% via urine, approximately 20% via faeces (approximately 7% via bile)
Potential for accumulation	Low; binding to rat haemoglobin, not relevant to humans
Metabolism in mammals	Extensive (> 95%) to at least 25 metabolites; major pathway is *N*-dealkylation
Toxicologically significant compounds in animals, plants and the environment	Parent compound, chloro-s-triazine metabolites DEA, DIA, DACT (animals, environment), hydroxyatrazine (plants, environment)
Acute toxicity	
Rat, LD_{50}, oral	1870–3090 mg/kg bw
Rat, LD_{50}, dermal	> 2000 mg/kg bw
Rat, $LC_{50,}$ inhalation	> 5.8 mg/L
Rabbit, skin irritation	Not an irritant
Rabbit, eye irritation	Not an irritant
Guinea-pig, skin sensitization	Sensitizer (Magnusson & Kligman; Maurer optimization test)
Short-term studies of toxicity	
Target/critical effect	Reduced body-weight gain, ovaries (inhibition of ovulation), cardiotoxicity (in dogs only)
Lowest relevant oral NOAEL	3.3 mg/kg bw per day (90-day study in rats)
Lowest relevant dermal NOAEL	100 mg/kg bw per day (25-day study in rabbits)

Lowest relevant inhalation NOAEC	No data
Genotoxicity	
	Unlikely to be genotoxic in vivo
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	Ovaries (inhibition of ovulation) and related endocrine changes
Lowest relevant NOAEL	1.8 mg/kg bw per day (6-month luteinizing-hormone surge study in Sprague-Dawley rats)
Carcinogenicity	No relevant carcinogenicity
Reproductive toxicity	
Reproductive target/critical effect	Reduced body weight gain in pups at parentally toxic doses
Lowest relevant reproductive NOAEL	3.6 mg/kg bw per day
Developmental target/critical effect	Increased resorptions and incomplete ossification at maternally toxic doses; delayed sexual development
Lowest relevant developmental NOAEL	6.25 mg/kg bw per day (rat; male pubertal development)
	5 mg/kg bw per day (rabbit)
Neurotoxicity	
	No evidence of neurotoxicity in standard toxicity tests; however, neuroendocrine mode of action has been established for atrazine and its chloro-s-triazine metabolites
Other toxicological studies	
Studies on metabolites	DEA, DIA, DACT have the same neuroendocrine mode of action and similar potency to atrazine
	Hydroxyatrazine has a different mode of action and toxicity profile to atrazine
Mode of neuroendocrine action	Atrazine and its chlorometabolites modify hypothalamic catecholamine function and gonadotrophin-releasing hormone (GnRH) regulation, leading to alterations in pituitary luteinizing hormone (LH) and prolactin secretion
Mode of carcinogenic action	The postulated mode of carcinogenic action in female Sprague-Dawley rats involves acceleration of the reproductive ageing process (suppression of LH surge, subsequent oestrous cycle disruption), which is not relevant to humans
Direct estrogenic activity	Atrazine has no intrinsic estrogenic activity
Aromatase expression	No effect on aromatase expression in rats
Effects on sexual development	Evidence of delayed sexual development in male and/or female rats by atrazine, DEA, DIA and DACT
Effects on neuronal development	Evidence of impaired post-natal CNS development (and subsequent alterations in prolactin regulation)
Immunotoxicity	Evidence for immune system modulation at doses above LOAELs for neuroendocrine disruption or reproductive and developmental effects
Medical data	
	No evidence of atrazine causing effects in manufacturing plant

		personnel. Epidemiology studies do not support a causal association between exposure to atrazine and cancer in humans.	
Summary			
Atrazine			
	Value	**Study**	**Safety factor**
Group ADI[a]	0–0.02 mg/kg bw	Sprague-Dawleys rat; 6-month study of LH surge/oestrous cycle disruption	100
Group ARfD[a]	0.1 mg/kg bw	Rat; special 4-day study of prolactin release, supported by studies of developmental toxicity in rats and rabbits	100
Hydroxyatrazine			
ADI	0–0.04 mg/kg bw	Sprague-Dawley rats; 2-year study	25
ARfD	Unnecessary	—	—

[a] Group ADI or ARfD for atrazine, deethyl-atrazine (DEA), deisopropyl-atrazine (DIA) and diaminochlorotriazine (DACT)

5.3 AZINPHOS METHYL (002)

TOXICOLOGY

Azinphos-methyl is the ISO approved common name for *S*-3,4-dihydro-4-oxo-1,2,3-benzotriazin-3-ylmethyl *O*,*O*-dimethyl phosphorodithioate (IUPAC) or *O*,*O*-dimethyl *S*-[(4-oxo-1,2,3-benzotriazin-3(4*H*)-yl)methyl] phosphorodithioate (CAS; CAS No. 86-50-0). It is a broad-spectrum organophosphorus pesticide. Its toxicity was first evaluated by the 1965 JMPR, when an ADI of 0–0.0025 mg/kg bw was established based on a NOAEL of 0.25 mg/kg bw per day for inhibition of cholinesterase activity in serum and erythrocytes in a repeat-dose study in rats. The 1968 JMPR considered a number of additional studies that were not available to the Meeting in 1965. The ADI established in 1965 was confirmed. The 1973 JMPR considered new studies that involved human volunteers but, owing to the absence of sufficient information on the conduct of these studies in humans, the existing ADI was re-affirmed. In 1991, the ADI was increased to 0–0.005 mg/kg bw on the basis of reduced body-weight gain and fertility observed in the multigeneration study in rats. Azinphos-methyl was reviewed by the present Meeting within the Periodic Re-evaluation Programme of the CCPR. All studies previously submitted to JMPR were available for consideration by the present Meeting. Several new studies, including two double-blind clinical studies in human volunteers, were also considered by the present Meeting.

Most studies, excluding some described in previous JMPR monographs, were certified as having been performed in compliance with good laboratory practice (GLP) and in accordance with the relevant Organization for Economic Co-operation and Development (OECD) test guidelines. The studies in humans were conducted in accordance with the principles of good clinical practice and the Declaration of Helsinki, or equivalent statements prepared for use by national and/or multinational authorities.

Biochemical aspects

After oral administration of radiolabelled azinphos-methyl, the radiolabel was rapidly and completely (90–100% of the administered dose) absorbed from the mammalian intestinal tract, widely distributed throughout the organs, and eliminated in the urine (60–70% of the administered dose) and faeces via bile (25–35% of the administered dose) within 48 h. The maximum concentration in blood was reached within 2–3 h after administration. Azinphos-methyl was rapidly cleared from the blood and tissues, and consequently there is negligible potential for accumulation. In rats, the initial steps of metabolism involved the formation of the highly reactive oxon metabolite and mercaptomethylbenzazimide by cytochrome P450. Glutathionyl methylbenzazimide and desmethyl isoazinphos-methyl were formed via glutathione transferase. Subsequent hydrolysis of glutathionyl methyl-benzazimide resulted in the formation of cysteinyl-methylbenzazimide, which was then oxidized to form its corresponding sulfoxide and sulfone.

Toxicological data

Azinphos-methyl was highly acutely toxic (LD_{50} range, 4.4–26 mg/kg bw) when administered orally in an aqueous or non-aqueous vehicle to rats, and its profile of clinical signs was similar to those of other cholinesterase-inhibiting organophosphorus pesticides. Clinical signs observed in experimental animals after acute exposure were salivation, lacrimation, vomiting, diarrhoea, anorexia, reduced locomotor activity, piloerection, staggering gait and muscular tremors. These signs were generally evident within 5–20 min after dosing. There was very little difference in the sensitivity of male and female rats to the acute effects of azinphos-methyl.

The main toxicological findings in repeat-dose studies in rodents and dogs were inhibition of cholinesterase activity and, at higher doses, reduced body-weight gain and signs of neurotoxicity. In short-term studies of toxicity of less than 12 months duration, the NOAEL for inhibition of erythrocyte acetylcholinesterase activity was 0.2 mg/kg bw per day in rats and dogs. The NOAEL for inhibition of brain cholinesterase activity was 0.9 mg/kg bw per day in rats, and 0.7 mg/kg bw per day in dogs. Toxicity observed in rats and dogs was limited to the characteristic muscarinic signs (diarrhoea, salivation) and reduced body-weight gain. The effect doses for these clinical signs in short-term studies correlated with the high levels of inhibition of brain cholinesterase activity (> 80%) in rats and dogs.

Azinphos-methyl was tested in an adequate range of studies of genotoxicity in vitro and in vivo and showed no evidence of genotoxicity. The Meeting concluded that azinphos-methyl is unlikely to be genotoxic.

In long-term studies of toxicity, inhibition of cholinesterase activity was again the main toxicological finding in mice and rats. In mice, erythrocyte and brain cholinesterase activities were inhibited at 3.8 mg/kg bw per day, with a NOAEL of 0.9 mg/kg bw per day. Reduced body-weight gain and clinical signs involving hyperactivity and convulsions were observed in mice at higher doses (6.25 mg/kg bw per day). At equivalent doses in rats, body tremors and deaths were reported, although reduced body-weight gain was observed at 2.7 mg/kg bw per day. In rats, the NOAEL for inhibition of erythrocyte acetylcholinesterase activity was 0.3 mg/kg bw per day, while for brain cholinesterase activity it was 0.9 mg/kg bw per day and the NOAEL for a reduction in body-weight gain was 0.9 mg/kg bw per day. There was no evidence of carcinogenicity with azinphos-methyl at dietary concentrations of up to 40 ppm (equal to 12.8 mg/kg bw per day) in mice and up to 45 ppm (equal to 2.7 mg/kg bw per day) in rats; these were the highest doses tested.

In the absence of any carcinogenic potential in rodents and the lack of genotoxic potential in vitro and in vivo, the Meeting concluded that azinphos-methyl is unlikely to pose a carcinogenic risk to humans.

In multigeneration studies of reproductive toxicity in rats, the treatment-related effects of azinphos-methyl were cholinergic signs at high doses, reductions in body-weight gain and inhibition

of cholinesterase activity. These effects were consistent with those seen in short- and long-term studies of toxicity. However, there was also evidence of reduced pup viability at 4.8 mg/kg bw per day. The NOAEL for inhibition of brain cholinesterase activity in dams was 5 ppm, equal to 0.5 mg/kg bw per day. The NOAEL for inhibition of brain cholinesterase activity in pups was 15 ppm, equal to 1.5 mg/kg bw per day.

In studies of developmental toxicity with azinphos-methyl in mice, rats and rabbits, teratogenicity was not observed at doses of up to 2, 3.6 and 15 mg/kg bw per day respectively. The only developmental effect noted in any of these studies was delayed ossification in rat and rabbit foetuses at doses that also caused inhibition of brain and erythrocyte cholinesterase activity in the dams. The NOAEL for developmental effects in foetuses was 2 mg/kg bw per day in rats and 1.5 mg/kg bw per day in rabbits. Inhibition of brain cholinesterase activity was not observed in rats at doses of 1 mg/kg bw per day or in rabbits at doses of 2.5 mg/kg bw per day.

In studies of delayed neurotoxicity, azinphos-methyl was administered to chickens either as a single dose at up to 330 mg/kg bw or as repeated doses of up to 225 mg/kg bw per day in the feed for 30 days; there was no evidence of delayed neuropathy.

In rats given azinphos-methyl as a single dose at up to 12 mg/kg bw by gavage or as repeated doses of up to 7.4 mg/kg bw per day in the diet for 13 weeks, cholinergic signs and significant inhibition of erythrocyte and brain cholinesterase activity were seen at a number of doses. In these studies, which included a functional observational battery (FOB) of tests, clinical signs of intoxication (perianal stain, red lacrimation, increased reactivity, uncoordinated gait, tremor) were observed. However, cholinergic signs were observed only when brain cholinesterase activity was inhibited by more than 70% or when erythrocyte acetylcholinesterase activity was inhibited by approximately 65–80%. This occurred after repeated doses in excess of 3.2 mg/kg bw per day or after a single dose of 6 mg/kg bw. The NOAEL for inhibition of cholinesterase activity in the brain after a single dose was 2 mg/kg bw or 1 mg/kg bw per day after repeat dosing.

In a randomized double-blind study in human volunteers (seven of each sex) given ascending single oral doses, azinphos-methyl did not induce cholinergic signs or changes in acetylcholinesterase activity in erythrocytes at doses of up to 1 mg/kg bw in males and up to 0.75 mg/kg bw in females; these were the highest doses tested.

When eight male volunteers were given azinphos-methyl as a daily oral dose at 0.25 mg/kg bw per day for 28 days, there were no cholinergic signs and erythrocyte acetylcholinesterase activity was not significantly inhibited. In another study, two groups of five male volunteers were given azinphos-methyl at a dose of 0.26 or 0.29 mg/kg bw per day for 30 days did not induce cholinergic signs or changes in cholinesterase activity in erythrocytes or plasma. In a third study, a similar outcome was reported when two male volunteers were given azinphos-methyl orally at a dose of 0.23 mg/kg bw per day for 30 days.

Regular medical examinations of workers involved in formulating products containing azinphos-methyl had revealed no effects, except for one case of possible dermatosis resulting in sensitive dry skin.

The Meeting concluded that the existing database on azinphos-methyl was adequate to characterize the potential hazards to foetuses, infants, and children.

Toxicological evaluation

The Meeting established an ADI of 0–0.03 mg/kg bw per day based on a NOAEL of 0.29 mg/kg bw per day for the absence of inhibition of erythrocyte acetylcholinesterase activity in a 30-day study of toxicity in male volunteers and a safety factor of 10. Since the database indicated that rodents and dogs of each sex and humans had similar NOAEL values for the most sensitive end-point, namely inhibition of acetylcholinesterase activity in erythrocytes, the NOAELs identified in the studies in humans were considered to be protective for the entire population. The Meeting also considered the

ADI to be protective for other, non-neurotoxic effects of azinphos-methyl observed in short- and long-term studies with repeated doses, and in studies of reproductive and developmental toxicity, where the use of a safety factor of 100 would be appropriate. The effect of azinphos-methyl on body-weight gain and fertility in dams at 15 ppm (0.5 mg/kg bw per day) in multigeneration studies of reproduction in rats was reconsidered. The Meeting concluded that it was a marginal effect that could not be directly attributed to treatment.

The Meeting established an ARfD of 0.1 mg/kg bw based on the NOAEL of 1 mg/kg bw and using a safety factor of 10. The NOAEL observed in a study of single doses in volunteers was the highest tested dose in males. Although the maximum dose given to females was only 0.75 mg/kg bw, there was no apparent observed difference in sensitivity between the sexes, so the NOAEL observed in males was also considered to be protective of effects in females. In a study of acute neurotoxicity in rats, the NOAEL was 2 mg/kg bw on the basis of inhibition of cholinesterase activity in the brain. At a dose of 2 mg/kg bw, significant inhibition of acetylcholinesterase activity in erythrocytes of male rats was observed, but not at 1 mg/kg bw in female rats. In rats, pup deaths as a result of inhibition of cholinesterase activity were observed at 6 mg/kg bw in females and at 12 mg/kg bw in males, suggesting a steep dose–response effect. Based on the median oral LD_{50} value of 13 mg/kg bw (range, 4.4–26 mg/kg bw) in all available studies in rats, there would be about a 130-fold margin between the ARfD and the LD_{50} in rats.

A toxicological monograph was prepared.

Levels relevant for risk assessment

Species	Study	Effect	NOAEL	LOAEL
Rat	Acute neurotoxicity[a]	Inhibition of brain cholinesterase activity	2.0 mg/kg bw	3.0 mg/kg bw
Human	Single dose[b,d]	No adverse effects	1.0 mg/kg bw per day	—
Mouse	Two-year study of toxicity and carcinogenicity[c]	Inhibition of erythrocyte and brain cholinesterase activity	5 ppm, equal to 0.9 mg/kg bw per day	20 ppm, equal to 3.8 mg/kg bw per day
		Carcinogenicity[d]	40 ppm, equal to 12.8 mg/kg bw per day	—
Rat	Three-month study of toxicity[c]	Inhibition of brain cholinesterase activity	0.9 mg/kg bw per day	3.4 mg/kg bw per day
	Two-year study of toxicity and carcinogenicity[c]	Reduced body-weight gain and inhibition of brain cholinesterase activity	15 ppm, equal to 0.9 mg/kg bw per day	45 ppm, equal to 2.7 mg/kg bw per day
		Carcinogenicity[d]	45 ppm, equal to 2.7 mg/kg bw per day	—
	Multigeneration study of reproductive toxicity[c,e]	Parental toxicity	5 ppm, equal to 0.5 mg/kg bw per day	15 ppm, equal to 1.5 mg/kg bw per day
		Offspring toxicity	15 ppm, equal to 1.5 mg/kg bw per day	45 ppm equal to 4.8 mg/kg bw per day
	Developmental toxicity[a,e]	Maternal toxicity	1.0 mg/kg bw per day	2.0 mg/kg bw per day

Species	Study	Effect	NOAEL	LOAEL
		Embryo/fetotoxicity	2.0 mg/kg bw per day	3.6 mg/kg bw per day
	Three-month study of neurotoxicity[c]	Inhibition of brain cholinesterase activity	15 ppm, equal to 1 mg/kg bw per day	45 ppm, equal to 3 mg/kg bw per day
Rabbit	Developmental toxicity[b,c]	Maternal toxicity	2.5 mg/kg bw per day	6.0 mg/kg bw per day
		Embryo/fetotoxicity	1.5 mg/kg bw per day	4.75 mg/kg bw per day
Dog	One-year study of toxicity[a]	Reduced body-weight gain and inhibition of brain cholinesterase activity	25 ppm, equal to 0.7 mg/kg bw per day	125 ppm, equal to 4.1 mg/kg bw per day
Human	Clinical 30-day study[b,d,e]	No adverse effects	0.29 mg/kg bw per day	—

[a] Gavage administration.

[b] Capsule administration.

[c] Dietary administration.

[d] Highest tested dose.

[e] Two or more studies combined

Estimate of acceptable daily intake for humans

0–0.03 mg/kg bw

Estimate of acute reference dose

0.1 mg/kg bw

Information that would be useful for the continued evaluation of the compound

Results from epidemiological, occupational health and other such observational studies of human exposures

Critical end-points for setting guidance values of exposure for azinphos-methyl

Absorption, distribution, excretion and metabolism in mammals	
Rate and extent of oral absorption	Almost complete absorption. Maximum plasma concentration 2–3 h after dosing.
Dermal absorption	See previous azinphos-methyl monographs
Distribution	Extensive
Potential for accumulation	Low, no evidence of accumulation
Rate and extent of excretion	Largely complete within 48 h; approximately 95% excreted in urine and bile.
Metabolism in animals	Extensive; two major urinary metabolites and six other products. Five faecal metabolites (10–12% of the administered dose).
Toxicologically significant compounds in	Azinphos methyl, azinphos-methyl oxon

animals, plants and the environment	
Acute toxicity	
Rat, LD_{50}, oral	4.4–26 mg/kg bw
Rat, LD_{50}, dermal	See previous azinphos-methyl monographs
Rat, LC_{50}, inhalation	See previous azinphos-methyl monographs
Skin sensitization (test method used)	See previous azinphos-methyl monographs
Short-term studies of toxicity	
Target/critical effect	Inhibition of brain cholinesterase activity
Lowest relevant oral NOAEL	0.7 mg/kg bw per day (dog)
Lowest relevant dermal NOAEL	See previous azinphos-methyl monographs
Lowest relevant inhalation NOAEC	See previous azinphos-methyl monographs
Genotoxicity	
	Unlikely to pose a genotoxic risk in vivo
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	Inhibition of brain cholinesterase activity
Lowest relevant NOAEL	0.9 mg/kg bw per day (rat)
Carcinogenicity	Not carcinogenic in rats and mice
Reproductive toxicity	
Reproduction target/critical effect	Inhibition of brain cholinesterase activity in dams
Lowest relevant reproductive NOAEL	0.5 mg/kg bw per day (rats)
Developmental target/critical effect	Delayed ossification at maternally toxic doses (rats, rabbits)
Lowest relevant developmental NOAEL	1.0 mg/kg bw per day (rats); 2.5 mg/kg bw per day (rabbits)
Neurotoxicity/delayed neurotoxicity	No evidence of delayed neuropathy observed in hens
	NOAEL: 1 mg/kg bw in a repeat-dose study of neurotoxicity in rats
Medical data	
	Medical examinations of workers involved in formulating azinphos-methyl products revealed no effects, except for one case of possible dermatosis resulting in sensitive dry skin.

Summary

	Value	Study	Safety factor
ADI	0–0.03 mg/kg bw per day	Humans, 30-day oral-dosing study	10
ARfD	0.1 mg/kg bw	Humans, study of acute toxicity	10

5.4 CAPTAN (007)

TOXICOLOGY

Evaluation for an acute reference dose

Captan, the ISO approved name for *N*-(trichloromethylthio)cyclohex-4-ene-1,2-dicarboximide, is a fungicide (CAS No. 133-06-2) registered for the control of fungal diseases in crops. The toxicology of captan was evaluated by the JMPR in 1963, 1965, 1969, 1973, 1978, 1982, 1984, 1990, 1995 and 2004. Toxicological monographs were prepared by the Meeting in 1963, 1965 and 1969, and monograph addenda were prepared in 1973, 1977, 1978, 1982, 1984, 1990, 1995 and 2004. In 1984, an ADI of 0–0.1 mg/kg bw was established based on a NOAEL of 12.5 mg/kg bw per day in studies of reproductive toxicity in rats and monkeys. This ADI was confirmed by JMPR in 1995. In 2004, the Meeting established an ARfD of 0.3 mg/kg bw, for women of childbearing age only, based on a NOAEL of 30 mg/kg bw per day for increased incidences of intrauterine deaths and malformations at 100 mg/kg bw per day in the study in rabbits and a safety factor of 100.

The Meeting concluded that the database was insufficient, particularly with regard to information about the possible developmental effects of the metabolite 1,2,3,6-tetrahydrophthalimide (THPI), to establish the mode of action by which the increased incidences of intrauterine deaths and foetuses with malformations were induced.

The sponsor conducted a study of developmental toxicity with THPI, and studies to evaluate the potential effects of captan and THPI on the intestinal flora of the rabbit. It was known that the rabbit is dependent on the presence of caecotrophs for adequate nutrition. The sponsor suggested that disruption of the intestinal flora might result in maternal malnutrition, with possible consequent adverse effects on foetal development.

At the request of the CCPR at its 39th Session,[22] the present Meeting reconsidered the ARfD on the basis of new data.

All pivotal studies with captan and THPI were certified as being compliant with GLP

Toxicological data

Data previously evaluated by the Meeting in 2004

With respect to the developmental toxicity of captan, the following description is quoted from JMPR 2004 (Annex 5, reference *101*, *103*):

> In a study from the published literature, the teratogenic effects of a number of phthalimide derivatives, including captan, were tested in pregnant golden hamsters. The Meeting noted that this study has major limitations (e.g., small number of animals per dose, limited reporting of the data) and is therefore of limited value. It does, however, suggest that developmental effects may occur after a single exposure to captan, albeit at maternally toxic doses.
>
> In a study of developmental toxicity in rats treated by gavage, captan was not teratogenic. The NOAEL for maternal toxicity was 18 mg/kg bw per day on the basis of a reduction in body weight and food consumption. The NOAEL for offspring toxicity was 90 mg/kg bw per day on the basis of the reduction in foetal body weight and an increased incidence of skeletal variations.
>
> In a study in rabbits treated by gavage, the NOAEL for maternal toxicity was 10 mg/kg bw per day on the basis of a markedly reduced body-weight gain and reduced food consumption at 30 mg/kg bw per day. The NOAEL for embryo- and fetotoxicity was 10 mg/kg bw per day on the basis of

[22] Codex Alimentarius Commission. *Report of the 39th Session of the Codex Committee on Pesticide Residues, 7–12 May 2007, Beijing, China* (ALINORM07/30/24).

increases in skeletal variations at 30 and 100 mg/kg bw per day. At 100 mg/kg bw per day, increased incidences of early and late intra-uterine deaths were observed, as were increased incidences of several malformations. The NOAEL for these effects was 30 mg/kg bw per day. Multiple malformations observed in two foetuses in the group receiving the intermediate dose were considered to be incidental. In another study in rabbits treated by gavage, the NOAEL for maternal toxicity was 10 mg/kg bw per day on the basis of reduced body-weight gain and food consumption at 40 mg/kg bw per day. On the basis of the increase in post implantation losses and the increase in incidence of minor skeletal variations at 160 mg/kg bw per day, the NOAEL for embryo- and fetotoxicity was 40 mg/kg bw per day. In a third study in rabbits treated by gavage, the NOAEL for maternal toxicity was 12 mg/kg bw per day on the basis of reductions in body-weight gain during the initial phase of treatment. The NOAEL for embryo- and fetotoxicity was 25 mg/kg bw per day on the basis of a reduction in foetal body weight at 60 mg/kg bw per day. The Meeting considered that maternal toxicity and the associated increases in skeletal variations and foetal body-weight reductions observed were likely to be caused by high local concentrations of captan produced by administration by gavage, and are not considered to be relevant to dietary exposure.

Toxicokinetics

In a study evaluated by the JMPR in 2004, in mice given captan at a dose of 400 or 3000 ppm (equivalent to 57 and 429 mg/kg bw per day) no captan was found in mouse duodenal tissue or its contents (extracts of 5 cm sections of the duodenum were analysed; limit of quantitation, 0.5–3 nmoles, i.e., 0.150–1 µg), indicating that in mice, captan is largely, if not completely, degraded to THPI in the stomach.

In a toxicokinetic study in rats (previously evaluated by the JMPR in 1995), concentrations of captan and its metabolites were measured in the faeces and urine. In order to establish whether captan reached the distal parts of the gastrointestinal tract in rats, the study was re-evaluated by the present Meeting.

Rats were given [^{14}C] labelled captan at a dose of 10 or 500 mg/kg bw by gavage. Extracts of urine and faeces were qualitatively analysed by thin-layer chromatography (TLC) through comparison with reference compounds. Quantification of metabolites was performed by linear plate scanner and autoradiography. Subsequently, some metabolites isolated by TLC were further identified by gas chromatography/mass spectrometry (GC/MS). Several compounds were identified in urine and faeces, including THPI, 3- and 5-hydroxylated THPI, THPI-diol, THPI-epoxide, cyclohexene acid amide and hydroxycyclohexene acid amide and parent captan. The presence of captan in extracts of urine and faeces was identified by TLC only (i.e., by comparison with the retention factor, Rf, of captan). No further identification was attempted. Toxicokinetic data are presented in Table 8.

Table 8. Toxicokinetic data for rats given [^{14}C] labelled captan by gavage.

Dose	Radioactivity excreted (% of administered dose)		Captan in urine (% of radioactivity)	Captan in faeces	
	Urine	Faeces		% of radioactivity (males/females)	% of total administered dose
10 mg/kg bw, single dose	81	8–9	ND	6.5/16.8	0.5–1.5
10 mg/kg bw, repeated dose	88–91	7–9	ND/0.7 (males/females)	ND/4.6	ND/0.4
500 mg/kg bw, single dose	69–73	23–25	1.3–1.6	44.1/40.9	± 12 (males and females)

From Lappin & Havell (1990). ND, not detected

After a single dose at 10 mg/kg bw, 81% and 8–9% of the administered radioactivity was recovered from urine and faeces, respectively. At this single dose, no captan was detected in the urine. Between 0.5% and 1.5% of the total dose recovered in the faeces was captan.

After 14 consecutive doses at 10 mg/kg bw, 88–91% and 7–9% of the administered radioactivity was recovered from the urine and faeces, respectively. At this repeated low dose, 0.7% of urinary radioactivity was detected as captan in the urine of females (not detected in males). Of the radioactivity recovered from the faeces up to 4.6% was captan.

At 500 mg/kg bw, about 71% and 24% of the administered radioactivity was recovered from the urine and faeces, respectively. At this dose, 1–2% of urinary radioactivity was provisionally identified as intact captan.[23]

Developmental toxicity

In a study of developmental toxicity, groups of 25 time-mated female New Zealand White rabbits received THPI (purity, 98.4%) at a dose of 0, 5, 10 or 22.5 mg/kg bw per day by gavage from days 6 to 28 after mating. The vehicle was water containing 0.5% w/v Tween 80 and 0.7% w/v carboxymethylcellulose. In view of the relative molecular masses of captan (300.6) and THPI (151.2), a dose of THPI of 22.5 mg/kg bw per day would be equimolar to a dose of captan of about 45 mg/kg bw per day. All animals were examined twice per day for clinical signs. Body weight was recorded daily from the day of mating until day 29 of gestation, when the animals were killed. Food intake was recorded daily from the first day after mating until day 29 of gestation. On day 29 of gestation, the animals were killed and examined macroscopically. In females of the control group and at the highest dose, the duodenum and sphincter of Oddi (hepatopancreatic sphincter) were examined microscopically. The ovaries and uterus were removed and the foetuses were weighed and examined for visceral and skeletal abnormalities.

One female in the control group died on day 12 of gestation. The cause of death could not be established. One animal at 10 mg/kg bw per day was killed in extremis on day 14 of gestation. At necropsy, in the control group and in the groups at 5, 10 and 22.5 mg/kg bw per day, six, one, three and one female respectively did not appear to be pregnant. In the dams, no treatment-related clinical signs or effects on body weight and food consumption, and no macroscopic or microscopic abnormalities were observed. In the foetuses, no treatment-related embryo/fetotoxicity or effects on visceral and skeletal parameters were observed. The NOAELs for maternal and embryo/fetotoxicity were 22.5 mg/kg bw per day i.e., the highest dose tested.[24]

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[23] Lappin, G.J. & Havell, M.L. (1990) Captan: biotransformation study in the rat. Unpublished report No CTL/P/2951 from ICI Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, England. Submitted to WHO by Makhteshim Chemical Works, Beer-Sheva, Israel.

[24] Blee, M.A.B. (2006) Tetrahydrophthalimide. Prenatal toxicity study in the rabbit by oral gavage administration. Unpublished report No R-18202, MAK 864/053232 from Huntingdon Life Sciences Limited, Woolley Road, Alconbury, Huntingdon, Cambridgeshire. Submitted to WHO by Makhteshim Chemical Works, Beer-Sheva, Israel.

Inhibition of microbial activity in vitro

A study was performed to determine minimum inhibitory concentrations (MIC) of captan (purity, 95.1%) against two bacterial species (*Bacteroides* sp. and *Enterococcus faecalis*) and one species of yeast (*Candida albicans*). These bacteria were considered to be representative of anaerobic bacteria in the rabbit gut. *Candida albicans* was considered to be representative of yeast that may occur in the rabbit gut. The MIC values for *Bacteroides* sp., *Enterococcus faecalis* and *Candida albicans* were 20–50, 50–500 and 2–5 µg/mL, respectively. The Meeting concluded that captan demonstrates antimicrobial activity against organisms considered representative of rabbit gut flora.[25]

In a study to determine MIC of THPI (purity, 98.4%), MIC values for *Bacteroides* sp., *Enterococcus faecalis* and *Candida Albicans* were all > 1000 µg/mL. The Meeting concluded that THPI demonstrates no antimicrobial activity against organisms considered representative of rabbit gut flora.[26]

The Meeting concluded that the existing database (i.e., the new available studies and the previously evaluated studies), was adequate to characterize the potential hazards of captan to foetuses, infants and children.

Toxicological evaluation

In 2004, the Meeting established an ARfD of 0.3 mg/kg bw for captan for women of childbearing age, based on a NOAEL of 30 mg/kg bw per day for increased incidences of intrauterine deaths and malformations at 100 mg/kg bw per day in a study in rabbits and using a safety factor of 100.

The new study of developmental toxicity with THPI did not elucidate the mode of action by which the increased incidences of intrauterine deaths and of foetuses with malformations (observed at 100 mg/kg bw per day expressed as captan) were induced. Because the maximum dose was similar to the NOAEL in the study of developmental toxicity with captan, it was not possible to use this study to determine the contribution of THPI to the developmental toxicity of captan.

Studies in vitro showed that captan, but not its metabolite THPI, has antimicrobial action on gut flora.

A toxicokinetic study in mice indicated that an oral dose of captan is largely, if not completely, metabolized in the stomach in this species. Toxicokinetic studies in rats given captan by gavage indicated that, at a high dose (500 mg/kg bw), a considerable amount of captan reaches the distal part of the gastrointestinal tract. At this dose, intact captan was also present in rat urine. At a single low dose of 10 mg/kg bw given by gavage, captan also reached the distal part of the gastrointestinal tract. It was not detected in urine after a single dose at 10 mg/kg bw, but was detected in the urine after 14 daily doses. No toxicokinetic data in rabbits, the species showing the developmental effect of concern, were provided.

There was some evidence that THPI can reach the caecum and that the developmental effects of captan in rabbits might be secondary to an effect on the gut flora of this species. The doses achieved in the study with THPI did not exclude a systemic role for this compound (and its further metabolites) in the developmental effects seen with captan in rabbits. Furthermore, it could not be excluded that the effects observed in a study of developmental toxicity in rabbits were a result of

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[25] Akhurst, L.C (2005a) Captan: determination of minimum inhibitory concentration against selected micro-organisms representative of rabbit gut microflora. Unpublished report No. R-18666, MAK 0888/052848 from Huntingdon Life Sciences Ltd, Huntingdon, Cambridgeshire, England. Submitted to WHO by Makhteshim Chemical Works, Beer-Sheva, Israel.

[26] Akhurst, L.C (2005b) THPI: determination of minimum inhibitory concentration against selected micro-organisms representative of rabbit gut microflora. Unpublished report No. R-18735, MAK 0890/053252 from Huntingdon Life Sciences Limited, Huntingdon, Cambridgeshire, England. Submitted to WHO by Makhteshim Chemical Works, Beer-Sheva, Israel.

direct action by captan or the thiocarbonyl chloride moiety released after metabolism to THPI. The presence of captan in the urine indicated that a certain amount of captan is available systemically.

In view of these considerations, the Meeting reconfirmed the ARfD of 0.3 mg/kg bw based on a NOAEL of 30 mg/kg bw per day for increased incidences of intrauterine deaths and malformations at 100 mg/kg bw per day in the study in rabbits and using a safety factor of 100. This ARfD applies to women of childbearing age. The Meeting concluded that it was unnecessary to establish an ARfD for the rest of the general population.

An addendum to the toxicological monograph was not prepared.

Estimate of acute reference dose

0.3 mg/kg bw for women of childbearing age

Unnecessary for the rest of the general population

Information that would be useful for the continued evaluation of the compound

Results from epidemiological, occupational health and other such observational studies of human exposures.

5.5 CARBARYL (008)

RESIDUE AND ANALYTICAL ASPECTS

The carbaryl was last evaluated for residues by the 2002 JMPR. Residue data on cranberries and chilli peppers were evaluated by the current Meeting for estimation of maximum residue levels.

Carbaryl is approved for the control of a range of insect pests in cranberries such as Cranberry fireworm, Cranberry fruitworm and Cranberry twig girdler as well various larvae and bugs in chilli peppers.

Results of supervised trials on crops

Supervised trials were carried out following the maximum registered dosage rate in cranberries in the USA and in chilli peppers in Thailand. The residues were determined with HPLC after post-column derivatisation in all trials. The limit of quantification was 0.02 mg/kg. The recoveries ranged between 81% and 110%.

Cranberries

The US GAP permits a maximum of 5 applications at 7 day intervals with a dosage rate of 1.68–2.24 kg ai/ha. Three replicate samples were taken from each plot. The highest residues derived from maximum application rates 7 days (PHI) after the last application was: 0.52, 0.94, 1.85, 2.95 mg/kg.

Taking into account that cranberry is a minor crop, the Meeting considered that four trials performed at maximum GAP were sufficient, and estimated a maximum residue level of 5 mg/kg, an STMR of 1.40 mg/kg and an HR of 2.95 mg/kg.

Chilli peppers

Residues in mature chilli peppers treated according to maximum GAP (0.425–0.6375 kg ai/ha at 7–10 day intervals with a PHI of 14 days) were: 0.05, 0.5, 0.09, 0.09, 0.10, 0.25 mg/kg.

The Meeting estimated a maximum residue level of 0.5 mg/kg, an STMR of 0.09 mg/kg and an HR of 0.25 mg/kg for fresh chilli peppers.

Based on the concentration factor of 7 (for explanation and rational see report section on Chilli peppers), the Meeting estimated an STMR of 0.63 (7 × 0.09) mg/kg and a maximum residue level of 2 (7 × 0.25=1.75) mg/kg to replace its previous recommendation of 50 mg/kg for dried chilli pepper, which was based on an MRL of 5 for sweet peppers, and the default concentration factor of 10.

DIETARY RISK ASSESSMENT

Long- term intake

Using the consumption figures for chilli peppers and the STMR value of 0.63 for dried chilli peppers, the long term intake from use of carbaryl on chilli peppers and cranberries amounts to 0–2% of the ADI (0-0.008 mg/kg bw) in the 13 regional diets.

The Meeting concluded that the long-term intake of residues derived from carbaryl use on cranberries and chilli peppers that have been considered by the present JMPR will not, in practical terms, change the total intake of residues from other uses considered by the 2002 JMPR.

Short-term intake

The rounded cranberry short term intake is 0% of the ARfD (0.2 mg/kg bw) for both children and for adults. The short term intake derived from the consumption of dried chilli pepper is 0% for adults and 1% for children.

The Meeting concluded that the short-term intake estimate derived from residues of carbaryl use on cranberries and chilli peppers that has been considered by the JMPR is unlikely to present a public health problem.

5.6 CLOFENTEZINE (156)

RESIDUE AND ANALYTICAL ASPECTS

Clofentezine, an acaricide first evaluated by the JMPR in 1986 and re-evaluated for residues several times up to 1992. A toxicological review was conducted in 2005, when an ADI of 0-0.02 mg/kg bw was established. The 2005 JMPR concluded that an ARfD was not necessary. At the 37th session of the CCPR, clofentezine was scheduled for Periodic Re-evaluation of residues by the 2007 JMPR.

The manufacturer supplied information on identity; metabolism and environmental fate; residue analysis; use patterns; residues resulting from supervised trials on citrus, pome fruits, stone fruits, grapes, strawberries, currants, melons, tree nuts, tomatoes and cucumbers; and the fate of residues on apple, peach, almond and animal tissues during storage and orange, apple, grape and strawberries in processing. GAP information and enforcement methods were supplied by the manufacturer and the governments of the Netherlands and Australia.

Animal metabolism

The Meeting received animal metabolism studies with clofentezine in lactating cows, goats and laying hens. Clofentezine [^{14}C] labelled in the tetrazine ring was used in the animal metabolism studies.

The metabolism of clofentezine in rat, mouse, rabbit, calf and cow, dog, baboon and hen was qualitatively similar (details on laboratory animal metabolism are given in the toxicology report), with

hydroxylation of the phenyl ring and/or replacement of chlorine with a methylthio group being the 2 major pathways.

A lactating cow was orally dosed with [^{14}C] labelled clofentezine for 5 consecutive days at about 0.27 mg/kg bw per day. Residues in milk reached a plateau level of approximately 0.007 mg/L on the second day. Residues were highest in bile (1.1 mg/kg) and liver (0.09 mg/kg). Heart, muscle and fat contained residues less than 0.01 mg/kg.

A lactating cow was orally administered with [^{14}C] labelled clofentezine for 3 consecutive days at an exaggerated rate (2.2 mg/kg bw per day) in order to produce quantifiable residues. Levels of radioactivity in milk were shown to plateau at a level of 0.17 mg/kg clofentezine equivalents on day 3 after treatment. The major component of the residue in milk was 4-OH clofentezine (75 % TRR, total radioactive residues). The [^{14}C] residue was higher in the liver (0.76 mg/kg) than in other tissues, of which at least 67 % was identified as 4-OH clofentezine. In renal fat, 90% of the TRR (0.24 mg equivalents/kg) was confirmed to be 4-OH clofentezine. Residues in kidney were also found to be composed predominantly of 4-OH clofentezine (83% TRR, 0.30 mg equivalents/kg). The remaining components appeared to be hydrolysis products of 4-OH clofentezine.

A lactating goat was given a single oral dose (0.63 mg/kg bw per day) of [^{14}C]clofentezine. The results showed [^{14}C] in all tissues at levels below 0.05 mg/kg, with all the [^{14}C] being excreted within 72 hours of dosing. Highest TRR was in goat milk at a level of 0.049 mg/L clofentezine equivalents at a time of 24 h after dosing.

Another study at an exaggerated rate (2.2 mg/kg bw per day) was undertaken for 7 consecutive days, in which a plateau for TRR in milk was reached at days 3 or 4 of the test, with a maximum residue of 0.2 mg/L being obtained. Over 95% of the TRR was confirmed as 4-OH clofentezine.

In summary, most of the [^{14}C]clofentezine fed to ruminants was excreted within 72 h. Liver was the target tissue and the major part of the residue was 4-OH clofentezine. There are no qualitative differences in the comparative metabolism studies of rodents (rats) and ruminants (goats and cattle).

Laying hens were administered [^{14}C]clofentezine orally for 3 consecutive days at a dose level of 17 mg clofentezine/kg bodyweight/day. By far the greatest [^{14}C] residue was found in fat (3.0 mg/kg equivalents). The majority of each daily dose of clofentezine (71–79%) was excreted by hens during the subsequent 24 hour period. The majority of the identified component of the residue found in all tissue samples, was the parent clofentezine (fat: 70%, muscle: 34%, unlaid developing eggs: 32% and skin: 7.0%), with varying quantities of both 3 and 4-OH clofentezine. The remaining residue most likely consisted of conjugates of the 3 and 4-OH clofentezine metabolites.

Plant metabolism

The Meeting received plant metabolism studies with clofentezine on lemon, apple, peach and grapes.

In plants, parent clofentezine was the major component of the residue at shorter and longer intervals with lower and higher application rates. Levels of metabolites were usually much lower than parent clofentezine. Residues were mostly found as a surface residue.

The metabolism of [^{14}C]clofentezine (applied at 0.3 kg ai/ha) on lemon leaves was studied. Parent clofentezine was the main residue component and 2-chlorobenzonitrile was also present, at levels of 88% TRR and 8.1% TRR 25 days post-treatment, and 77% TRR and 6.8% TRR 103 days post-treatment, respectively.

The metabolism of [^{14}C]clofentezine in apple foliage was studied following application at a nominal dosage of 0.5 kg ai/ha. The main component of the residue found 25 days after treatment was parent clofentezine present amounting to 87% of TRR. Levels of parent clofentezine decreased over time to a level of 66% of TRR, with an increase of fibre bound residue. The metabolite NC 22505 (3, 6-bis(2-chlorophenyl)-1,2-dehydro -1,2,4,5-tetrazine) was present 10 and 100 days post-treatment but

was not found at intermediate time points. Other single metabolites appeared in concentrations less than 1% of TRR.

The metabolism of [^{14}C]clofentezine was investigated in apples treated at a field spray concentration of 0.03 kg ai/hL and the exaggerated spray concentration of 0.76 kg ai/hL. Residues in mature apple fruit 72 days post-treatment consisted predominantly of parent clofentezine and peel fibre bound residues. However, both residues were at levels of 0.012 mg/kg or less at a rate of 0.03 kg ai/hL. At the exaggerated spray concentration, the same components were present, however the level of the parent clofentezine was much higher, i.e., 82% of TRR (0.81 mg/kg).

Further investigation was made into the components of the fibre bound residue, with apples being treated at spray concentrations of 0.06 kg ai/hL and 0.48 kg ai/hL. Samples were taken at 25 and 64 days post-treatment. Only limited quantities (approximately 0.01 mg/kg) of fibre bound radioactivity was recovered in this trial. Base and enzyme hydrolysis revealed that approximately 50% of bound residue was likely to be unchanged clofentezine, with the remainder consisting of 2-chlorobenzoic acid, 2-chlorobenzylacohol and 2-chlorobenzaldehyde.

Peach trees in a glasshouse were treated with [^{14}C]clofentezine at spray concentrations of 0.01 and 0.1 kg ai/hL and peaches were harvested for analysis 62 days post-treatment. Following the application at 0.01 kg ai/hL the overall TRR was only 0.047 mg/kg, of which 0.036 mg/kg was parent clofentezine. At the higher treatment rate, the TRR was 0.70 mg/kg consisting of 0.63 mg/kg parent clofentezine and 0.038 mg/kg 2-chlorobenzonitrile.

Grape vines were treated in a glasshouse with [^{14}C]clofentezine at spray concentrations of 0.01 and 0.1 kg ai/hL (equivalent to application rates of 0.1 and 1.0 kg ai/ha). Grape samples were collected for analysis 25 and 46 days post-treatment. At 25 days post-treatment, the total radioactive residue found at the 0.1 kg ai/ha rate was 0.38 mg/kg and 2.5 mg/kg at the 1.0 kg ai/ha rate. At the lower rate, the majority of the residue was found to be parent clofentezine (0.29 mg/kg) followed by 2-chlorobenzonitrile (0.04 mg/kg), the remainder of the residue comprised of polar materials (< 0.01 mg/kg). At 46 DAT the overall residue levels were much lower (0.11 mg/kg at 0.1 kg ai/ha and 0.45 mg/kg at 1.0 kg ai/ha), and the parent clofentezine remained the prevalent component (69% of TRR or 0.31 mg/kg).

Environmental fate in soil

The Meeting received information on the environmental fate of clofentezine in soil, including studies on aerobic soil metabolism, field dissipation and crop rotational studies.

The environmental fate of clofentezine was investigated in a number of laboratory studies using either unlabelled or [^{14}C] tetrazine ring labelled material under aerobic conditions for various durations. The degradation rates were not strongly affected by soil organic carbon content, but greatly influenced by the soil pH, with the faster degradation at higher soil pH. The aerobic soil metabolism half-lives for clofentezine ranged from approximately 2 to 12 weeks. After one year, in the loamy sand, clay and clay loam, approximately 56%, 38% and 25% of the applied radioactivity respectively had been mineralized to [^{14}C]O_2, and 30–40% of the initial dose was extractable residue in the loamy sand, clay and clay loam respectively.

During the study period, the maximum concentrations of the major metabolites, expressed as the percentage of the initial dose, were: 13% of AEC 593600 [2-chlorobenzoic (2-chlorobenzylidene) hydrazide], 1.6% of AEC 512898 [N, N'-bis-(2-chlorobenzoyl)-hydrazine], 0.8% of AEF 092117 [2-chlorobenzamide] and 6.2% of AEC 500233 [2-chlorobenzoic acid].

Very little of the applied clofentezine moved below the top 15 cm of the soil during field dissipation trials of up to 8 months' duration in several different soils. Clofentezine concentrations declined to half of their initial values within 14 days to approximately 6 months. In orchard soil residue decline trials, quantifiable residues of clofentezine were mostly detected in the top soil layer and declined below the limit of determination within 60 days.

The low water solubility and relatively high octanol/water partition coefficient of clofentezine lessen the uptake of clofentezine residues from soil into following crops. A crop uptake study with orange and apple trees grown under glasshouse conditions indicated that the potential for uptake of clofentezine residues from the previously treated soil was low.

Methods of analysis

The Meeting received analytical methods descriptions and validation data for residues of clofentezine in a number of crops, and residues of clofentezine or 4-OH clofentezine or total residues of all compounds containing the 2-chlorobenzoyl moiety in animal tissues, milk and eggs.

Methods rely on HPLC-UV, HPLC-DAD, GC-ECD and GC-MSD for analysis of clofentezine or 4-OH clofentezine and all compounds containing the 2-chlorobenzoyl moiety in the various matrices. Several multi-residue methods with HPLC-DAD and GC-MSD were suitable for enforcement for plant and animal commodities (LOQ values 0.01–0.05 mg/kg).

In summary, numerous recovery data on a wide range of substrates showed that the methods for data collection and enforcement were valid over the relevant concentration ranges.

Stability of residues in stored analytical samples

The Meeting received information on the freezer storage stability of residues of clofentezine in apple, peach, almond (hulls and nutmeats), muscle, liver, fat and milk.

Residues were stable in apple, almond/nutmeat and peach samples for a period of at least one year when stored frozen.

After 6 months storage, the mean percentage of clofentezine fortified had fallen to 38% (muscle), 72% (liver), 50% peritoneal fat), and 50% (milk). The percentage of clofentezine-derived residues (all metabolites containing the 2-chlorobenzoyl moiety) determined by derivation to 2-chlorobenzoic acid was more than 90% of the original residue in muscle, liver and fat, and approximately 84% in milk after 15 months storage. Parent clofentezine is relatively unstable in products of animal origin, but the total residue of all metabolites containing the 2-chlorobenzoyl moiety was stable in animal products for at least 15 months.

Definition of the residue

The main residues in fruit crops were the parent clofentezine, and metabolite 2-chlorobenzonitrile. The levels of 2-chlorobenzonitrile found were < 0.05 mg/kg, which was approximately a tenth of those of the parent residue. Other metabolites identified were present only at low levels and these metabolites were not considered to be of toxicological significance. Therefore the parent compound is only included in the residue definition for plant matrices.

The metabolism data submitted for clofentezine in animal products showed the vast majority of the residue in cattle and goat tissues is 4-OH clofentezine. Poultry studies however, showed more significant quantities of parent clofentezine, in addition to 3 and 4-OH clofentezine. Quantities of 3 and 4-OH clofentezine were not separated in the poultry study, but quantities of 3-OH clofentezine are much smaller than the combined totals of parent and 4-OH clofentezine.

In the cow metabolism study, the TRRs in subcutaneous fat and muscle were about 0.02 mg/kg, but TRR in renal fat was about 16 times as high as that in muscle. The main component of the residue in poultry commodities is the parent clofentezine and the TRR in fat was approximately 22 times higher than in the muscle. Based on the above results and the octanol-water partition coefficient of clofentezine (log P_{OW}=4.1), clofentezine is considered as fat-soluble.

Based on the available comparative animal and plant metabolism studies, the Meeting recommended a residue definition for clofentezine as follows:

Definition of the residue (for compliance with the MRL and for estimation of dietary intake) for plant commodities*: clofentezine.*

Definition of the residue (for compliance with the MRL and estimation of dietary intake) for animal commodities: *sum of clofentezine, and* a*ll metabolites containing the 2-chlorobenzoyl moiety, expressed as clofentezine.*

The Meeting decided that residue is fat-soluble.

Results of supervised residue trials on crops

The Meeting received supervised trial data for clofentezine uses on orange, lemon, mandarin, apple, pear, peach, apricot, cherry, nectarine, plum, grapes, strawberry, currant, gherkin, cucumber, melon, tomato, walnut and almond. Residue data were also provided on almond hulls.

Labels (or translations of labels) were available to the Meeting from Argentina, Australia, Belgium, Canada, France, Germany, Greece, Italy, the Netherlands, Portugal, South Africa, Spain, Switzerland, UK, and USA describing the relevant GAP for evaluation of clofentezine.

Citrus fruits

Supervised trials were conducted on orange trees in Greece (citrus GAP 0.015 kg ai/hL, one application, 30-day PHI), Italy (citrus GAP 0.015–0.02 kg/hL, one application, 30-day PHI) and Spain (citrus GAP 0.005–0.01 kg/hL, 21-day PHI) in 1984, 1990 and 2001.

In two orange trials from Greece with application conditions in line with GAP, clofentezine residues were 0.10 and 0.18 mg/kg, with residues in flesh at 0.02 and 0.03 mg/kg.

In six orange trials from Spain and two trials from Italy with application conditions matching Spanish GAP, clofentezine residues were: 0.06, 0.07, 0.09(3), 0.10, 0.12 and 0.14 mg/kg, with some residues in flesh at < 0.01, 0.01, 0.02(3) and 0.03 mg/kg.

In one trial on lemons from Greece with application conditions in line with GAP, clofentezine residue was 0.15 mg/kg, with residue in flesh at 0.03 mg/kg.

In one trial on lemons from Italy matching Spanish GAP, clofentezine residue in lemon was 0.09 mg/kg, with residue in flesh at 0.02 mg/kg.

In one trial on tangerines from Italy matching Spanish GAP, clofentezine residue was 0.24 mg/kg, with residue in flesh at 0.03 mg/kg.

In six mandarin trials from Spain with application conditions in line with GAP, clofentezine residues were 0.08(3), 0.15, 0.17 and 0.18 mg/kg, with residues in flesh for two trials at 0.02 and 0.17 mg/kg.

The Meeting noted that the residue data populations for orange, lemon, tangerine and mandarin were from similar populations and can be combined. The residues in ranked order on citrus fruits were: 0.06, 0.07, 0.08(3), 0.09(4), <u>0.10</u> (2), 0.12, 0.14, 0.15(2), 0.17, 0.18(2) and 0.24 mg/kg (n=19). A similar situation exists for the flesh and the ranked order of concentrations in flesh was: < 0.01, 0.01, <u>0.02</u>(5), 0.03(3) and 0.17 mg/kg (n=11).

The Meeting estimated a maximum residue level for citrus fruits and an STMR value for flesh of 0.5 and 0.02 mg/kg respectively. The Meeting also estimated an STMR value for clofentezine in whole citrus fruits of 0.10 mg/kg (for estimating STMR-R value in orange juice). The recommendation for a maximum residue level of 0.5 mg/kg for citrus fruits confirms the previous recommendation of 0.5 mg/kg.

Pome fruits

Supervised trials were conducted on apple trees in Australia (pome fruit GAP 0.015 kg/hL, one application, 21-day PHI), Canada (GAP 0.15–0.30 kg ai/ha, one application, 45-day PHI), UK (GAP 0.2 kg ai/ha, one application, 28-day PHI), France (GAP 0.02 kg ai/hL, one application, 42-day PHI), Greece (GAP 0.015 kg ai/hL, one application, 45-day PHI), Germany (pome fruit GAP 0.02 kg ai/hL, one application per year, 35-day PHI), Belgium (GAP 0.13 kg ai/ha, one application, no PHI), South Africa (GAP 0.02 kg ai/hL, 30-day PHI), USA (GAP 0.12–0.24 kg ai/ha, one application, 45-day PHI) annually from 1980 to 1987 and then 1992 and 1993.

In one trial from Canada with application conditions in line with GAP, the residue of clofentezine found in apple was 0.04 mg/kg.

In fifteen apple trials from France with application conditions in line with GAP, clofentezine residues were < 0.01(3), 0.01, 0.03, 0.05(2), 0.06, 0.07(3), 0.08, 0.10, 0.11 and 0.22 mg/kg.

In one apple trial from Greece with application conditions in line with GAP, clofentezine residue was 0.04 mg/kg.

In two apple trials from South Africa with application conditions in line with GAP, clofentezine residues were 0.09(2) mg/kg.

In sixteen apple trials from USA with application conditions in line with GAP, clofentezine residues were 0.01(2), 0.02(3), 0.04(3), 0.05(3), 0.07(2), 0.11 and 0.12(2) mg/kg.

In five apple trials from Germany with application conditions in line with GAP, clofentezine residues were 0.02, 0.03, 0.04, 0.05 and 0.09 mg/kg.

In four apple trials from UK with application conditions matching French GAP, clofentezine residues were 0.10, 0.16, 0.17 and 0.24 mg/kg.

The Meeting noted that the residues in apples from the above countries were from similar populations and could be combined. The ranked order of residues were: < 0.01(3), 0.01(3), 0.02(4), 0.03(2), 0.04(6), 0.05(6), 0.06, 0.07(5), 0.08, 0.09(3), 0.10(2), 0.11(2), 0.12(2), 0.16, 0.17, 0.22 and 0.24 mg/kg (n=44).

Supervised trials were conducted on pear trees in Australia (pome fruit GAP 0.015 kg/hL, one application, 21-day PHI), Canada (GAP 0.15-0.30 kg ai/ha, one application, 21-day PHI), Italy (GAP 0.02 kg ai/hL, one application, 30-day PHI), South Africa (GAP 0.02 kg ai/hL, 30-day PHI), USA (GAP 0.12-0.24 kg ai/ha, one application, 21-day PHI) in 1982, 1984, 1985, 1986, 1987, 1988 and 1993.

In one pear trial from Australia with application conditions in line with GAP, clofentezine residue was 0.02 mg/kg.

In four pear trials from Canada with application conditions in line with GAP, clofentezine residues were 0.12, 0.13, 0.14 and 0.19 mg/kg.

In one pear trial from Italy with application conditions in line with GAP, clofentezine residue was 0.04 mg/kg.

In two pear trials from South Africa with application conditions in line with GAP, clofentezine residues were 0.20 and 0.22 mg/kg.

In thirteen pear trials from USA with application conditions in line with GAP, clofentezine residues were 0.04, 0.05, 0.06(3), 0.08(2), 0.09(3), 0.15, 0.18 and 0.20 mg/kg.

The Meeting noted that the residues in pears from the above countries were from similar populations and could be combined. The residues in ranked order were: 0.02, 0.04(2), 0.05, 0.06(3), 0.08(2), 0.09(3), 0.12, 0.13, 0.14, 0.15, 0.18, 0.19, 0.20(2) and 0.22 mg/kg.

The Mann-Whitney test indicated the residue data populations for apple and pear were not significantly different and could be combined to support a pome fruit MRL. The ranked order of concentrations, median underlined, were < 0.01(3), 0.01(3),0.02(5), 0.03(2), 0.04(8), 0.05(7), 0.06(4), 0.07(5), 0.08(3), 0.09(6), 0.10(2), 0.11(2), 0.12(3), 0.13, 0.14, 0.15, 0.16, 0.17, 0.18, 0.19, 0.20(2), 0.22(2) and 0.24 mg/kg (n=65). The Meeting estimated a maximum residue level and an STMR value for clofentezine in pome fruits of 0.5 and 0.05 mg/kg respectively. The recommendation for a maximum residue level of 0.5 mg/kg for pome fruits confirms the previous recommendation.

Stone fruits

Supervised trials were conducted on peach in Australia (stone fruit GAP 0.015 kg ai/hL, one application, 21-day PHI), in Italy (no GAP), and USA (GAP 0.059–0.24 kg ai/ha, one application, 21-day PHI) in 1984, 1986, 1987, 1988, 1991, 1993 and 2002.

In two peach trials from Australia with application conditions in line with GAP, clofentezine residues in flesh were 0.06 and 0.13 mg/kg.

In eighteen peach trials conducted at GAP in USA, clofentezine residues were 0.02, 0.03, 0.04, 0.05, 0.06, 0.08(2), 0.09(2), 0.11, 0.12, 0.13, 0.14(2), 0.18(2), 0.24 and 0.35 mg/kg.

The Meeting noted that the residue data populations from Australia and USA for peach were from similar populations and should be combined. The residues in ranked order were: 0.02, 0.03, 0.04, 0.05, 0.06(2), 0.08(2), 0.09(2), 0.11, 0.12, 0.13(2), 0.14(2), 0.18(2), 0.24 and 0.35 mg/kg.

Supervised trials were conducted on apricot in Greece (GAP 0.015 kg ai/hL, one application, 45-day PHI) and USA (GAP 0.059-0.24 kg ai/ha, one application, 21-day PHI) in 1987, 1989 and 1993.

In one apricot trial conducted at GAP in Greece, clofentezine residue was 0.16 mg/kg.

In two apricot trials conducted at GAP in USA, clofentezine residues were 0.13 and 0.14 mg/kg.

Combined residues from Greek and USA apricot trials were 0.13, 0.14 and 0.16 mg/kg.

Supervised trials were conducted on cherries in UK (0.2 kg ai/ha, one application, 56-day PHI) in 1983.

In two cherry trials conducted in accordance with British GAP, clofentezine residues were 0.01 and 0.02 mg/kg.

Supervised trials were conducted on nectarines in USA (GAP 0.059–0.24 kg ai/ha, one application, 21-day PHI) in 1986 and 1987.

In three nectarine trials conducted in accordance with USA GAP, clofentezine residues were 0.04, 0.11 and 0.17 mg/kg.

Supervised trials were conducted on plums in Germany (GAP 0.02 kg ai/hL, one application limited by growth stage of the crop, no PHI) in 1985 and 1986. The last application was made during fruit development, which is not in accordance with German GAP, as a result the residue data could not be used for the evaluation.

The Meeting combined the residue data in peach, apricot, cherry and nectarine. The residues in ranked order were: 0.01, 0.02(2), 0.03, 0.04(2), 0.05, 0.06(2), 0.08(2), 0.09(2), 0.11(2), 0.12, 0.13(3), 0.14(3), 0.16, 0.17, 0.18(2), 0.24 and 0.35 mg/kg (n=28).

The Meeting estimated a maximum residue level and an STMR value for clofentezine in stone fruits of 0.5 and 0.11 mg/kg respectively. The recommendation for a maximum residue level of 0.5 mg/kg for stone fruits replaces the previous recommendation of 0.2 mg/kg.

Grapes

Supervised trials were conducted on grapes in France (GAP 0.2 kg ai/ha, one application, 42-day PHI), in Greece (no GAP, use that of Spain), in Germany (GAP 0.06–0.24 kg ai/ha, one application, 35-day PHI), in Italy (GAP 0.01-0.015 kg ai/hL, one application, 30-day PHI) and in Spain (GAP 0.01-0.03 kg ai/hL, 30-day PHI) in 1984, 1985, 1986, 1987, 1991, 1992 and 2001.

In twelve trials conducted in line with German GAP, clofentezine residues were 0.09, 0.12, 0.14, 0.20, 0.22, 0.23, 0.39, 0.61, 0.69, 0.73, 0.79 and 0.89 mg/kg.

In one trial conducted in accordance with Italian GAP, clofentezine residue was 0.35 mg/kg.

In two trials conducted in accordance with Spanish GAP, clofentezine residues were 0.25 and 0.27 mg/kg.

In one trial in Greece conducted in accordance with Spanish GAP, clofentezine residue was 0.67 mg/kg.

In one trial in Italy conducted in accordance with Spanish GAP, clofentezine residue was 0.12 mg/kg.

In two trials in France conducted in accordance with Spanish GAP, clofentezine residues were 0.09 and 0.11 mg/kg.

The Meeting noted that the residues in grapes were from similar populations and could be combined. The residues in ranked order were: 0.09(2), 0.11, 0.12(2), 0.14, 0.20, 0.22, 0.23, 0.25, 0.27, 0.35, 0.39, 0.61, 0.67, 0.69, 0.73, 0.79 and 0.89 mg/kg (n=19).

The Meeting estimated a maximum residue level and an STMR value for clofentezine in grapes of 2 and 0.25 mg/kg respectively. The recommendation for a maximum residue level of 2 mg/kg for grapes replaces the previous recommendation of 1 mg/kg.

Strawberries

Supervised trials were conducted on strawberries in France (GAP 0.2 kg ai/ha, 3-day PHI), in Germany (GAP 0.3 kg ai/ha, one application, no PHI, growth-stage restriction), in the Netherlands (GAP 0.075–0.15 kg ai/ha, one to two applications, no PHI, growth-stage restriction) and in Spain (GAP 0.01–0.02 kg ai/hL, 3-day PHI) in 1989, 1990, 1992, 2000 and 2001.

In eight outdoor trials in France conducted in line with French GAP, clofentezine residues were 0.08(2), 0.09, 0.13, 0.19, 0.20 and 0.24(2) mg/kg.

In two outdoor trials in the Netherlands conducted in accordance with Dutch GAP, clofentezine residues were 0.08 and 0.13 mg/kg.

In nine outdoor trials in Spain conducted in accordance with Spanish GAP, clofentezine residues were 0.50, 0.56, 0.60, 0.70, 0.72, 0.73, 0.75, 0.81 and 1.10 mg/kg.

In five outdoor trials in Germany conducted in line with French GAP, clofentezine residues were 0.09(2), 0.16, 0.18 and 0.23 mg/kg.

The data populations from France and those from the Netherlands and Germany were not significantly different and should be combined. The data from Spain were significantly different from those from France, Germany and the Netherlands in strawberries on a Mann-Whitney test.

Based on data from Spain, the Meeting estimated a maximum residue level and an STMR value for clofentezine in strawberries of 2 and 0.72 mg/kg respectively. The recommendation for a maximum residue level of 2 mg/kg for strawberry confirms the previous recommendation of 2 mg/kg.

Black, red and white Currants

Four supervised trials were conducted on blackcurrants in France (maximum GAP: 0.2 kg ai/ha, 45-day PHI) in 2001. The residues in ranked order on currants were: < 0.04(3) and 0.09 mg/kg.

The Meeting agreed to extrapolate from blackcurrants to red and white currants and estimated a maximum residue level and an STMR value for clofentezine in currants of 0.2 and 0.04 mg/kg respectively. The recommendation for a maximum residue level of 0.2 mg/kg for currants replaces the previous recommendation of 0.05 mg/kg.

Cucurbits

Supervised trials were conducted on cucumbers in France (cucurbits GAP 0.2 kg ai/ha, 3-day PHI), in Greece (cucumber GAP 0.015 kg ai/hL, one application, 4-day PHI) and in Switzerland (cucumber GAP 0.02 kg ai/hL, one application, 14-day PHI) in 1985, 1987, 1988 and 1991.

In one trial in France conducted on cucumber in accordance with French GAP, clofentezine residue was 0.07 mg/kg.

In four trials in Greece conducted on cucumber in accordance with Greek GAP, clofentezine residues were 0.12(2), 0.14 and 0.16 mg/kg.

In one trial in Switzerland conducted on cucumber in accordance with French GAP, clofentezine residue was 0.13 mg/kg.

The Meeting noted that the residue data in cucumber were from similar populations and could be combined. The residues in ranked order were: 0.07, 0.12(2), 0.13, 0.14 and 0.16 mg/kg (n=6).

The Meeting estimated a maximum residue level and an STMR value for clofentezine in cucumber of 0.5and 0.125 mg/kg respectively. The recommendation for a maximum residue level of 0.5 mg/kg for cucumber replaces the previous recommendation of 1 mg/kg.

Melons

Supervised trials were conducted on melons in France (GAP 0.2 kg ai/ha, 3-day PHI), in Greece (no GAP, use that of France), in Italy (GAP 0.015–0.02 kg ai/hL, one application, 15-day PHI), in Portugal (no GAP, use that of France) and in Spain (GAP 0.01–0.02 kg ai/hL, 3-day PHI) in 1999 and 2000.

In two trials in France conducted in line with French GAP, clofentezine residues were < 0.05 and 0.05 mg/kg, with no detectable residue in pulp.

In one trial in Greece conducted in accordance with Greek GAP, clofentezine residue was 0.03 mg/kg, with no detectable residue in pulp.

In two trials in Portugal conducted in accordance with Portuguese GAP, clofentezine residues were < 0.05 mg/kg, with no detectable residue in pulp.

In two trials in Spain conducted in accordance with Spanish GAP, clofentezine residues were < 0.01 and < 0.05 mg/kg, with no detectable residue in pulp.

In two trials in Italy conducted in accordance with French GAP, clofentezine residues were 0.03 and 0.06 mg/kg, with no detectable residue in pulp.

The Meeting noted that the residues in melons were from similar populations and could be combined. The residues in ranked order were: < 0.01, 0.03(2), < 0.05(4), 0.05 and 0.06 mg/kg (n=9). The residues in all pulp samples were below the limit of quantification (n=9).

The Meeting estimated a maximum residue level of 0.1 mg/kg. Taking into account that the parent compound practically did not translocate in plants, the Meeting estimated an STMR value of 0 mg/kg for clofentezine in melons.

Tomato

Supervised trials were conducted on tomato in France (no GAP, use that of the Netherlands), in Germany (no GAP, use that of the Netherlands), in Greece (no GAP, use that of the Netherlands), in Italy (GAP 0.02-0.03 kg ai/hL, one application, 15-day PHI), in the Netherlands (GAP 0.075–0.23 kg ai/ha, 1-2 applications, 3-day PHI) and in Spain (0.01-0.02 kg ai/hL, one application, 3-day PHI) in 1986, 1992, 1999, 2000 and 2005.

In seven trials in Italy conducted in accordance with Italian GAP, clofentezine residues were 0.01, 0.03, 0.05(2), 0.06, 0.07 and 0.10 mg/kg.

In seven glasshouse trials in the Netherlands conducted in accordance with Dutch GAP, clofentezine residues were < 0.05, 0.09, 0.10, 0.11, 0.12, 0.16 and 0.18 mg/kg.

In four trials in France conducted matching Dutch GAP, clofentezine residues were < 0.05, 0.05, 0.06 and 0.09 mg/kg.

In three trials in Germany conducted matching Dutch GAP, clofentezine residues were < 0.05, 0.06 and 0.11 mg/kg.

In one trial in Greece conducted matching Dutch GAP, clofentezine residue was < 0.05 mg/kg.

In one trial in Italy conducted matching Dutch GAP, clofentezine residue was < 0.05 mg/kg.

In one trial in Spain conducted matching Dutch GAP, clofentezine residue was 0.09 mg/kg.

The Meeting noted that the residues from France, Germany and the Netherlands, in line with Dutch GAP, were from similar populations and could be combined. The data populations from France, Germany and the Netherlands and from Greece, Italy and Spain were not from similar populations based on the Mann-Whitney test, and could not be combined. The residues in ranked order based on France, Germany and the Netherlands were: < 0.05(3), 0.05, 0.06(2), 0.09(2), 0.10, 0.11(2), 0.12, 0.16 and 0.18 mg/kg (n=14).

The Meeting estimated a maximum residue level and an STMR value for clofentezine in tomato of 0.5 and 0.09 mg/kg respectively.

Tree nuts

Eight supervised trials were conducted on walnut in USA (maximum GAP: 0.24 kg ai/ha, one application, 30-day PHI) in 1987 and 1988. The ranked order of concentrations on walnut was: < 0.02(8) mg/kg.

Thirty four supervised trials were conducted on almond in USA (maximum GAP: 0.24 kg ai/ha, 30-day PHI) in 1985, 1987, 1993, 1998 and 2002. The ranked order of concentrations on almond was: < 0.01(9), < 0.02(3), < 0.05(13), 0.10(3), 0.20(2), and 0.30(4) mg/kg.

The residue data for walnut and almond were from similar populations and could be combined. The residues in ranked order on tree nuts were: < 0.01(9), < 0.02(11), < 0.05(13), 0.10(3), 0.20(2), and 0.30(4) mg/kg (n=42).

The Meeting estimated a maximum residue level and an STMR value for clofentezine in tree nuts of 0.5 and 0.05 mg/kg respectively.

Animal feedstuffs

Almond hull

In 34 supervised trials on almond compliant with US GAP, residues of clofentezine in almond hulls in rank order, median and highest residue underlined, were: 0.06, 0.10, 0.11, 0.12(2), 0.20(2), 0.30,

0.40(2), 0.50(2), 0.60(2), 0.70(2), 0.90, 0.91, 1.00, 1.10(2), 1.20, 1.40(2), 1.50(2), 1.60, 1.70, 1.80, 2.00, 2.20, 2.30, 2.50 and 2.70 mg/kg (fresh weight) (n=34).

The meeting estimated an STMR value of 0.91 mg/kg and a highest residue of 2.70 mg/kg for clofentezine in almond hulls (fresh weight).

Allowing for the standard 90% dry matter for almond hulls (*FAO Manual*, p. 147) the residues in almond hulls were: 0.07, 0.11, 0.12, 0.13(2), 0.22(2), 0.33, 0.44(2), 0.56(2), 0.67(2), 0.78(2), 1.00, 1.01, 1.11, 1.22(2), 1.33, 1.56(2), 1.67(2), 1.78, 1.89, 2.00, 2.22, 2.44, 2.56, 2.78 and 3.00 mg/kg. The Meeting estimated a maximum residue level of 5 mg/kg and an STMR of 1.01 mg/kg for almond hulls (dry weight). A highest residue level of 3.00 mg/kg was estimated for calculating the dietary burden of farm animals.

Fate of residues during processing

The Meeting received information on the fate of clofentezine residues during aqueous hydrolysis under conditions representing pasteurisation, baking, brewing, boiling and sterilisation. Information was also provided on the fate of clofentezine residues during the food processing of citrus, apples, grapes and strawberries.

Clofentezine was stable at pH 4 for 20 minutes at 90 °C with no degradation products formed, and moderately stable at pH 5 at 100 °C for 60 minutes. In this latter instance, clofentezine degraded slightly (by approximately 10%) to form metabolite 2-chlorobenzoic (2-chlorobenzylidene) hydrazide (AEC 593600). The parent clofentezine was rapidly hydrolysed at pH 6 and 120 °C and it was not detected after 20 minutes. The major reaction products as a percentage of the applied radioactivity were 2-chlorobenzoic (2-chlorobenzylidene) hydrazide (78%), 2-chlorobenzonitrile (4.9%) and 2-chlorobenzamide (17%).

The processing was carried out to produce apple sauce from samples spiked with clofentezine in the laboratory. The time of cooking and pasteurizing was approximately 15 minutes at a temperature of over 97 °C. The treated apples, the apple sauce and the processing by-products (washed apple, apple cores, peeled apples, wash water), were analysed for the potential degradation products of clofentezine (AEC 593600, 2-chlorobenzonitrile and 2-chlorobenzamide), but none of the compounds was present in quantifiable concentration in any of the samples. One uncooked apple peel sample contained 0.02 mg/kg for 2-chlorobenzonitrile. The clofentezine residue in the pasteurized apple sauce was reduced from 0.40 mg/kg in the apple in one study, and from 0.41 mg/kg to < 0.02 mg/kg in three samples in a follow up test, where the three degradation products were not detectable. The Meeting noted that the 3 degradation products found in the above hydrolysis study, performed at pH 6 and 120 °C, were not present in apple sauce prepared following a normal processing procedure.

Processing studies for the conversion of oranges, apples, grapes and strawberries to various processed products were reported from Germany, Italy, Spain and USA. In most cases, the raw agricultural commodities had quantifiable field incurred clofentezine residue. Calculated processing factors and the mean or best estimate for the processing factors are summarized in the following table.

Raw agricultural commodity (RAC)	Processed commodity	Calculated processing factors. [1/]	Median or best estimate
Orange	Juice	< 0.08, < 0.11, < 0.14, 0.14, < 0.17(3), < 0.20, < 0.25(2), < 0.33(2)	0.14
Apples	Wet pomace	< 0.50, 1.20, 1.50 (2), 2.00 (4), 2.11, 2.40, 3.00, 3.44, 5.50, 5.69, 5.79, 6.00	2.06
	Juice	0.016, 0.11, 0.20, < 0.5 (3)	0.11
Grapes	Raisins	0.22, 0.28, 0.64, < 0.67, 1.09, 1.12, 1.70, 2.33, 2.92	1.11
	Juice	nd	0
	Wet pomace	1.88, 1.89	1.89
	White wine making	< 0.042, < 0.50 (2)	< 0.042

[1/] 'Less-than' (<) values are derived from cases where residues were not detected in the processed commodity. The 'less-than' processing factor is then calculated from the LOQ of the analyte in the processed commodity and the residue in the raw agricultural commodity.

The processing factor for orange juice (0.14) was applied to the estimated STMR for orange (0.10 mg/kg) to produce STMR-P values for orange juice (0.014 mg/kg).

The processing factors for wet apple pomace (2.06) and apple juice (0.11) were applied to the estimated STMR for apple (0.05 mg/kg) to produce STMR-P values for wet apple pomace (0.103 mg/kg) and apple juice (0.0055 mg/kg).

The processing factors for grapes to raisins (1.11), grape juice (0), white wine (0.042) and wet pomace (1.89) were applied to the estimated STMR for grapes (0.25 mg/kg) to produce an STMR-P value for dried grapes (0.28 mg/kg), grape juice (0), white wine (0.011 mg/kg) and wet pomace (0.47 mg/kg). The processing factors for raisins (1.09) were applied to the grape residue data (highest value 0.89 mg/kg) to produce estimated highest values for dried grapes (0.99 mg/kg).

The Meeting estimated a maximum residue level for clofentezine in dried grapes of 2 mg/kg.

Residues in animal commodities

Farm animal feeding studies

The Meeting received feeding studies on lactating dairy cows, calves and laying hens, which provided information on likely residues appearing in animal tissues, milk and eggs from residues in the animals' diet.

Lactating Friesian cows were dosed with clofentezine at the equivalent of 10 (1), 30 (3 ×) and 100 (10 ×) ppm in the dry-weight diet using an average feed consumption of 20 kg for 28 consecutive days. Milk was collected twice daily for analysis. Animals were sacrificed at 1 or 3 days after the final dosing.

No residues (total clofentezine=clofentezine and metabolites hydrolysable to 2-chlorbenzoic acid and expressed as clofentezine) were detected in milk samples taken from the control and the 1 × dose groups. From day 7, total residues between < 0.05 and 0.14 mg/kg were detected in the milk of cows from the 3 × dose group. In the 10 × dose group, residues occurred regularly from day 7 in the concentration range of 0.11 to 0.27 mg/kg.

The total residue was below the LOQ (0.05 mg/kg) in all tissue samples except liver from the treatment rate of 1 ×. No residue was detectable in heart, muscle and fat samples at any dose level. The average residues were present in liver (0.26, 1.15, 2.20 mg/kg) and in kidney (< 0.05, 0.18, 0.40 mg/kg) at the dose rates of 1 ×, 3 × and 10 ×, respectively.

Calves were dosed at a rate equivalent to 0.5 ppm feed (dry weight) using an average feed consumption of 3.5 kg for 28 days. Animals were sacrificed at 19 h after the final dosing. The total

clofentezine residues were below the limit of quantification (0.05 mg/kg clofentezine equivalents) in the liver and kidney samples.

Laying hens were fed clofentezine at 0.05, 0.15, 0.50 and 6.0 ppm in the diet (dry weight) for 28 days. Egg samples were taken daily during the study and kept frozen. Birds were sacrificed 1 day after the final dosing. Only one egg sample obtained from the highest dose rate group contained quantifiable residues (0.06 mg/kg). From the dose groups of 0.05, 0.15, 0.50 ppm, no residue was present above the LOQ (0.05 mg/kg) in any tissue samples. Quantifiable residues were only present at the exaggerated 6.0 ppm dosage rate: liver (0.08 mg/kg), kidney (0.06 mg/kg) and abdominal and subcutaneous fat (0.13, 0.09 mg/kg).

Livestock dietary burden

The Meeting estimated the dietary burden of clofentezine in farm animals on the basis of the diets listed in the Annex 6 of the 2006 JMPR Report. Calculation from highest residue and STMR-P values provides the levels in feed suitable for estimating MRLs, while calculation from STMR and STMR-P values for feed is suitable for estimating STMR values for animal commodities.

Estimated maximum and mean dietary burdens of farm animals

Dietary burden calculations for beef cattle, dairy cattle and turkey are provided in Annex 6. The calculations were made according to the animal diets from USA, Canada, EU and Australia in the OECD Table (Annex 6 of the 2006 JMPR Report).

The calculations are then summarized and the highest dietary burdens (underlined) are selected for MRL and STMR estimates on animal commodities.

	Animal dietary burden, clofentezine, ppm of dry matter diet					
	USA-Canada		EU		Australia	
	max	mean	max	mean	max	mean
Beef cattle	0.35	0.15	0.05	0.05	<u>0.98</u> [1/]	<u>0.78</u> [2/]
Dairy cattle	0.33	0.13	0.03	0.03	<u>0.95</u> [3/]	<u>0.75</u> [4/]
Poultry - layer	0	0	0	0	0	0
Poultry - layer	0	0	0	0	0	0

[1/] Highest maximum beef or dairy cattle dietary burden suitable for MRL estimates for mammalian meat.

[2/] Highest mean beef or dairy cattle dietary burden suitable for STMR estimates for mammalian meat.

[3/] Highest maximum dairy cattle dietary burden suitable for MRL estimates for milk.

[4/] Highest mean dairy cattle dietary burden suitable for STMR estimates for milk.

The dietary burden for both beef and dairy cattle was 0.93 mg/kg, below the lowest feeding level (10 ppm in the feed). Therefore, the resulting residues in milk and cattle tissues were calculated by applying the respective transfer factors (transfer factor=residue level in tissue or milk ÷ residue level in feed) to the estimated dietary burden. In the feeding study the highest residue levels in tissues were used to calculate the highest likely mammal commodity residue levels and mean residue levels in milk and tissues were used to estimate the mammal commodity STMRs. In the table below, dietary burdens and the corresponding estimated residues in brackets are indicated with Italic fonts.

	Feeding level (mg/kg) actual	Clofentezine residues, mg/kg									
		Milk		Muscle		Fat		Liver		Kidney	
		Highest	Mean	Highest	Mean	Highest	Mean	Highest	Mean	Highest	Mean
MRL	*0.98*			*(< 0.005)*		*(< 0.005)*		*(0.031)*		*(< 0.005)*	
beef cattle	10			< 0.05		< 0.05		0.33		< 0.05	

MRL	*0.95*		*(< 0.005)*								
dairy cow	10		< 0.05								
STMR	*0.78*				*(< 0.004)*		*(< 0.004)*		*(0.019)*		*(< 0.004)*
beef cattle	10				< 0.05		< 0.05		0.26		< 0.05
STMR	*0.75*		*(< 0.004)*								
dairy cow	10		< 0.05								

The dietary burden for laying hens was 0 mg/kg, therefore the table of calculation of MRLs and STMRs for poultry meat and eggs is not necessary.

The Meeting estimated maximum residue levels of 0.05 (*) mg/kg for mammalian meat (fat), mammalian edible offal, and milks to replace the present recommendations of 0.05 (*) mg/kg for cattle meat, 0.01 (*) mg/kg and 0.1 mg/kg for edible offal of cattle. The Meeting also estimated the following STMR values: muscle 0 mg/kg, fat 0 mg/kg, edible offal 0.05 mg/kg, and whole milk 0 mg/kg.

The Meeting estimated maximum residue levels of 0.05 (*) mg/kg for eggs, poultry meat (fat), and poultry edible offal, based on the limit of quantification for poultry commodities to confirm the present recommendation of 0.05 (*) mg/kg. Also estimated were STMRs of 0 mg/kg for eggs, meat, and edible offal of poultry.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes (IEDIs) of clofentezine, based on the STMRs estimated for sixteen commodities, were 0–3% of the maximum ADI of 0.02 mg/kg bw for the thirteen GEMS/Food regional diets. The Meeting concluded that the long-term intake of residues of clofentezine resulting from its uses that have been considered by JMPR is unlikely to present a public health concern.

Short-term intake

The 2005 JMPR decided that an ARfD was unnecessary. The Meeting therefore concluded that the short-term intake of clofentezine residues is unlikely to present a public health concern.

5.7 CYFLUTHRIN (157)/ BETA-CYFLUTHRIN (228)

RESIDUE AND ANALYTICAL ASPECTS

Cyfluthrin was identified as a priority compound under the Periodic Re-evaluation Programme at the 37th Session of the CCPR. The Meeting received information on cyfluthrin metabolism and environmental fate, methods of residue analysis, freezer storage stability, national registered use patterns, supervised residue trials, farm animal feeding studies, fate of residues in processing and national MRLs. The Meeting also received information on beta-cyfluthrin methods of residue analysis, freezer storage stability, national registered use patterns and supervised residue trials. The metabolism and environmental fate, transfer from feeds to farm animals and fate of residues in processing provided for cyfluthrin are used to support both pesticides.

Cyfluthrin was evaluated by the 48th JECFA for residues in animal commodities arising from direct animal treatment. In the case of animal commodities, the maximum residue limit recommendations of the 48th JECFA for cattle are fat 0.2 mg/kg, muscle, liver and kidney 0.02 mg/kg and milk 0.04 mg/kg. The residue definition (marker residue) chosen by JECFA was cyfluthrin.

The 2006 JMPR established common ADIs and ARfDs for beta-cyfluthrin and cyfluthrin of 0-0.04 mg/kg bw per day and 0.04 mg/kg bw respectively.

Cyfluthrin is a mixture of 8 stereoisomeric esters derived from esterification of the dichloro analogue of chrysanthemic acid, (2,2-dimethyl-3-(2,2-dichlorovinyl)cyclopropane carboxylic acid, DCVA) with α -cyano-3-phenoxy-4-fluorobenzyl alcohol. Beta-cyfluthrin is an enriched isomeric form of the 2 biologically active diastereoisomeric pairs of isomers.

Conclusions reached in discussing cyfluthrin equally apply to beta-cyfluthrin. In the presence of water and other protic solvents, the isomer composition of beta-cyfluthrin changes through epimerisation such that with sufficient time the isomer ratio becomes the same as cyfluthrin.

The following abbreviations are used for the metabolites discussed below:

DCVA	2,2-dimethyl-3-(2,2-dichlorovinyl)cyclopropane carboxylic acid
FPBald	4-fluoro-3-phenoxybenzaldehyde
FPBacid	4-fluoro-3-phenoxybenzoic acid
FPBalc	3-phenoxy-4-fluorobenzyl alcohol
OH-FPBacid	3-(4'-hydroxyphenoxy)-4-fluorobenzoic acid
Me-FPBacid	methyl 4-fluoro-3-phenoxybenzoate
FPBamide	4-fluoro-3-phenoxybenzamide
FPB	1-fluoro-2-phenoxybenzene
COOH-cyfluthrin	α-[[[3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropyl]carbonyl]oxy]-4-fluoro-3-phenoxybenzeneacetic acid

Animal metabolism

Two radiolabelled cyfluthrin preparations separately [^{14}C] labelled at the phenyl-UL-^{14}C- and fluorophenyl-UL positions, were used in the metabolism and environmental studies. The metabolism of laboratory animals was qualitatively the same as for farm animals. The proposed major route of cyfluthrin metabolism in livestock is via hydrolysis of the ester linkage. Hydrolysis gives initially DCVA and the unstable cyanohydrin which rapidly breaks down to the aldehyde (FPBald) and is oxidized to the corresponding acid/or hydroxylated acids (FPBacid, OH-FPBacid). A very minor route was observed in which a small amount of FPBald was converted to its corresponding alcohol, FPBalc.

Lactating cows were orally dosed with [phenyl-UL-^{14}C]-cyfluthrin at 0.5 mg/kg bw for 5 consecutive days. Cyfluthrin was the major identifiable product in milk (98% TRR, 0.039–0.079 mg/kg). The radiocarbon content of tissues, reported in cyfluthrin equivalents, was highest in liver (0.62 mg/kg), kidney (0.19 mg/kg), and fat (0.12–0.23 mg/kg) with low levels (< 0.05 mg/kg) present in other tissues. Cyfluthrin was the main component of the [^{14}C] in liver and kidney (56–86%) and in muscle and fat (93–100%). Hydrolysis products, formed from hydrolysis of the ester and oxidation, were only detected in liver (14% FPBald), kidney (43% FPBalc) and heart (29%, FPBalc).

Laying hens were orally dosed with [phenyl-UL-^{14}C]-cyfluthrin for 3 consecutive days at 5 mg/kg bw/hen/day. Radioactive residues in eggs collected in the 24 hour period prior to slaughter were 0.05 mg/kg cyfluthrin equivalents. Radioactive residues in tissues of birds slaughtered at 2 h after the last dose were highest in kidney (4.7 mg/kg cyfluthrin equivalents) and liver (3.0 mg/kg) with low levels observed in other tissues. Residues of [^{14}C] in fat were 0.1–0.2 mg/kg while those in muscle were 0.2–0.3 mg/kg, both expressed in cyfluthrin equivalents. The major radiolabelled fraction identified in eggs (56%), fat (75%) and muscle (21–39%) was cyfluthrin. Significant metabolites were FPBacid (12% liver, 11% kidney, 15–21% muscle) and OH-FPBacid (10% liver, 12% kidney, 11-20% muscle).

Plant metabolism

The Meeting received information on the fate of [phenyl-UL-^{14}C]cyfluthrin after foliar application to on apple, cotton, potato, soya bean and wheat and of [cyclopropyl-1-^{14}C]cyfluthrin on wheat. Studies were also available on the fate of [fluorophenyl-UL-^{14}C]cyfluthrin on tomatoes and stored wheat grain.

The metabolism of [^{14}C]cyfluthrin was studied in apples. The majority of the [^{14}C] was associated with the fruit surface (rinses and peel) with 4% or less associated with pulp. Cyfluthrin was the major component of the radioactivity detected at 0 to 28 days after application accounting for 91–84% of the [^{14}C] in rinse solutions and peel. Several minor components, principally FPBald and FPBacid, were present at ≤ 2% of the [^{14}C].

Unchanged cyfluthrin accounted for > 90% of the TRR present tomato fruit and leaves from 1 to 35 days after application to both fruit and leaves.

Potato plants were treated in a greenhouse study with [phenyl-UL-^{14}C]cyfluthrin as a foliar treatment. There was limited translocation of [^{14}C] to potato tubers. Residues in leaves sampled at 0–98 days after application mostly comprised unchanged cyfluthrin (70–95%) together with a number of free and conjugated metabolites (FPBald, FPBacid, OH-FPBacid, FPB) each present at < 5%TRR.

Cyfluthrin was also the major component of [^{14}C] residues following application of [phenyl-UL-^{14}C]cyfluthrin to soya bean plants raised in a greenhouse (43–92% TRR at 4–88 days after application). Individual metabolites identified in whole plants, leaves and stalks were present in both free and conjugated forms and were all individually < 10% TRR (FPBald, OH-FPBacid, FPBacid, FPBalc, Me-FPBacid, FPBamide, FPB). There was limited translocation of [^{14}C] to pods. Incubation of [phenyl-UL-^{14}C]cyfluthrin with soya bean tissue cultures produced a similar range of metabolites.

Cotton plants were treated with [phenyl-UL-^{14}C]cyfluthrin as a foliar treatment and exposed to natural sunlight or grown in a greenhouse. Cyfluthrin was the major component of the [^{14}C] accounting for 61–99% of the TRR at 0–63 days after application. All metabolites identified were present at levels ≤10% TRR in free and conjugated forms (FPBald, FPBalc, FPBacid, Me-FPBacid, OH-FPBacid). Little translocation was observed when individual leaves or bolls were treated. Degradation of cyfluthrin was greater for plants exposed to field conditions than those grown in the glasshouse.

The metabolism of [phenyl-UL-^{14}C]cyfluthrin was also studied in wheat. In forage, straw and heads at up to 21 days after application, 51–69% of [^{14}C] residues were identified as cyfluthrin. Minor metabolites were present at ≤ 5% TRR and occurred in both free and conjugated forms (COOH-cyfluthrin, FPBacid, OH-FPBacid). In a study where [cyclopropyl-1-^{14}C]cyfluthrin and [phenyl-UL-^{14}C]cyfluthrin were applied to wheat plants as seven applications with harvest one day after the last application, cyfluthrin was the major component of [^{14}C] in both heads and straw (77–86%). Metabolites were individually < 10% of TRR as would be expected with application of the last spray so close to harvest. Metabolites identified were DCVA, COOH-cyfluthrin, FPBald, FPBacid, FPBalc and OH-FPBacid.

In a study of the degradation of cyfluthrin on stored wheat grain treated with [fluorophenyl-UL-^{14}C]cyfluthrin at 0.3–0.8 mg/kg, the majority of the radioactivity was located on the grain surface and released into rinse solutions. Unchanged cyfluthrin was the major component identified. After 9 months of storage, 79% of the TRR was cyfluthrin with a further 1.9% identified as FPBald and 0.8% as FPBalc.

Metabolism studies in apples, tomato, cotton, potatoes, soya beans and wheat demonstrated that cyfluthrin was slowly degraded and that the degradation pattern was similar in all crops. The major identified products of cyfluthrin metabolism in plants are analogous to those in mammals. The proposed degradation pathway consists of epimerisation, hydrolysis, ester cleavage, reduction, oxidation and hydroxylation. Cyfluthrin is not systemic, with only limited translocation in plants.

Environmental fate in soil

The half-life for degradation of cyfluthrin in soil is estimated to be < 6 months. Degradation occurred via ester hydrolysis followed by oxidation and mineralisation to $[^{14}C]O_2$.

Photodegradation on soil surfaces is fast with half-lives for degradation of cyfluthrin that are < 20 days. During irradiation with artificial or natural sunlight cyfluthrin in soils underwent ester hydrolysis with FPBald, FPBacid and DCVA identified as degradates.

Hydrolysis in water is pH dependent. Cyfluthrin is considered stable at pH 4 and 7 but is rapidly hydrolysed at pH 9 with a half-life of < 2 days. Two degradation products were identified, FPBald and traces of DCVA, presumably formed from cyfluthrin on hydrolysis of the ester. Abiotic hydrolysis is unlikely to contribute significantly to the degradation of cyfluthrin residues in aquatic systems unless the pH is high.

In confined and field rotational crop studies, no significant residues of cyfluthrin (< 0.01 mg/kg) were found in any crop material. It is concluded that succeeding or rotational crops are unlikely to contain significant residues of cyfluthrin.

Analytical methods

Several different analytical methods have been reported for the analysis of cyfluthrin (and isomers) in plant material and animal commodities. The basic approach involves extraction by homogenisation with an organic solvent mixture incorporating varying proportions of polar and non-polar solvents depending upon the nature of the matrix being extracted and its water content. In general, a primary liquid – liquid partition follows extraction to transfer cyfluthrin residues to less polar solvents prior to column clean-up. Residues are finally determined by gas chromatography with electron capture or mass spectra detectors. In a small number of the methods the four pairs of diastereoisomeric enantiomers that make up cyfluthrin were resolved.

The methods for cyfluthrin and beta-cyfluthrin have been extensively validated with numerous recoveries on a wide range of substrates with LOQs typically in the range 0.01 to 0.05 mg/kg.

Stability of pesticide residues in stored analytical samples

Freezer storage stability was tested for a range of representative substrates. Residues of cyfluthrin were generally stable in crops and their processed products.

Cyfluthrin was stable in homogenized samples fortified at 1 mg/kg and stored frozen for at least 1118 days for apple, 1145 days for cantaloupe, 1130 days for corn, 1145 days for corn oil, 1125 days for corn starch, 1145 days for cucumber, 739 days for oranges, 1145 days for orange juice, 739 days for orange pulp, 1145 days for peanut shells, 1126 days for potatoes, 1130 days for potato chips, 1126 days for potato granules, 95 days for potato peel (wet), 1146 days for potato peel (dry), 102 days for rice, 207 days for rice hulls, 1155 for sugar cane stalks, 1125 days for molasses, 1151 days for tomatoes, 1130 days for wheat and for wheat bran, 1118 days for wheat flour and 1126 days for wheat dust. Incurred cyfluthrin residues were stable in bovine muscle, fat, milk and kidney tissues for at least 6 months and liver for at least 1 month. Fortified liver samples were stable on freezer storage for at least 1 year.

Residue definition

The residue following use of cyfluthrin on crops is predominantly cyfluthrin. Methods are available that can measure cyfluthrin however they do not generally resolve the individual diastereoisomers.

The ratio of cyfluthrin to major metabolites differed in the lactating cow metabolism and feeding studies. In the feeding study, cyfluthrin is the major component of the residue in edible animal commodities, tissues, milk and eggs. Major metabolites derived from hydrolysis of the ester are

DCVA and FPBald, FPBacid and FPBalc. None of these metabolites are unique to cyfluthrin. DCVA is a metabolite common to permethrin, cypermethrin and cyfluthrin while metabolites derived from FPBald are common to cyfluthrin and flumethrin. Separate methods are required for measuring the metabolites. The metabolites were not identified in the evaluation of the toxicological data for cyfluthrin and cypermethrin by the 2006 JMPR as being of toxicological concern.

No metabolism studies were available that specifically used beta-cyfluthrin however the data for cyfluthrin can be used to support beta-cyfluthrin. The residue following its use on crops is predominantly cyfluthrin. Methods are available that can measure both cyfluthrin and beta-cyfluthrin however they do not generally resolve the individual diastereoisomers. Epimerisation of beta-cyfluthrin leads to a change in isomer composition.

Based on the actual residue measured, the Meeting recommended that the residue definition for plant and animal commodities for compliance with MRLs and for estimation of dietary intake should be cyfluthrin. The log K_{ow} of cyfluthrin (pH 6) and the animal metabolism and feeding studies suggest that cyfluthrin should be described as fat-soluble. In the lactating cow metabolism study cyfluthrin residues were approximately 10 times greater in fat than muscle.

Definition of the residue (for compliance with MRL and for estimation of dietary intake) for plant and animal commodities: cyfluthrin (sum of isomers).

The residue is fat-soluble.

Results of supervised residue trials on crops

Supervised trials were available for the use of cyfluthrin on numerous crops: apples, pears, Brassica vegetables (broccoli, Brussels sprouts, cabbage, cauliflower and Chinese cabbage), cotton, oranges, grapefruit, lemons, peppers, potatoes, rape, soya beans, sunflower, sweet corn, mangoes and tomatoes. Specific supervised trials based on unvalidated analytical data (from Craven Laboratories) could not be considered further for sweet corn and soy beans.

Supervised trials were also available for the use of beta-cyfluthrin on several crops: mango, cabbage, cotton, soya beans and rape.

Trial data or relevant GAP was not submitted for maize for which there is a current recommendation for a maximum residue level. The Meeting agreed to withdraw its previous maximum residue level recommendation of 0.05 mg/kg for maize.

Citrus (cyfluthrin)

Cyfluthrin is registered in the USA for use on citrus fruits at 28–112 g ai/ha, PHI 0 days with a maximum seasonal application of 112 g ai/ha and no more than 112 g ai/ha to be applied in a seven day period. Trials conducted in the USA that approximated GAP were often conducted such that more than one plot was treated per trial location. Often treatments involved high and low spray volumes and in some cases different formulations (EC and WP). The Meeting decided that for the purposes of estimation of maximum residue levels that only one result per trial location be used. Seven trials from the USA on grapefruit were selected as complying with US GAP. Residues in whole fruit (n=7) were 0.02, 0.02, 0.03, 0.04, 0.04, 0.07 and 0.11 mg/kg. Residues in oranges from US trials conducted according to GAP (n=7) were 0.03, 0.05, 0.05, 0.05, 0.06, 0.06 and 0.2 mg/kg. Residues in lemons from US trials conducted according to GAP (n=5) were 0.08, 0.08, 0.10, 0.10 and 0.11 mg/kg.

The Meeting decided to combine the trials in the various citrus fruit for the purposes of estimating a maximum residue level and STMR. Residues in rank order are: 0.02, 0.02, 0.03, 0.03, 0.04, 0.04, 0.05, 0.05, 0.05, 0.06, 0.06, 0.07, 0.08, 0.08, 0.10, 0.10, 0.11, 0.11 and 0.2 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for cyfluthrin in citrus whole fruit of 0.3, 0.06 and 0.2 mg/kg respectively.

Apples and pears (cyfluthrin)

Data were available from supervised trials on apples in the USA (GAP: 25–49 g ai/ha, PHI 7 days with a maximum seasonal application of 49 g ai/ha and no more than 49 g ai/ha to be applied in a fourteen day period). Residues of cyfluthrin from twelve trials in USA at 49 g ai/ha with a PHI of 7 days were 0.01, 0.01, 0.02, 0.02, 0.02, 0.02, 0.02, 0.03, 0.03, 0.03, 0.04 and 0.06 mg/kg.

Data were available from supervised trials on pears in the USA (GAP: 25–49 g ai/ha, PHI 7 days with a maximum seasonal application of 49 g ai/ha and no more than 49 g ai/ha to be applied in a fourteen day period). Residues of cyfluthrin from six trials in USA at 49 g ai/ha with a PHI of 7 days were 0.02, 0.02, 0.02, 0.02, 0.04 and 0.05 mg/kg.

The Meeting noted that the use patterns for apple and pears in the USA were the same and that the residues populations for each crop could be used to support the other. Therefore the Meeting decided to combine the data for apples and pears to increase the database for the purposes of estimating a maximum residue level, STMR and HR but to make separate recommendations as a general pome fruit use pattern does not exist in the USA.

Residues in rank order (n=18), median underlined, were: 0.01, 0.01, 0.02, 0.02, 0.02, 0.02, 0.02, 0.02, 0.02, 0.02, 0.02, 0.02, 0.03, 0.03, 0.03, 0.04, 0.04, 0.05 and 0.06 mg/kg.

The Meeting estimated maximum residue levels, STMR values and HR values for cyfluthrin in apples and pears of 0.1, 0.02 and 0.06 mg/kg respectively. The Meeting agreed to withdraw its previous recommendation of 0.5 mg/kg for apples.

Mangoes - cyfluthrin

Results from three supervised trials on mangoes conducted in the Philippines were made available to the Meeting. One trial was conducted using cyfluthrin and two with beta-cyfluthrin.

One cyfluthrin trial matched GAP for the Philippines (2.5 g ai/hL, PHI 14 days) with residues of 0.02 mg/kg in whole fruit. The Meeting considered a single trial insufficient to estimate a maximum residue level for cyfluthrin in mangoes.

Mangoes (beta-cyfluthrin)

Results from two supervised trials on mangoes conducted in the Philippines were made available to the Meeting. One beta-cyfluthrin residue trial matched GAP of the Philippines (10 g ai/hL, PHI 28 days) with residues in fruit of < 0.01 mg/kg. The Meeting considered one trial insufficient to estimate a maximum residue level.

Brassica vegetables (cyfluthrin)

Cyfluthrin is registered in the USA for use on Brassica vegetables at 15–56 g ai/ha, PHI of 0 days and a maximum application per season of 224 g ai/ha and a maximum of 56 g ai/ha in a 7 day period.

Trials were available from USA of Brussels sprouts approximating GAP with residues of 0.39 and 0.44 mg/kg. The Meeting considered two trials are not sufficient to recommend a maximum residue level.

Thirteen trials approximating GAP were available for broccoli: 0.04, 0.05, 0.19, 0.19, 0.19, 0.19, 0.20, 0.26, 0.28, 0.29, 0.30, 0.46 and 1.5 mg/kg. The Meeting estimated a maximum residue level of 2 mg/kg, STMP of 0.20 mg/kg and an HR of 1.5 mg/kg for residues of cyfluthrin in broccoli.

Six trials on cauliflower that matched GAP of the USA were: < 0.01, 0.11, 0.17, 0.31, 0.32 and 0.91 mg/kg. The Meeting estimated a maximum residue level of 2 mg/kg, STMR of 0.24 mg/kg and HR of 0.91 mg/kg for cauliflower.

In eighteen trials on cabbage from the USA that matched GAP residues were: 0.01, 0.03, 0.03, 0.06, 0.07, 0.10, 0.10, 0.18, 0.24, 0.25, 0.33, 0.42, 0.58, 0.62, 1.0, 1.2, 1.3 and 2.1 mg/kg for cabbage. The Meeting estimated a maximum residue level, an STMR value and an HR value for cyfluthrin in cabbages of 4, 0.25 and 2.1 mg/kg respectively.

Cabbage (beta-cyfluthrin)

Results from four supervised trials on cabbage conducted in Germany (no GAP) were made available to the Meeting. The Meeting decided to evaluate the German trials against the GAP of Sweden (10 g ai/ha, PHI 7 days). Four trials matched the GAP of Sweden with beta-cyfluthrin residues of < 0.01, < 0.01, 0.06 and 0.08 mg/kg.

Tomatoes (cyfluthrin)

Trials on tomatoes were reported from the USA (GAP: 28–49 g ai/ha, PHI of 0 days and a maximum application per season of 295 g ai/ha and a maximum of 49 g ai/ha in a 7 day period). All trials were for field grown tomatoes with no data for tomatoes grown under protective cover.

Cyfluthrin residues in eleven trials from the USA matching GAP in rank order were (median underlined): < 0.01, 0.01, 0.02, 0.06, 0.07, 0.07, 0.07, 0.08, 0.08, 0.09 and 0.10 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for cyfluthrin in tomatoes of 0.2, 0.07 and 0.10 mg/kg respectively. The recommendation replaces the previous recommendation of 0.5 mg/kg for tomatoes.

Peppers (cyfluthrin)

Trials on peppers were reported from the USA (GAP: 28–49 g ai/ha, PHI of 7 days and a maximum application per season of 295 g ai/ha and a maximum of 49 g ai/ha in a 7 day period). All trials were for field grown peppers (including chilli) with no data for peppers grown under protective cover.

The Meeting agreed to combine the three trials on chilli peppers (0.06, 0.08, 0.08 mg/kg) with the six trials on sweet peppers (0.01, 0.01, 0.05, 0.06, 0.12 and 0.12 mg/kg) matching GAP in the USA. Residues matching GAP in rank order were (median underlined): 0.01, 0.01, 0.05, 0.06, 0.06, 0.08, 0.08, 0.12 and 0.12 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for cyfluthrin in peppers of 0.2, 0.06 and 0.12 mg/kg respectively. The recommendation for peppers replaces the previous recommendation of 0.2 mg/kg for peppers sweet.

Egg plant (cyfluthrin)

The Meeting noted that the registered use of cyfluthrin in the USA also includes egg plant (GAP: 28–49 g ai/ha, PHI of 7 days and a maximum application per season of 295 g ai/ha and a maximum of 49 g ai/ha in a 7 day period). The meeting considered the results from the trials conducted on peppers and tomatoes that comply with GAP for egg plants could be extrapolated to egg plants for the purposes of estimating maximum residue, STMR and HR levels. Residues on tomatoes that matched GAP for egg plants were < 0.01, 0.01, 0.02, 0.02, 0.03, 0.03, 0.04, 0.04, 0.04, 0.05, 0.05, 0.05, 0.05, 0.05, 0.06, 0.08 and 0.09 mg/kg. Residues on peppers that matched GAP for egg plants were 0.01, 0.01, 0.05, 0.06, 0.06, 0.08, 0.08, 0.12 and 0.12 mg/kg. The Meeting estimated a maximum residue level, an STMR value and an HR value for cyfluthrin in egg plant of 0.2, 0.05 and 0.12 mg/kg respectively.

Sweet corn (cyfluthrin)

Trials on sweet corn were reported from the USA (GAP: 15–49 g ai/ha, PHI of 0 days and a maximum application per season of 493 g ai/ha and a maximum of 49 g ai/ha in a 2 day period).

Cyfluthrin residues in three trials from the USA matching GAP in rank order were (median underlined): < 0.01 (2) and 0.01 mg/kg.

The Meeting considered three trials insufficient to estimate a maximum residue level for cyfluthrin in sweet corn.

Potatoes (cyfluthrin)

Trials on potatoes were reported from Canada (no GAP) and the USA (GAP: 15–49 g ai/ha, PHI of 0 days and a maximum application per season of 295 g ai/ha and a maximum of 49 g ai/ha in a 7 day period).

Cyfluthrin residues in seventeen trials from the USA matching GAP in rank order were (median underlined): < 0.01 (17) mg/kg. Residues were not detected in residue trials and metabolism results on plants including potatoes confirm that cyfluthrin is not translocated by plants. The Meeting considered detectable residues in potato tubers to be unlikely.

The Meeting estimated a maximum residue level, an STMR value and an HR value for cyfluthrin in potatoes of 0.01*, 0 and 0 mg/kg respectively.

Soya beans (cyfluthrin)

Trials on soya beans were reported from the USA (GAP: 15–49 g ai/ha, PHI of 45 days and a maximum application per season of 196 g ai/ha and a maximum of 49 g ai/ha in a 7 day period).

Cyfluthrin residues in five trials from the USA matching GAP in rank order were (median underlined): < 0.01 (5) mg/kg. In addition, residues ranging from < 0.01 to 0.02 mg/kg were reported in unvalidated trials.

The Meeting considered five trials insufficient to estimate a maximum residue level for cyfluthrin in soya beans (dry).

Soya beans (beta-cyfluthrin)

Four trials on soya beans employing beta-cyfluthrin were reported from Brazil (12.5 g ai/ha, PHI 21 days) that complied with GAP for Brazil. Residues were < 0.01 and < 0.05 (3) mg/kg. The Meeting considered four trials on soya beans insufficient to estimate a maximum residue level for residues arising from the use of beta-cyfluthrin in soya beans.

Cotton seed (cyfluthrin)

Trials on cotton were reported from the USA (GAP: 15–49 g ai/ha, PHI of 0 days and a maximum application per season of 560 g ai/ha and a maximum of 56 g ai/ha in a 3 day period).

Cyfluthrin residues in seven trials from the USA matching GAP in rank order were (median underlined): < 0.01, 0.02, 0.03, < 0.1, < 0.1, 0.1 and 0.52 mg/kg.

The Meeting estimated a maximum residue level and an STMR value for cyfluthrin in cotton seed of 0.7 and 0.1 mg/kg respectively. The recommendation for cotton seed replaces the previous recommendation of 0.05 mg/kg.

Cotton seed (beta-cyfluthrin)

Beta-cyfluthrin trials on cotton were reported from the USA (GAP: 7–28 g ai/ha, PHI of 0 days and a maximum application per season of 280 g ai/ha and a maximum of 28 g ai/ha in a 3 day period). Beta-cyfluthrin residues in three trials from the USA matching GAP in rank order were: < 0.1, < 0.1 and 0.38 mg/kg.

Rape seed (cyfluthrin)

Cyfluthrin trials on rape were reported from Germany (no GAP). The Meeting decided to assess the German trials against the GAP of Belgium (15 g ai/ha, application according to growth stage, maximum 2 applications per crop, one spray from seed to 3 leaf BBCH 10–13, one at bud development BBCH 50–59 and one at pod development BBCH 70-75). Seven trials matched GAP of Belgium with residues of < 0.05 (6) and 0.05 mg/kg.

The Meeting estimated a maximum residue level and an STMR value for cyfluthrin in rape seed of 0.07, 0.05 and < 0.05 mg/kg respectively. The recommendation for rape seed replaces the previous recommendation of 0.05 mg/kg.

Rape seed (beta-cyfluthrin)

Trials conducted on rape using beta-cyfluthrin trials were reported from the Germany (GAP: 5.2–7.7 g ai/ha, 0.2-0.3 g ai/hL, PHI of 56 days). Beta-cyfluthrin residues in nine trials from the Germany matching GAP in rank order were (median underlined): < 0.01, < 0.01, 0.01, < 0.02 (4), < 0.05, and < 0.05 mg/kg.

Sunflower seed (cyfluthrin)

Trials on sunflower were reported from Canada (no GAP) and the USA (GAP: 15–49 g ai/ha, PHI of 30 days and a maximum application per season of 147 g ai/ha and a maximum of 49 g ai/ha in a 7 day period).

Cyfluthrin residues in five trials from Canada and the USA matching GAP of the USA in rank order were (median underlined): < 0.01 (3) and 0.01 (2) mg/kg.

The Meeting considered five trials insufficient to estimate a maximum residue level for cyfluthrin in sunflower seed.

Animal feedstuffs

Sweet corn forage (cyfluthrin)

Field trials on sweet corn were made available to the Meeting from the USA (GAP: 15–49 g ai/ha, PHI of 0 days and a maximum application per season of 493 g ai/ha and a maximum of 49 g ai/ha in a 2 day period).

Residues on sweet corn forage were 3.7, 3.7 and 7.7 mg/kg (fresh weight basis).

Residues on sweet corn cannery waste were 0.20, 0.43 and 0.90 mg/kg (fresh weight basis).

The Meeting considered three trials insufficient to estimate median and high residues for sweet corn livestock feeds.

Cotton gin-trash (cyfluthrin)

Cyfluthrin field trials on cotton were made available to the Meeting from the USA (GAP: 15–49 g ai/ha, PHI of 0 days and a maximum application per season of 560 g ai/ha and a maximum of 56 g ai/ha in a 3 day period; Do not graze treated fields).

Cyfluthrin residues on cotton gin-trash were 2.4, 2.8 and 9.2 mg/kg (fresh weight basis). The Meeting considered three trials insufficient to estimate median residues for cotton gin-trash as a livestock feed.

Cotton gin-trash (beta-cyfluthrin)

Beta-cyfluthrin field trials on cotton were made available to the Meeting from the USA (GAP: 7–28 g ai/ha, PHI of 0 days and a maximum application per season of 280 g ai/ha and a maximum of 28 g ai/ha in a 3 day period; Do not graze treated fields).

Beta-cyfluthrin residues on cotton gin-trash were 2.3, 2.6, 2.9 mg/kg (fresh weight basis). The Meeting considered three trials insufficient to estimate median residues for cotton gin-trash as a livestock feed.

Rape forage and straw (cyfluthrin)

Field trials on rape seed were made available to the Meeting from the Germany (GAP: 15 g ai/ha, application according to growth stage, maximum 2 applications per crop, one spray from seed to 3 leaf BBCH 10–13, one at bud development BBCH 50-59 and one at pod development BBCH 70–75).

Residues on rape straw were < 0.02, < 0.02, < 0.02, < 0.02, < 0.02 and 0.06 mg/kg. The Meeting estimated an STMR and a high residue value for cyfluthrin in rape straw of < 0.02 and 0.06 mg/kg, respectively, both on an as received basis.

As the registered use pattern for rape in Germany does not restrict grazing, the Meeting assumed that according to GAP in Germany rape could be grazed at the earliest time after application. Residues on rape forage were 0.13, 0.15, 0.18, 0.20, 0.21, 0.27, 0.32 and 0.34 mg/kg (fresh weight basis). The Meeting estimated an STMR and a high residue value for cyfluthrin in forage of 0.205 and 0.34 mg/kg, respectively, both on a fresh weight basis.

Rape fodder (beta-cyfluthrin)

For beta-cyfluthrin trials on rape were reported from Germany (GAP: 5.2–7.7 g ai/ha, 0.2–0.3 g ai/hL, PHI of 56 days). Beta-cyfluthrin residues from rape straw in seven trials from Germany matching GAP in rank order were (median underlined): < 0.05, < 0.05, < 0.05, 0.02, 0.06, 0.07, 0.08 mg/kg (fresh weight basis). As the directions for use in Germany do not provide specific guidance for livestock feeding it is assumed forage rape can be grazed without restriction anytime after application. Residues in rape forage at 0 days after application were: < 0.05, 0.08, 0.16, 0.17, 0.19, 0.24, 0.26, 0.27 and 0.33 mg/kg. The Meeting estimated an STMR and a high residue value for cyfluthrin in rape forage of 0.19 and 0.33 mg/kg, respectively, both on a fresh weight basis.

Soya bean forage and vines (cyfluthrin)

Field trials on soya beans were made available to the Meeting from the USA (GAP: 15–49 g ai/ha, PHI of 45 days and a maximum application per season of 196 g ai/ha and a maximum of 49 g ai/ha in a 7 day period; dry vines and green forage may be fed 45 and 15 days, respectively after last application).

Residues on soya bean forage were 0.10, 0.26, 0.33, 0.34, 0.38, 0.45, 0.96 and 3.3 mg/kg (fresh weight basis). The Meeting estimated an STMR and a high residue value for cyfluthrin in soya bean forage of 0.36 and 3.3 mg/kg, respectively, both on a fresh weight basis.

Residues on soya bean dry vines were 0.01, 0.09, 0.21, 0.31 and 2.66 mg/kg (fresh weight basis). The Meeting considered five trials insufficient to estimate median and high residues for soya vines that may be used as livestock feed.

Sunflower fodder (cyfluthrin)

Trials on sunflowers were reported from Canada (no GAP) and the USA (GAP: 15–49 g ai/ha, PHI of 30 days and a maximum application per season of 147 g ai/ha and a maximum of 49 g ai/ha in a 7 day period; pre-grazing or foraging interval, 30 days).

Cyfluthrin residues in sunflower fodder in five trials from Canada and the USA matching GAP of the USA were 0.04, 0.13, 0.30, 0.33 and 0.63 mg/kg (fresh weight basis). The Meeting estimated an STMR and a high residue value for cyfluthrin in sunflower fodder of 0.30 and 0.63 mg/kg, respectively, both on a fresh weight basis.

Fate of residues during processing

The fate of cyfluthrin residues has been examined in potato, cabbage, tomato, citrus fruit, apples and oil seed crops processing studies. Processing of tomatoes into pulp and paste showed a slight increase of cyfluthrin residues in the processed commodities compared to the RAC. Whilst there was a decrease in residues found in the corresponding juice, ketchup and purée. Citrus and apples also both showed a decrease in residues found in the juice, but a slight increase in pomace and/or oil and molasses. There was a concentration into the oil of cottonseed and sunflower. Processing studies on potatoes, cabbages, soya bean and rape seed did not show any indication regarding the fate of beta-cyfluthrin/cyfluthrin residues during processing as residues in the RAC or processed products were all below the LOQ. Estimated processing factors, HRs and STMRs are summarized below.

Summary of processing factors for cyfluthrin residues.

Raw agricultural commodity (RAC)	Processed commodity	Calculated processing factors	PF (Mean, median or best estimate)	RAC-STMR	RAC-STMR×PF
Orange	Pulp dry	5.3	5.3	0.06	0.318
Apple	Pomace, dry	0.11, 16	16	0.02	0.32
Cotton	Hulls	1.9	1.9	0.1	0.19
Cotton	Meal	0.08	0.08		0.008
Cotton	Oil, crude	1.9	1.9		0.19
Cotton	Oil, refined	1.2	1.2		0.12

The Meeting decided to make maximum residue level recommendations for citrus pulp (dry) and cotton seed hulls. Based on an estimated high residue value of 1.06 mg/kg (5.3 × 0.2 mg/kg) for citrus pulp (dry), the meeting recommended a maximum residue level of 2 mg/kg for citrus pulp (dry). The Meeting also recommended a maximum residue level of 1 mg/kg for cotton seed oil, crude based on an estimated high residue of 0.988 mg/kg (1.9 × 0.22 mg/kg).

The Meeting also decided to use the default generic processing factor of 7 to estimate a maximum residue level for chilli pepper (dry) of 1 mg/kg based on an HR-P of 0.84 mg/kg (7 × 0.12) and STMR-P of 0.42 mg/kg (7 × 0.06).

Residues in animal commodities

Farm animal dietary burden

The Meeting estimated the dietary burden of cyfluthrin in farm animals on the basis of the diets listed in Annex 6 of the 2006 JMPR Report (OECD Feedstuffs Derived from Field Crops). Calculation from highest residue, STMR (some bulk commodities) and STMR-P values provides the levels in feed suitable for estimating MRLs, while calculation from STMR and STMR-P values for feed is suitable for estimating STMR values for animal commodities. The percentage dry matter is taken as 100% when the highest residue levels and STMRs are already expressed as dry weight.

Estimated maximum and mean dietary burdens of farm animals

Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are provided in Annex 6. The calculations were made according to the animal diets from US-Canada, EU and Australia in the OECD Table (Annex 6 of the 2006 JMPR Report).

	Animal dietary burden, cyfluthrin, ppm of dry matter diet					
	US-Canada		EU		Australia	
	max	mean	max	mean	max	mean
Beef cattle	1.87	0.31	3.00	0.49	5.89 [1]	0.68 [3]
Dairy cattle	1.84	0.26	3.00 [2]	0.49 [4]	2.47	0.36
Poultry - broiler	0.009	0.009	0.0152	0.015	0.003	0.003
Poultry - layer	0.009	0.009	1.3 [5]	0.16 [6]	0.003	0.003

[1] Highest maximum beef or dairy cattle dietary burden suitable for MRL estimates for mammalian meat

[2].Highest maximum dairy cattle dietary burden suitable for MRL estimates for mammalian milk

[3]Highest mean beef or dairy cattle dietary burden suitable for STMR estimates for mammalian meat.

[4] Highest mean dairy cattle dietary burden suitable for STMR estimates for milk.

[5]Highest maximum poultry dietary burden suitable for MRL estimates for poultry meat and eggs.

[6]Highest mean poultry dietary burden suitable for STMR estimates for poultry meat and eggs.

The cyfluthrin dietary burdens for animal commodity MRL and STMR estimation (residue levels in animal feeds expressed on dry weight) are: beef cattle 5.89 and 0.68 ppm, dairy cattle 3.06 and 0.50 ppm and poultry 1.3 and 0.16 ppm.

Farm animal feeding studies

The Meeting received information on the residue levels arising in animal tissues and milk when dairy cows were dosed with cyfluthrin for 28 days at the equivalent of 4.5, 13 and 40 ppm in the diet. Average residues in milk of the 40 ppm dose group were 0.22 mg/kg at day 14 and 0.14 mg/kg at day 28. Cyfluthrin residues in the fat were higher than in other tissues. Transfer factors (average residue level in tissue ÷ residue level in feed) for each tissue and milk for the three dosing levels (3 animals per dose group) were: fat, 0.056, 0.054, 0.066; muscle, < 0.002, < 0.001, 0.00075; kidney, 0.0042; liver, 0.0032; milk 28 days, 0.0037, 0.0036, 0.0036.

In an additional dosing study conducted at levels equivalent to 11, 36 and 112 ppm in the diet average residues in milk at day 28 were 0.45 mg/kg for the 112 ppm dose group. As for the previous study, residues were highest in fat with only low levels of cyfluthrin detected in other tissues. Transfer factors for each tissue and milk for the three dosing levels (3 animals per dose group) were: fat, 0.11, 0.074, 0.061; muscle, < 0.0009, 0.001, 0.00063; kidney, < 0.0009, < 0.0008, 0.00045; liver, < 0.0036, < 0.00028, 0.00018; milk 28 days, 0.0055, 0.0033, 0.0041.

The Meeting also received information on the residue levels arising in tissues and eggs when laying hens were dosed with cyfluthrin for 28 days at the equivalent of 6 and 20 ppm in the diet. Residues in eggs were below the LOQ for both feed levels. At the 2 ppm feeding level the residues in tissues were below the LOQ of the analytical methods. For the 20 ppm feed level, residues in fat were substantially higher than residues in other tissues 0.05 mg/kg compared to < 0.01-0.01 mg/kg. Transfer factors based on residues for fat were 0.0025 for the 20 ppm feed levels. Transfer factors (mean residue) for muscle and liver were < 0.0005 and < 0.0005 respectively for the 20 ppm feeding level while that for skin was 0.0005.

Farm animal direct treatment

No studies were received on the residues of cyfluthrin arising from direct animal treatment. The Meeting noted that JECFA has evaluated cyfluthrin residues arising from direct animal treatment at its 48th Meeting in 1997 and recommended maximum residue limits for cattle of 20 μg/kg for muscle, liver and kidney, 40 μg/kg for milk and 200 μg/kg for fat. The marker residue that applied to the residue limits was cyfluthrin.

Animal commodity maximum residue levels

The maximum dietary burden for beef and dairy cattle is 5.89 and 3.06 ppm respectively, so the levels of residues in tissues can be obtained by interpolation between the high residues obtained in tissues and at the 4.5 and 13 ppm feeding levels for milk, muscle and fat and from the 40 ppm feed level for kidney and liver as these are the only kidney and liver samples subjected to strong extraction required to release the majority of cyfluthrin residues. Maximum residues expected in tissues are: fat 0.37 mg/kg, muscle < 0.01 mg/kg, liver 0.021 mg/kg, kidney 0.027 mg/kg and the mean residue for milk 0.0136 mg/kg. No data was available on the partitioning of residues in milk between aqueous and fat phases of milk.

The Meeting estimated maximum residue levels for meat (from mammals other than marine mammals) 1 mg/kg (fat); kidney of cattle, goats, pigs and sheep 0.05 mg/kg; liver of cattle, goats, pigs and sheep 0.05 mg/kg and milks 0.04 mg/kg. The recommendation of 0.04 mg/kg milk replaces the previous recommendation of ML 0812 Cattle milk 0.01 F mg/kg, which also incorporated direct animal treatment. The Meeting noted the recommendation for cattle milk arising from exposure to cyfluthrin through the cattle diet is the same as proposed by JECFA for direct animal treatment.

The STMR dietary burdens for beef and dairy cattle are 0.68 and 0.50 ppm respectively. Transfer factors from the average residues from the 4.5 ppm feeding level were used to estimate STMR values as for cyfluthrin. The estimated STMRs are: meat (from mammals other than marine mammals) < 0.01 mg/kg, fat (from mammals other than marine mammals) 0.0378 mg/kg, kidney of cattle, goats, pigs and sheep < 0.01 mg/kg, liver of cattle, goats, pigs and sheep < 0.01 mg/kg and milks 0.0027 mg/kg.

The highest individual tissue residue from the relevant feeding group was used in conjunction with the highest residue dietary burden to calculate the likely highest animal commodity residue level. As only a single animal is available per feeding group, the tissue residues from the animals in the relevant feeding groups were used in conjunction with the STMR dietary burden to estimate the animal commodity STMR values. For milk, the mean milk residue at the plateau level from the relevant feeding group was used to estimate both the maximum residue level and the STMR.

Dietary burden (mg/kg)[1] Feeding level [ppm][2]		Cyfluthrin residues, mg/kg[3]								
		Milk	Fat		Muscle		Liver		Kidney	
		Mean	High	mean	High	mean	high	mean	High	mean
MRL beef	(5.89) [4.5] high		*(0.37)* 0.30		*(< 0.01)* < 0.01		*(0.021)* 0.14[4]		*(0.027)* 0.18[4]	
MRL dairy	(3.06) [4.5] av	*(0.0136)* 0.02								
STMR beef	(0.68) [4.5] av		*(0.0378)* 0.25		*(< 0.01)* < 0.01		*(< 0.01)* < 0.01		*(< 0.01)* < 0.01	
STMR dairy	(0.50) [4.5] av	*(0.0022)* 0.02								

[1] Values in parentheses are the estimated dietary burdens

[2] Values in square brackets are the actual feeding levels in the transfer study

[3] Residue values in parentheses in italics are interpolated from the dietary burden, feeding levels in the transfer study and the residues found in the transfer study. High is the highest individual animal tissue residue in the relevant feeding group. Mean is mean animal tissue (or milk) residue in the relevant feeding group.

[4]Residue values for kidney and liver were obtained from the dosing level equivalent to 40 ppm in the feed as only these samples were subject to reanalysis using a stronger extraction process

The maximum dietary burden for poultry is 1.3 ppm. No residues above the LOQ of the analytical method used were observed in the feeding study for laying hens at the lowest dose level equivalent to 2 ppm in the diet. Maximum residues expected are: muscle, fat, liver, kidney and eggs are all < 0.01 mg/kg.

The Meeting estimated maximum residue levels for poultry meat 0.01(*) mg/kg (fat); poultry offal 0.01(*) and eggs 0.01 (*) mg/kg.

As no residues are observed at the maximum feeding level for poultry, the STMRs for poultry meat, edible offal and eggs are the same as the maximum residue levels.

DIETARY RISK ASSESSMENT

Long-term intake

The evaluation of cyfluthrin has resulted in recommendations for MRLs and STMRs for raw and processed commodities. Consumption data were available for 22 food commodities and were used in the dietary intake calculation. The results are shown in Annex 3.

The International Estimated Daily Intakes for the 13 GEMS/Food regional diets, based on estimated STMRs were in the range 0–2% of the maximum ADI of 0.04 mg/kg bw (Annex 3). The Meeting concluded that the long-term intake of residues of cyfluthrin from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The international estimated short-term intake (IESTI) for cyfluthrin was calculated for the food commodities (and their processing fractions) for which maximum residue levels and HRs were estimated and for which consumption data were available. The results are shown in Annex 4.

For the general population the IESTI varied from 0–120% of the ARfD (0.04 mg/kg bw) while for children the IESTI varied from 0–240% of the ARfD. The IESTI (as a% of the ARfD) for broccoli for children was 120% and 70% for the general population, 240% for head cabbage for children and 100% for the general population.

The Meeting concluded that the short-term intake of residues of cyfluthrin resulting from uses that have been considered by the JMPR, except the uses on broccoli and head cabbage, is unlikely to present a public health concern.

The Meeting noted that no residue data relating to alternative GAP were submitted for broccoli and head cabbage. The information provided to the JMPR precludes an estimate that the dietary intake would be below the ARfD for consumption for broccoli and head cabbage by children.

5.8 LAMBDA-CYHALOTHRIN (146)

TOXICOLOGY

Lambda-cyhalothrin, the ISO approved common name for (*R*)-cyano(3-phenoxyphenyl)methyl (1*S*,3*S*)-rel-3-[(1*Z*)-2-chloro-3,3,3-trifluoro-1-propenyl]-2,2-dimethylcyclopropanecarboxylate is a synthetic cyano-containing type II pyrethroid insecticide (CAS No. 91465-08-6).

Cyhalothrin (CAS No. 68085-85-8) was evaluated by JMPR in 1984, when an ADI of 0–0.02 mg/kg bw was established based on a NOAEL of 20 ppm, equal to 2 mg/kg bw per day, identified on the basis of clinical signs in a 2-year study in mice; a NOAEL of 30 ppm, equal to

1.5 mg/kg bw per day, identified on the basis of decreased body-weight gain in a three-generation study in rats; and a NOAEL of 2.5 mg/kg bw per day, identified on the basis of neurotoxicity in a 6-month study in dogs, and using a safety factor of 100.

At its meeting in 2000, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) established a temporary ADI of 0–0.002 mg/kg bw based on a LOEL of 1 mg/kg bw per day for induction of liquid faeces in dogs in a 26-week study, and using a safety factor of 500. The high safety factor was used to compensate for the absence of a no-observed-effect level (NOEL) in this study.

At its meeting in 2004, JECFA concluded that the toxicity of cyhalothrin is similar in rats and dogs. The Committee decided that the temporary ADI could be replaced by an ADI of 0–0.005 mg/kg bw, which was determined by dividing the LOEL of 1 mg/kg bw per day in dogs (also the NOEL for rats) by a safety factor of 200. The safety factor incorporated a factor of 2 to compensate for the absence of a NOEL in dogs.

Lambda-cyhalothrin consists of two of the four enantiomers (i.e., the *cis* 1*R*α*S* and *cis* 1*S*α*S* enantiomeric pair) of cyhalothrin. One of the two enantiomers of lambda-cyhalothrin is the insecticidally active gamma-cyhalothrin (CAS No. 76703-62-3). Cyhalothrin comprises about 50% lambda-cyhalothrin.

Lambda-cyhalothrin was evaluated by the present Meeting within the Periodic Re-evaluation Programme of the CCPR. For the present re-evaluation, studies with cyhalothrin and lambda-cyhalothrin were available.

For lambda-cyhalothrin, specifications were established by the FAO/WHO Joint Meeting on Pesticide Specifications (JMPS) and published as *WHO specifications and evaluations for public health pesticides: lambda-cyhalothrin* [27] (technical material, 2003). For other formulations, specifications also exist.

All pivotal studies with cyhalothrin and lambda-cyhalothrin were certified as being compliant with GLP.

Biochemical aspects

Oral doses of cyhalothrin were readily but incompletely absorbed (30–40% of radiolabel was recovered in urine) in rats and dogs. Peak blood concentrations were reached after 4–7 h. In male rats treated with replacement bile obtained from treatment-naive rats, biliary excretion was about 11%. At a low dose, most (70%) of the administered material was excreted in the faeces and urine within 24 h. After 7 days, 2–3% of the cyhalothrin administered persisted as unchanged residue in fat. Metabolism in rats and dogs was similar, involving initial cleavage of the molecule at the ester bond. In rats dosed with cyhalothrin, major metabolites identified in urine were the sulfate conjugate of 3-(4'-hydroxyphenoxy) benzoic acid (compound XXIII) glucuronide conjugate of (1*RS*)-*cis*-3-(2-chloro-3,3,3-trifluoropropenyl)-2,2-dimethylcyclopropanoic acid (i.e., the compound 1a glucuronide). Minor metabolites identified were unconjugated compound XXIII and 3-phenoxybenzoic acid (compound V).

In volunteers given a single dose of lambda-cyhalothrin in capsules, serum and urine contained the metabolites compound XXIII, compound V and compound 1a ((1*RS*)-*cis*-3-(*Z*-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanoic acid, TMFVCA). Their presence suggests that the initial metabolism of this compound in humans is similar to that in rats and dogs.

[27] Available from: http://www.who.int/whopes/quality/en/Lambda-cyhalothrin_eval_specs_WHO_2003.pdf

Toxicological data

The acute oral LD_{50} of lambda-cyhalothrin in rats was 79 mg/kg bw in males and 56 mg/kg bw in females. The observed clinical signs (ataxia, decreased activity, tiptoe gait, splayed gait, loss of stability, dehydration, urinary incontinence, hunched posture, piloerection, salivation, ungroomed appearance and pinched-in sides) were typical of this class of pyrethroids.

In studies with lambda-cyhalothrin in rats, the inhalation LC_{50} value was 60 mg/m^3 (0.06 mg/L), and the dermal LD_{50} was 632 mg/kg bw in males and 696 mg/kg bw in females. Lambda-cyhalothrin was not irritating to the skin and only slightly irritating to the eyes. With respect to dermal sensitization, the results of a maximization test with lambda-cyhalothrin in guinea-pigs were inconclusive. Technical-grade cyhalothrin has been reported to cause skin sensitization in a Buehler test and a maximization test in guinea-pigs.

In a 90-day feeding study in rats given cyhalothrin, the NOAEL was 50 ppm, equal to 2.6 mg/kg bw per day, on the basis of reduced body-weight gain and food consumption. In a 90-day feeding study in rats given lambda-cyhalothrin, the NOAEL was 50 ppm, equivalent to 2.5 mg/kg bw per day, on the basis of reduced body-weight gain and food consumption. In a 26-week study in dogs fed capsules containing cyhalothrin and a 1-year study in dogs fed capsules containing lambda-cyhalothrin, increased incidences of liquid faeces was observed, with an overall NOAEL of 0.1 mg/kg bw per day. The increased incidences of liquid faeces were observed from the first week of treatment. Other pyrethroids produce this effect, which may be the consequence of the local gastrointestinal equivalent of paraesthesia in the skin. In the two studies in dogs, signs of systemic neurotoxicity (ataxia, tremors, and occasionally convulsions) were observed, with an overall NOAEL of 0.5 mg/kg bw per day. Signs of systemic neurotoxicity were observed from the first week and generally occurred within a few hours after treatment.

In a 2-year dietary study with cyhalothrin in mice, the NOAEL was 20 ppm, equal to 1.8 mg/kg bw per day, on the basis of clinical signs (piloerection and hunched posture) in males. An increase in the incidence of mammary adenocarcinomas in the groups receiving the intermediate or highest dose was at the upper limit of the range for historical controls and was not dose-related. The Meeting therefore considered that it was unlikely that these tumours were caused by treatment with cyhalothrin.

In a 2-year dietary study with cyhalothrin in rats, the NOAEL was 50 ppm, equal to 2.3 mg/kg bw per day, on the basis of a reduction in body-weight gain. No treatment-related changes in tumour incidence were observed in this study.

The Meeting concluded that cyhalothrin is not carcinogenic in rodents.

Lambda-cyhalothrin was tested for genotoxicity in an adequate range of assays, both in vitro and in vivo. No evidence for genotoxicity was observed in any test. A number of published studies, largely from the same laboratory, have reported significant increases in DNA damage in vitro (Comet assay) and chromosomal aberrations in vitro and in vivo. The materials tested in these studies were either commercial formulations of unknown composition or were inadequately described. In view of the uniform finding of a lack of genotoxicity in those studies in which lambda-cyhalothrin was adequately characterized, the Meeting concluded that lambda-cyhalothrin is unlikely to be genotoxic.

In view of the lack of genotoxicity of lambda-cyhalothrin and the absence of carcinogenicity shown by cyhalothrin in mice and rats, the Meeting concluded that lambda-cyhalothrin is unlikely to pose a carcinogenic risk to humans.

In a multigeneration dietary study with cyhalothrin in rats, the NOAEL for parental toxicity was 30 ppm, equivalent to 2.0 mg/kg bw per day, on the basis of a reduction in body-weight gain. The NOAEL for offspring toxicity was 30 ppm, equivalent to 2 mg/kg bw per day, on the basis of reduced body-weight gain during lactation. The NOAEL for reproductive toxicity was 100 ppm, equivalent to 6.7 mg/kg bw per day, i.e., the highest dose tested.

The effect of oral exposure to cyhalothrin on prenatal development was investigated in rats and rabbits. In a study of developmental toxicity in rats treated by gavage, the NOAEL for maternal toxicity was 10 mg/kg bw per day on the basis of a reduction in body weight and loss of limb coordination. The NOAEL for foetal toxicity was 15 mg/kg bw per day, i.e., the highest dose tested. In a study of developmental toxicity in rabbits treated by gavage, the NOAEL for maternal toxicity was 10 mg/kg bw per day on the basis of reduced body-weight gain and food consumption. The NOAEL for fetotoxicity was 30 mg/kg bw per day, i.e., the highest dose tested.

In a study of acute neurotoxicity in rats given lambda-cyhalothrin by gavage, the NOAEL was 2.5 mg/kg bw per day on the basis of signs of neurotoxicity (increased breathing rate, urinary incontinence, salivation, reduced response to sound).

In a comparative study on the acute effects of pyrethroids in rats treated by oral gavage, in which the data were analysed using a nonlinear exponential threshold model, lambda-cyhalothrin showed decreased motor activity with a benchmark threshold dose (estimate of the highest no-effect level at which the rats would not display any decrease in motor activity) of 0.5 mg/kg bw. In a 90-day dietary study, the NOAEL was 150 ppm (equal to 11 mg/kg bw per day), i.e., the highest dose tested.

In a study of developmental neurotoxicity in rats, the NOAEL for maternal toxicity was 60 ppm, equal to 4.9 mg/kg bw per day, on the basis of reduced body-weight gain during gestation. The NOAEL for offspring toxicity was 60 ppm, equal to 10.7 mg/kg bw per day, based on maternal lambda-cyhalothrin intake, on the basis of reduced body-weight gain during lactation. No evidence for developmental neurotoxicity was observed.

In case reports in humans, no systemic effects were reported. In most cases exposure was by the dermal and inhalation routes. Predominant signs were skin paraesthesia, numbness, irritation of the skin, red eyes, coughing and sneezing.

No toxicological studies on metabolites of cyhalothrin were available. However, the Meeting considered it likely that the metabolites would be less neurotoxic than cyhalothrin, as none contains an intact pyrethroid structure.

The Meeting concluded that the existing database on lambda-cyhalothrin was adequate to characterize the potential hazards to foetuses, infants and children.

Toxicological evaluation

Although increased incidences of liquid faeces were observed in dogs given lambda-cyhalothrin/cyhalothrin, which may represent a consequence of a local gastrointestinal equivalent of paraesthesia in the skin, the Meeting considered that it was not appropriate to base the ADI and ARfD on local effects on the gastrointestinal tract, observed after bolus administration.

The most sensitive systemic effect of lambda-cyhalothrin/cyhalothrin was neurotoxicity (decreased motor activity), which was observed in a study of acute toxicity in rats given lambda-cyhalothrin orally, with a threshold dose of 0.5 mg/kg bw, and in repeat-dose studies with cyhalothrin and lambda-cyhalothrin in dogs treated orally (ataxia, tremors, occasionally convulsions) with a NOAEL of 0.5 mg/kg bw per day. On the basis of these effects, the Meeting established a group ADI for cyhalothrin and lambda cyhalothrin of 0–0.02 mg/kg bw, using a safety factor of 25. Because lambda-cyhalothrin is relatively rapidly absorbed and excreted and the neurotoxic effects are rapidly reversible and dependent on C_{max}, the Meeting considered it appropriate to adjust the safety factor for the reduced variability in C_{max} compared with AUC. The Meeting considered that the ADI of 0.02 mg/kg bw is adequately protective against the other, non-neurotoxic effects of lambda-cyhalothrin/cyhalothrin observed in short- and long-term studies with repeated doses, and in studies of reproductive and developmental toxicity, where the use of a safety factor of 100 would be appropriate.

The Meeting established a group ARfD for cyhalothrin and lambda-cyhalothrin of 0.02 mg/kg bw on the basis of systemic neurotoxicity (decreased motor activity) observed in a study of acute toxicity in rats given lambda-cyhalothrin orally with a threshold dose of 0.5 mg/kg bw per day, and in repeat-dose studies with cyhalothrin and lambda-cyhalothrin in dogs treated orally, in which neurotoxic effects (ataxia, tremors, occasionally convulsions) occurred during the first week, within a few hours after treatment, with an overall NOAEL of 0.5 mg/kg bw per day, and using a safety factor of 25. For the same reasons as described above, the Meeting considered it appropriate to adjust the safety factor for the reduced variability in C_{max} compared with AUC.

A toxicological monograph was prepared.

Levels relevant for risk assessment

(a) Cyhalothrin

Species	Study	Effect	NOAEL	LOAEL
Mouse	Two-year study of toxicity and carcinogenicity [a]	Toxicity	20 ppm, equal to 1.8 mg/kg bw per day	100 ppm, equal to 9.2 mg/kg bw per day
		Carcinogenicity	500 ppm, equal to 51 mg/kg bw per day[c]	—
Rat	Ninety-day study of toxicity[a]	Toxicity	50 ppm, equal to 2.6 mg/kg bw per day	250 ppm, equal to 14 mg/kg bw per day
	Two-year study of toxicity and carcinogenicity [a]	Toxicity	50 ppm, equal to 2.3 mg/kg bw per day	250 ppm, equal to 12 mg/kg bw per day
		Carcinogenicity	250 ppm, equal to 12 mg/kg bw per day[c]	—
	Two-generation study of reproductive toxicity[a]	Parental toxicity	30 ppm, equivalent to 2.0 mg/kg bw per day	100 ppm, equivalent to 6.7 mg/kg bw per day [d]
		Offspring toxicity	30 ppm, equivalent to 2.0 mg/kg bw per day	100 ppm, equivalent to 6.7 mg/kg bw per day [d]
		Reproductive toxicity	100 ppm, equivalent to 6.7 mg/kg bw per day[c]	—
	Developmental toxicity[b]	Maternal toxicity	10 mg/kg bw per day	15 mg/kg bw per day
		Fetotoxicity	15 mg/kg bw per day [c]	—
Rabbit	Developmental toxicity[b]	Maternal toxicity	10 mg/kg bw per day	30 mg/kg bw per day
		Fetotoxicity	30 mg/kg bw per day [c]	—
Dog	Twenty-six-week study[b]	Toxicity	2.5 mg/kg bw per day	10 mg/kg bw per day

[a] Dietary administration.

[b] Gavage administration.

[c] Highest dose tested.

(b) Lambda-cyhalothrin

Species	Study	Effect	NOAEL	LOAEL
Rat	Ninety-day study of toxicity[a]	Toxicity	50 ppm, equivalent to 2.5 mg/kg bw per day	250 ppm, equivalent to 12.5 mg/kg bw per day
	Acute neurotoxicity[b]	Neurotoxicity	0.5 mg/kg bw [e]	1.3 mg/kg bw [f]

	Ninety-day study of neurotoxicity [a]	Neurotoxicity	150 ppm, equal to 11 mg/kg bw per day [c]	—
	Developmental neurotoxicity [a]	Maternal toxicity	60 ppm, equal to 4.9 mg/kg bw per day	150 ppm, equal to 11.4 mg/kg bw per day
		Offspring toxicity	60 ppm, equivalent to 10.7 mg/kg bw per day [d]	150 ppm, equivalent to 26.3 mg/kg bw per day [d]
		Developmental (neuro)-toxicity	150 ppm, equivalent to 11.4 mg/kg bw per day[c]	—
Dog	One-year study[b]	(Neuro)toxicity	0.5 mg/kg bw per day	3.5 mg/kg bw per day

[a] Dietary administration.

[b] Gavage administration.

[c] Highest dose tested.

[d] Based on maternal intake of lambda-cyhalothrin during lactation.

[e] Threshold dose obtained using a nonlinear exponential threshold model.

[f] ED_{30} (dose associated with a 30% decrease in motor activity) obtained using a nonlinear exponential threshold model.

Estimate of acceptable daily intake for humans

0–0.02 mg/kg bw

Estimate of acute reference dose

0.02 mg/kg bw

Information that would be useful for the continued evaluation of the compound

Results from epidemiological, occupational health and other such observational studies of human exposures

Critical end-points for setting guidance values for exposure to cyhalothrin/lambda-cyhalothrin

Absorption, distribution, excretion and metabolism in animals	
Rate and extent of absorption	Rapid, incomplete absorption (about 40–50% in rats)
Distribution	Highest concentrations in fat, followed by liver and kidney (rats)
Potential for accumulation	Low
Rate and extent of excretion	Rapid (70% in faeces and urine within 24 h in rats)
Metabolism in animals	Sulfate conjugate of 3-(4'-hydroxyphenoxy) benzoic acid (compound XXIII) and glucuronide conjugate of (1RS)-cis-3-(2-chloro-3,3,3-trifluoropropenyl)-2,2-dimethylcyclopropane carboxylic acid. Unconjugated compound XXIII and 3-phenoxybenzoic acid (compound V) were minor metabolites.
Toxicologically significant compounds in animals, plants and the environment	Cyhalothrin, lambda-cyhalothrin
Acute toxicity	
Rat, LD_{50}, oral	56 mg/kg bw
Rat, LD_{50}, dermal	632 mg/kg bw
Rat, LC_{50}, inhalation	0.060 mg/L
Rabbit, skin irritation	Not an irritant (cyhalothrin)

Rabbit, eye irritation	Slightly irritating (lambda-cyhalothrin)
Guinea-pig, skin sensitization	Sensitizing (cyhalothrin, Buehler test and Magnusson & Kligman)
Short-term studies of toxicity	
Target/critical effect	Neurotoxicity, i.e., ataxia, tremors, occasionally convulsions (dogs)
Lowest relevant oral NOAEL	0.5 mg/kg bw per day (lambda-cyhalothrin, dogs)
Lowest relevant dermal NOAEL	No data
Lowest relevant inhalation NOAEC	No data
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	Decreased body weight gain (rats)
Lowest relevant NOAEL	50 ppm, equal to 2.3 mg/kg bw per day (cyhalothrin, rats)
Carcinogenicity	Not carcinogenic (cyhalothrin, mice, rats)
Genotoxicity	
	Not genotoxic (lambda-cyhalothrin)
Reproductive toxicity	
Reproduction target/critical effect	No reproductive effects (rats)
Lowest relevant reproductive NOAEL	100 ppm, equal to 6.7 mg/kg bw per day, i.e., highest dose tested (cyhalothrin, rats)
Developmental target	No developmental effects (rabbits)
Lowest relevant developmental NOAEL	30 mg/kg bw per day (lambda-cyhalothrin, rabbits)
Neurotoxicity/delayed neurotoxicity	
Neurotoxicity	Type II pyrethroid toxicity (choreoathetosis/salivation syndrome)
Lowest relevant oral NOAEL	0.5 mg/kg bw (lambda-cyhalothrin, rats, dogs)
Other toxicological studies	
	No data
Medical data	
	No systemic poisoning reported.
	Skin paraesthesia, numbness, irritation of the skin, red eyes, coughing and sneezing.

Summary for cyhalothrin and lambda-cyhalothrin

	Value	Study	Safety factor
Group ADI	0–0.02 mg/kg bw	Rat, acute neurotoxicity, lambda-cyhalothrin;[a] dog, 1-year, lambda-cyhalothrin	25
Group ARfD	0.02 mg/kg bw	Rat, acute neurotoxicity, lambda-cyhalothrin; dog, 1-year, lambda-cyhalothrin[b]	25

[a] The most sensitive NOAEL for the primary action the chemical and considered protective of other non-neurotoxic effects from studies of repeated doses.

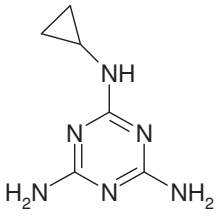
[b] Neurotoxicity occurred a few hours after dosing during the first week of treatment.

5.9 CYROMAZINE (169)

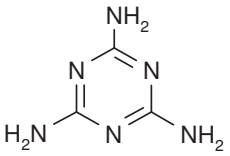
RESIDUE AND ANALYTICAL ASPECTS

Cyromazine was last evaluated by the JMPR in 2006 for toxicology within the Periodic Re-evaluation Programme, where an ADI of 0-0.06 mg/kg bw and an ARfD of 0.1 mg/kg bw were established. The compound was listed at the 38th Session of the CCPR for periodic re-evaluation for residues by the 2007 JMPR. Data submitted by the manufacturer include physical and chemical properties, metabolism in animals and plants, environmental fate in soils, residues in succeeding crops, analytical methods, storage stability, supervised trial on mangos, vegetables and animal commodities and processing studies. Residue and information on good agricultural practices (GAP) was also submitted by the Netherlands.

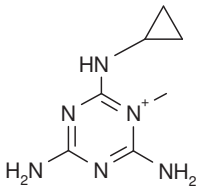
Cyromazine is a selective insecticide that acts by inhibiting the moulting process in insects, particularly in members of the Dipteran family. The figure below shows the compound structure and its main metabolites or degradation products found in animals, plants and/or soils. Metabolism and environmental fate studies submitted to the Meeting were conducted with [triazine-U-^{14}C]cyromazine.



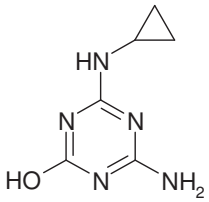
CYROMAZINE



MELAMINE



1-METHYL CYROMAZINE



HYDROXY CYROMAZINE

Animal metabolism

Metabolism studies in rats evaluated by the 2006 JMPR showed that more than 97% of the administered [^{14}C]cyromazine dose was excreted within 24 h, almost exclusively in the urine. Cyromazine was the major compound found in urine (71.5% of the applied radioactivity), with a further 7% attributed to melamine and 8–11% to hydroxy-cyromazine and 1-methyl-cyromazine.

Laying hens that received cyromazine at 5.0 ppm in the feed (equivalent to 0.5 mg/kg body weight/day) for 7 consecutive days had > 99% of the applied radioactivity recovered in the excreta. Egg white and egg yolk had 0.4% and 0.2% of the total applied radioactive dose, respectively; for egg white and egg yolk, an average of 0.15 and 0.12 mg/kg cyromazine equivalents were found in the daily collected eggs of two animals, respectively. Cyromazine represented about 64% TRR in eggs; a metabolite (15.6% TRR) had the same retention volume in an ion exchange column as melamine, but no confirmation of the identity of this compound was performed. Hen tissue residues accounted for 0.1% of the total applied dose, with the highest radioactive levels found in liver, kidney, heart and muscle (0.032, 0.019, 0.10 and 0.09 mg/kg cyromazine equivalents, respectively). The residues in tissues were not characterized. Expired CO_2 and other volatiles accounted for < 0.1% of the applied dose.

Lactating goats dosed with [^{14}C]cyromazine for ten consecutive days at levels of 4.6 ppm (low rate) and 48.4 ppm (high rate) in the feed had most of the administered dose excreted in the urine (86%) and faeces (6.6%). Residues in tissues represented < 2% of the applied dose, mostly found in liver (0.79 and 1.5 mg/kg cyromazine eq. for the low and higher dose, respectively) and kidney (0.043 and 0.44 mg/kg cyromazine eq). About 93% TRR was extracted from the liver, the majority (> 70%) as a non-identified metabolite with cyromazine and melamine representing 2 and 5.6% TRR, respectively. Radioactivity in milk accounted for < 0.4% of the applied dose and plateaued rapidly at both dose levels, with a mean of 0.017 and 0.32 mg/kg cyromazine eq found in the samples collected daily at the low and high dose levels, respectively. The radioactivity in the day 7 milk was mostly associated with the whey fraction, with cyromazine representing about 37% TRR and melamine 9.2 and 4.5% TRR for the low and higher dose, respectively.

In a second study, goats were dosed with cyromazine at 100 ppm in the feed for 4 consecutive days. The TRR was 74% of the applied dose, with 2.7 and 59% eliminated via faeces and urine, respectively; 7.4% of the total dose was found in the gastrointestinal tract. About 6% of the applied dose was recovered in the tissues, mostly in muscle (mean of 2.6%). Highest levels were found in kidney and liver (4.6 and 2.7 mg/kg cyromazine eq, respectively). In liver, the metabolite 1-methylcyromazine was the major compound found (42% TRR), followed by the parent cyromazine (34% TRR). Kidney and muscle had mostly cyromazine (> 70% TRR) and only cyromazine was detected in fat. On average, a total of 0.76% of the applied dose was recovered in the milk, with an average of 0.66 mg/kg cyromazine eq/day. Cyromazine was the major identified compound in milk (68% TRR) followed by melamine (2.9% TRR).

In one study conducted with a mature female sheep fed with [^{14}C]cyromazine for 9 consecutive days at a level of 5 ppm in the diet (equivalent to 0.15 mg/kg bw per day), 94% of the applied radioactivity was recovered, mostly in urine (89%). Tissues represented 0.09% of the applied radioactivity, mostly found in liver (0.17 mg/kg cyromazine eq), kidney (0.048 mg/kg eq) and muscle (0.13 mg/kg eq). While the excreta extracts contained mostly cyromazine, the main compound found in liver extract was melamine (44% total radioactivity), with cyromazine corresponding to 12%.

In summary, animals dosed daily with [^{14}C]cyromazine excreted over 90% of the radioactivity, mainly in urine. Eggs and milk represented < 0.5% and tissues < 2% of the applied or recovered radioactivity. Metabolism of cyromazine involves mainly dealkylation to melamine. Alkylation to 1-methylcyromazine was specific to ruminants; hydroxylation was identified in goats fed at 100 ppm. Cyromazine was the major compound found in hen eggs and milk of goats and sheep. The major compounds found in liver of goat and sheep were the metabolites 1-methylcyromazine and melamine, respectively.

Metabolism in plants

In one greenhouse study conducted at a 0.28 kg ai/ha foliar rate in two phases, celery plants received 2 (1st phase) or 6 applications (2nd phase) and were sampled 7 days after the second application (mature) in the 1st phase or third application (immature) and 14 days after the sixth application (mature) in the 2nd phase. Lettuce received 2 or 4 applications and heads were sampled 7 days after the second application (mature or immature) and 7 days after the fourth application (mature). Radioactivity in the plants was mostly extracted in the aqueous phase (> 74% TRR), with cyromazine representing the major residues (48 to 74% TRR in both plants) and melamine was the only metabolite found (11 to 33% TRR).

In a study conducted with tomatoes in a California field, 6 foliar applications at 0.28 kg ai/ha were made to the crop at 2 weeks intervals. Tomato samples were taken at 0, 7, and 14 days after the 4th or 6th applications and a stalk sample after the last application. TRR in the samples ranged from 64–98% of the applied radioactivity, mostly found in the aqueous extract (56 to 87% TRR) and being characterized as cyromazine (29 to 76% TRR) and melamine (11 to 44% TRR). While the residues ranged from 0.08 to 0.44 mg/kg cyromazine eq. in tomato samples, they reached 37 mg/kg eq in the stalk sample (aerial portion of the plant after removal of the tomato fruits).

Five trials conducted with non-radioactive cyromazine demonstrated that residues did not accumulate significantly in mushrooms under normal use conditions when the crop was grown in amended compost. Cyromazine residues were < 0.05 mg/kg in mushrooms in all trials/flushes with the exception of one trial at a target cyromazine concentration in the compost of 10 mg/kg for which the sample from the third flush contained a residue of 0.08 mg/kg. Residues of melamine were in the range 1.5–6.6 mg/kg at a compost of 5 mg ai/kg, and in the range 3.1–17 mg/kg at a compost of 10 mg/kg.

The results indicated that the major pathway of cyromazine in lettuce, celery and tomato was by dealkylation to form melamine, which can represent about 40% TRR. Melamine was the major compound found in cold treated mushroom.

Environmental fate in soil

Fourteen cyromazine aerobic degradation laboratory studies conducted with a variety of soils were submitted to the Meeting. Soil samples containing from 0.25 to 10.7 mg ai/kg (0.33 to 9.5 kg ai/ha) cyromazine were incubated for up to 12 months in the dark at temperatures ranging from 10 to 25 ˚C. In most studies, TRR was over 90% of the applied radioactivity. Melamine was the only or major degradation product found in the soils. In a 12 months/25 ˚C study conducted with a sandy loam soil (9 mg/kg cyromazine) 15% of the applied dose, at the end of the study, was identified as the carboxylic acid of cyromazine, formed through oxidative opening of the cyclopropane ring. Cyromazine half lives (DT_{50}) varied widely, ranging from 2.9 to 107 days, being lesser at lower temperatures, organic matter content and microbial biomass. In general, the degradation rate of melamine was slower than that of cyromazine.

The photolytic degradation of cyromazine was studied at 20 ˚C under artificial light on soil at a rate of 3.2 µg ai/cm^2 (corresponding to a field rate of 0.32 kg ai/ha). Samples were irradiated for 240 h, equivalent to 30 days natural summer sunlight. In moist irradiated soil, cyromazine degraded rapidly with a calculated DT_{50} of 3.5 days; in dry irradiated soil the level fell rapidly during the first 24 h and the degradation was slow thereafter (DT_{50} > 1 year). In both moist and dry soils, melamine was the major degradation product observed (53 and 15% of applied radioactivity in the moist and dry soil, respectively).

Eleven field soil studies conducted with cyromazine were submitted to the Meeting. In one study cyromazine was applied to bare soil at four different sites in various states in the USA during 1982/83. Plots were treated at an exaggerated rate of 5.6 kg ai/ha as a single application with a second application in Year 2. Residues in the soil at day 0 in both years ranged from 0.39 to 6.6 mg/kg in the 0–15 cm layer, with the highest value occurring from one site in Florida. Cyromazine dissipated at a slow rate at all 4 sites, and could remain unchanged for over 100 days. At the sites in California and Nebraska, essentially no movement of cyromazine was observed below a depth of 15 cm; at the two sites in Florida, cyromazine residues were found to a depth of 30–45 cm in both years. Melamine was detected at all sites down to a depth of 30–45 cm towards the end of each year of the trial.

In four field studies carried out on bare soil plots in potato growing areas of Canada during 1993 and 1994, cyromazine was applied twice at 0.28–0.48 kg ai/ha. Cyromazine residues declined rapidly after the second application and continued to decline over the winter period at a slower rate, with half-lives ranging from 29 to 42 days. The majority of the parent residue was retained in the upper soil layer (0–15 cm) and most of the melamine residues remained in the top 30 cm. Melamine was present from background sources in the three topsoil layers up to 0.011 mg/kg.

In two field studies conducted in Switzerland and France in 2002/2003, soil samples (0–30 cm deep) from plots treated at 0.30 kg ai/ha were taken up to 360 days. In France, no residues were detected in soil below a depth of 20 cm and in Switzerland; no cyromazine residues were found in soil below a depth of below a depth of 10 cm. DT_{50} for cyromazine calculated from the 0–10 cm layer residue data was 17 days and 2.3 days for France and Switzerland, respectively.

In one study conducted in Greece from 2001 to 2003, cyromazine was applied annually 4 times at a rate of 0.30 kg ai/ha at approximately 7 day intervals to bare ground (sandy loam soil type). The plot was cultivated with mustard 1–2 days before the first application in each year. Cyromazine and melamine were found in some occasions at depths of up to 50–70 cm. The degradation of cyromazine was slower during a drought season of the first year (low biological activity) and during the winter.

In a study conducted in Spain, cyromazine was applied yearly to a loamy silt soil in four subsequent early summer applications at 0.30 kg ai/ha (2000–2003). Tomatoes were planted in the second year of the experiment just prior to the cyromazine application. Cyromazine residues were not found in soil layers deeper than 30 cm; melamine could be detected in soil layers up to 100 cm deep in the second and third year of the study, a possible result of higher than average rainfall during this period of the study. DT_{50} for cyromazine, calculated from the first year data, was 51 days.

The proposed metabolic pathway of cyromazine in soil involves the initial cleavage of the cyclopropyl ring moiety to form melamine, with a possible involvement of the carboxylic acid of cyromazine as intermediate. The rate of degradation of cyromazine under laboratory or field conditions vary widely, with estimated half lives ranging from a few days to over 100 days, depending on the soil type and environmental conditions.

Succeeding Crops

Five studies on succeeding crops conducted in USA were submitted to the Meeting. In a greenhouse study conducted in Florida in 1982, celery seedlings were transplanted into a muck soil and [^{14}C]cyromazine mixed with a sample of the soil applied as a top dressing to the crop at 1 kg ai/ha. Celery plants were harvested after 84 days and radishes or sweet corn immediately planted in the same container. About 78% TRR in celery stalks was found the aqueous extract, with cyromazine being the main residue found after 42 and 82 days after treatment (up to 0.45 mg/kg). Radioactivity in radish and mature sweet corn planted 84 days following foliar application of the compound to celery and harvested after 130 or 159 days after planting ranged from 0.01 to 0.02 mg/kg cyromazine eq and were too low for characterization.

In a field study conducted in California, tomatoes were treated in the fall with [^{14}C]cyromazine at 6 × 0.28 kg ai/ha. Tomato plants were harvested 14 days after the last application and winter wheat planted immediately after that. Lettuce, carrot, soy bean and sugar beet were planted the following spring. Two samplings (immature and mature harvest) were taken from each crop for analysis. Radioactive residues in succeeding crops were ≤ 0.05 mg/kg for all crop parts other than half-mature carrot tops (0.19 mg/kg cyromazine eq). Most of the residues in this sample (93%) was partitioned into the aqueous layer and was characterized as 14% cyromazine and 79% melamine.

A study was performed in Georgia to determine the fate of cyromazine in chicken manure amended soil and the uptake and metabolism of cyromazine residues by rotational cops. The soil was prepared by incorporating manure fortified with [^{14}C]cyromazine at 5 mg/kg at a rate of 11.2 t manure/ha and aged for 30 days. Spring wheat, lettuce and sugar beets were planted in buckets containing a 7.6 cm top layer of cyromazine-treated soil and grown to maturity in the greenhouse. TRR ranged from < 0.01 to 0.011 mg/kg cyromazine eq in mature and immature lettuce leaves, sugar beet tops and beets and wheat grain. Immature stalks and mature wheat straw and hulls contained residues between 0.022 to 0.11 (straw) mg/kg eq, greater than the initial soil concentration of 0.064 mg/kg. Cyromazine and melamine accounted for 43% and 28% TRR in wheat straw, respectively.

In a study carried out in Mississippi, tomato crops were treated with 12 applications of cyromazine at 0.14 or 0.28 kg ai/ha, the tomatoes harvested at 14 days after last application and wheat planted 10 weeks after the last application. Cyromazine residues in samples of forage, straw and grain harvested 23 to 43 weeks after planting ranged from < 0.05 to 0.08 mg/kg with the highest value in forage. In California and Florida, 21 field trials were carried with celery treated with 11–15 foliar

applications of cyromazine at rates from 0.14 to 0.28 kg ai/ha. Celery was harvested at 0–14 days after the last application and following a post-harvest interval of 1–6 weeks (Florida) or 8 weeks (California) the field plots were re-planted with sweet corn (eight trials), radishes (eight trials) and lettuce (five trials). Residues of cyromazine were detected in sweet corn forage (0.08 to 0.19 mg/kg), radish roots and tops (0.09 to 0.22 mg/kg) and lettuce leaf (0.05 to 0.08 mg/kg).

In summary, detectable residues of cyromazine and melamine can be found in crops cultivated after cyromazine treated plants have been harvested. Crops planted in cyromazine fortified manure amended aged soil also showed detectable residues.

Analytical methods

Four analytical methods for the analysis of cyromazine and melamine in vegetable crops were provided. In methods developed in the 1980´s, residues can be extracted with water/methanol or pure methanol, cleaned up and partitioned with dichloromethane and hexane, followed by C18 and/or cation exchange columns and additional clean-up with amino column or gel permeation chromatography. The analytes are quantified by HPLC with an amino column and UV detection at 214/215 nm or by GC/NPD. Samples of lettuce, celery, tomato, mushrooms, cucurbits, peppers, grapes, peas and alfalfa, cotton, Sudan grass and/or barley products were fortified at levels that varied from 0.04 to 10 mg/kg level of cyromazine and melamine. In most cases, recoveries were within 70−120% range, however only in few cases replicate samples were analysed.

In a method reported in 2001 (REM 174.02), samples of crops with high water content and fruits with high acid content, are macerated with an acidic solution of potassium dihydrogen phosphate and extracted with methanol. Crops with high fat content, cereals and other dry crops are macerated with water and then extracted with methanol by mechanical shaking. Celite is added, the mixture centrifuged, filtered, and the filtrate acidified. Analysis is by column switching HPLC using two cation exchange columns and detection within the range 215−245 nm depending on crop type and co-extractives. This method was fully validated for sunflower seeds, tomatoes, oranges, beans and potatoes fortified at 0.05 and 0.5 mg/kg (n=5 in each case). Recoveries of cyromazine and melamine ranged from 80 to 110%, with a coefficient of variation (CV) up to 5.2%.

Twelve methods for the analysis of cyromazine and melamine in food of animal origin were provided. The analytes could be extracted with methanol, methanol/water, ethanol or acetone, and the extracts cleaned-up on cation exchange, silica and/or celite column. In some methods, a solvent partitioning step was included before the clean-up, or replaced the clean-up. Quantification was by GC/NPD or MS in most cases, but also by HPLC/UV 214 nm. The methods were validated for eggs, milk and tissues fortified at 0.04 to 1 mg/kg. Recoveries were satisfactory in most cases, and whenever replicate samples were analysed, CV were < 20%. In one method reported in 2003 (RAM 394/01), cyromazine and melamine residues are extracted from liver, kidney, muscle tissue and milk with acetonitrile/water and from eggs with methanol/water. After centrifugation, aliquots are adjusted to pH 4 with glacial acetic acid, subjected to cation exchange clean-up and the compounds quantified by HPLC-MS/MS. This method was fully validated at 0.01 and 0.1 mg/kg levels, with recoveries from 70 to 107% and CV up to 16% (n=5).

Stability of pesticide residues in stored analytical samples

Residues of cyromazine and melamine in crop samples fortified at 0.5 or 1.0 mg/kg levels were stable after being frozen for up to 2 years, with the amount remaining in the range of 80 to 110%. Residues of cyromazine, melamine and 1-methylcyromazine in beef tissues, eggs and milk fortified at 0.5 or 1.0 mg/kg levels were also stable for over 3 years under freezer conditions. Field-incurred residues of cyromazine and melamine in lettuce, celery and tomatoes samples at levels from 0.07 to 21.5 mg/kg increased more than 150% of the initial concentration after stored for up to 23 months under freezer conditions.

Definition of the residue

In 1990, the JMPR defined the residue for cyromazine in food as cyromazine. At the 1992 JMPR, the possibility of including melamine in the definition was discussed, but the Meeting decided to maintain the previous definition in light of melamine was considered to be less toxic than cyromazine, and that melamine may have originated from sources other than from the use of cyromazine. Nevertheless the Meeting recognized that the monitoring of good agricultural practice in growing mushrooms under certain conditions was not possible when melamine was omitted from the residue definition.

Data submitted to the present Meeting have shown that melamine is the main metabolite found in all crops and most animal products. Cyromazine is the major compound found in all crops, with the exception of mushroom, where melamine can be present at levels higher than cyromazine. Most analytical methods analyse cyromazine and melamine and most of the supervised trials submitted to the Meeting contained data for both compounds. It is known that cyromazine is not the only source of melamine in agriculture and in the environment and that melamine can be a component in fertilizers and is used in a variety of manufacturing processes, including plastics. Data provided by the manufacturer have shown that, with the exception of Switzerland, the residue definition in most countries in all foods is cyromazine.

Based on the present knowledge and for practical purposes, the Meeting agreed that the residue definition for cyromazine for enforcement purposes for food of plant and animal origin should continue to be cyromazine.

Toxicological data evaluated by the 2006 JMPR confirmed that melamine is less toxic than the parent compound. The Meeting agreed that the definition for cyromazine in food of plant and animal origin, for dietary intake purposes, is cyromazine.

The octanol-water partition coefficient of cyromazine is < 1 and the compound does not accumulate in fat of animals dosed with cyromazine. The Meeting concluded that cyromazine is not fat soluble.

Definition of residues (for compliance with MRL and for estimation of dietary intake) for plants and animal commodities: *cyromazine.*

Results of supervised trials on crops

Metabolism studies conducted in plants and plant residue data for melamine (not included in this evaluation) indicate that cyromazine is always present at a higher concentration than melamine in the treated crops considered in this evaluation. Cyromazine might be absent or present at lower concentration than melamine in treated mushrooms.

Mango

Mango is registered in Mexico to be used as a foliar application in the field at rates from 0.07 to 0.10 kg ai/ha. The maximum number of application is not specified on the label and the PHI is 0 day. Six trials were conducted with cyromazine in mango in Mexico from 1984 to 1993. The compound was applied 5 times at 0.09 kg ai/ha and samples harvested from day 0 to day 28 after the last application. Residues of cyromazine in the whole fruit at 0 day PHI were: 0.06, 0.10, 0.11, 0.14(2) and 0.25 mg/kg.

The Meeting estimated a maximum residue level of 0.5 mg/kg, an STMR of 0.125 mg/kg and an HR of 0.25 mg/kg for cyromazine in mango.

Onions

The registered use of cyromazine in bulb vegetables in the USA recommends up to 6 foliar applications at 0.14 kg ai/ha rate with a 7 day PHI. A seed treatment at 5 g ai/100 g seed is also recommended, but with no PHI specified. Eight trials were conducted in 1993 with bulb onions using

the seed treatment at the GAP rate and resulted in residues in the onion bulbs at 98 to 207 days PHI of < 0.05 (7) and 0.06 mg/kg. Residues in the whole plant at 60–75 days PHI were 0.09, 0.16, 0.27, 0.34, 0.35, 0.44, 0.83 and 1.7 mg/kg. Dried onion bulb samples (fresh bulbs dried in the field) from all trials gave residues of < 0.05 and 0.06 mg/kg. In nine trials conducted in 1999, using foliar application within US GAP, residues found in onion bulbs were: < 0.05 (7) and 0.07 (2) mg/kg.

The Meeting agreed that trials conducted at GAP using foliar and seed application gave residues in onion bulbs at the same level and could be combined. Residues in ranked order (median underlined) were: < 0.05 (14), 0.06 and 0.07 (2) mg/kg. The Meeting estimated a maximum residue level of 0.1 mg/kg, an STMR of 0.05 mg/kg and an HR of 0.07 mg/kg for cyromazine in bulb onions.

Four trials were conducted with cyromazine in spring (green) onions in USA in 1999 using 6 foliar applications at 0.14 to 0.17 kg ai/ha. Residues in the whole plant within 7 days PHI were 0.26, 0.30, 0.75 and 0.78 mg/kg. Data from immature plant from the bulb onion trials can be considered for the estimation for spring onion and the results from the trials can be combined. Residues in ranked order (median underlined) were: 0.09, 0.16, 0.26, 0.27, 0.30, 0.34, 0.35, 0.44, 0.75, 0.78, 0.83 and 1.7 mg/kg.

The Meeting estimated a maximum residue level of 3 mg/kg, a STMR of 0.35 mg/kg and a HR of 1.7 mg/kg for cyromazine in spring onion.

Broccoli and cabbage

In the USA, cyromazine is registered for the brassica leafy vegetable group to be applied 6 times as a foliar application in the field at 0.41 kg ai/ha and 7 days PHI. In six trials conducted in broccoli at GAP, residues found in flower head and stem at 7 days PHI were: < 0.05, 0.05, 0.09, 0.21, 0.26 and 0.51 mg/kg.

The Meeting estimated a maximum residue level of 1 mg/kg, an STMR of 0.15 mg/kg and an HR of 0.51 mg/kg for cyromazine in broccoli.

In six trials conducted at GAP rate in USA, residues in cabbage head (with wrapper leaves) were: 0.06, 0.10, 0.24, 0.28, 0.50 and 6.1 mg/kg.

The Meeting estimated a maximum residue level of 10 mg/kg, an STMR of 0.26 mg/kg and an HR of 6.1 mg/kg for cyromazine in cabbage, head.

The IESTI calculation indicates that the consumption of cabbage at the HR level of 6.1 mg/kg will lead to an exceedance of the ARfD, but no residue data was available from an alternative GAP to estimate a lower maximum residue level.

Fruiting vegetables, cucurbits

Cyromazine is registered for use in cucumber, melon and summer squash in many European countries at similar rates, with the PHI ranging from 3 to 14 days. In France, the maximum GAP rate is 0.3 kg ai/ha (field and protected), with a PHI of 3 days for cucumber and summer squash. Fifteen protected cropping or field trials were conducted in cucumber from 1999 to 2001 in France (6), Greece (2), Italy (5), Spain (1) and Switzerland (1) using 3 to 4 applications at 0.30−0.34 kg ai/ha rate. Residues found at 3 days PHI, in ranked order were: 0.30, 0.32, 0.33, 0.40, 0.43, 0.46, 0.50, 0.52(2), 0.62, 0.71, 0.74, 0.79, 0.88 and 1.3 mg/kg.

In USA, cyromazine is registered for the Cucurbits crop group with a recommendation of a maximum of 6 foliar applications at 0.14 kg ai/ha at 7 day intervals with a 0 day PHI. Due to the rapid rate of growth exhibited by cucurbits, it was considered unlikely that early applications would contribute significantly to the final residues. As a result, trials conducted with a higher number of applications were considered to comply with the US GAP. In five trials conducted in the USA on cucumbers in 1986 and 1990 where 6 or 8 applications, at the GAP rate were made, residues at 0 days

PHI were: 0.16 (2), 0.20, 0.22 and 0.56 mg/kg. In four trials conducted at the double rate, residues found were within the same range.

The Meeting considered that the data from the 20 trials conducted in cucumbers according to the GAPs of Europe and the USA belonged to the same population and could be combined. Residues in ranked order (median underlined) were: 0.16 (2), 0.20, 0.22, 0.30, 0.32, 0.33, 0.40, 0.43, 0.46, 0.50, 0.52(2), 0.56, 0.62, 0.71, 0.74, 0.79, 0.88 and 1.3 mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg, an STMR of 0.048 mg/kg and an HR of 1.3 mg/kg for cyromazine in cucumbers.

The Meeting recommended withdrawing the previous recommendation of 0.2 mg/kg for cyromazine in cucumbers.

In eight field trials conducted in summer squash in France, Italy and Spain, between 2000 and 2003, using 3 applications of 0.3 to 0.35 kg ai/ha (0.03 kg ai/hL) with a 3 day PHI, residues found in ranked order were: 0.11, 0.14, 0.15, 0.16, 0.18, 0.21 and 0.27 (2) mg/kg.

In seven trials conducted in the USA from 1986 to 1990 based on the cucurbits GAP rate (6 or 8 applications), residues at 0 days PHI were 0.07 (2), 0.11(2), 0.18, 0.22 and 1.0 mg/kg. In five trials conducted at double rate, residues were within the same range.

The Meeting considered that the residues from 15 trials conducted in summer squash according to European GAP at 3 days or 14 days PHI and in USA according to US GAP belonged to the same population and could be combined. Residues in ranked order (median underlined) were: 0.07 (2), 0.11 (3), 0.14, 0.15, 0.16, 0.18(2), 0.21, 0.22, 0.27 (2) and 1.0 mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg, an STMR of 0.16 mg/kg and an HR of 1 mg/kg for cyromazine in summer squash.

GAP for melons in Spain is 0.3 kg ai/ha (14–30 days interval) with a PHI of 3 days. In France, the rate is also 0.3 kg ai/ha (10–15 days interval) and a PHI of 7 days. A total of fourteen trials (field and glasshouse) matching French GAP were conducted in melons in France, Italy and Spain from 1998 to 2001 using 3 applications of 0.28 to 0.33 kg ai/ha (7 days interval). Residues in the whole fruit were: < 0.05, 0.06 (3), 0.07, 0.08, 0.09(2), 0.11, 0.12, 0.13, 0.16, 0.18 and 0.25 mg/kg.

In seven trials conducted in the USA in 1986 in melons and cantaloupe using 8 applications at the GAP rate, residues at 0 days PHI were: < 0.05, 0.08, 0.09, 0.11(2), 0.13 and 0.45 mg/kg. In one trial conducted in watermelon at the same rate, residues found were 0.13 mg/kg.

The Meeting considered that residues from trials conducted in melons according to GAP in Europe and USA appeared to be from similar populations and could be combined. Residues in melons from the 21 trials, in ranked order (median underlined), were: < 0.05 (2), 0.06 (3), 0.07, 0.08 (2), 0.09 (3), 0.11 (3), 0.12, 0.13 (2), 0.16, 0.18, 0.25 and 0.45 mg/kg.

In some of 3 day PHI trials conducted in melons in Europe, residues in fruit were calculated from the levels found in the pulp and in the peel; residues in the pulp were < 0.05(4) mg/kg. The residue ratio fruit/pulp calculated from these and other trials was 1.1, > 1.6, > 2.4, > 2.6, > 3 and > 3.2, with an estimated mean of > 2.3. A fruit/pulp ratio of 2.3 was applied to the median and highest residues for melons (0.09 and 0.45 mg/kg), estimating the median and the highest residue in melon pulp as 0.04 and 0.19 mg/kg.

The Meeting estimated a maximum residue level of 0.5 mg/kg for cyromazine in melons, except watermelons, an STMR of 0.04 mg/kg and an HR of 0.19 mg/kg for cyromazine in melons (pulp).

The Meeting recommends withdrawing of the previous recommendation of 0.2 mg/kg for cyromazine in melons, except watermelons.

Fruiting vegetables, other than cucurbits

Cyromazine is registered in tomato and eggplant in many European countries for either in the field or under protected cropping. In France (F&P) and Italy (F) the maximum application rate is 0.3 mg/kg ai/ha. The recommended PHI is 3 days in France and 14 days in Italy. Eighteen foliar trials complying with French GAP were conducted in France, Greece, Italy and Spain under field or glasshouse conditions with 4 foliar applications at 0.3 to 0.34 kg ai/ha. Residues at 3 days PHI were: 0.05, 0.09, 0.11(3), 0.13 (2), 0.14, 0.15, 0.16, 0.18, 0.21, 0.22, 0.23, 0.29, 0.34, 0.42 and 0.58 mg/kg.

Application through irrigation is also recommended in Italy and Greece, at rates of 0.75 and 0.98 kg ai/ha with a PHI of 14 days. Only one of the four trials conducted in Greece, Italy and Spain using either drip or soil drench irrigation matched the GAP of Italian and Greece, giving residues of cyromazine at 14 days PHI of < 0.05 mg/kg.

In the USA, cyromazine can be applied to tomatoes up to 6 times at a rate of 0.14 kg ai/ha with a 0 day PHI. In 13 trials conducted according to GAP, residues at day 0 were: 0.09, 0.10, 0.11, 0.12, 0.13, 0.14, 0.18, 0.21(2), 0.22, 0.26, 0.28 and 0.30 mg/kg. Five trials conducted at double rate gave residues in the same range.

The Meeting considered that residues in tomatoes from 31 foliar trials conducted in Europe and USA matching GAP belonged to the same population and could be combined. Residues found, in ranked order (median underlined) were: 0.05, 0.09(2), 0.10, 0.11 (4), 0.12, 0.13(3), 0.14 (2), 0.15, 0.16, 0.18 (2), 0.21(3), 0.22(2), 0.23, 0.26, 0.28, 0.29, 0.30, 0.34, 0.42 and 0.58 mg/kg.

In four field trials conducted with eggplant in France and Switzerland 3 applications were made at 0.30 to 0.36 kg ai/ha, residues found at a 3 day PHI were: 0.05, 0.14, 0.23 and 0.26 mg/kg.

The Meeting considered that the residues of cyromazine found in tomatoes and eggplant belonged to the same population and could be combined. Residues from the trials, in ranked order (median underlined) were: 0.05 (2), 0.09 (2), 0.10, 0.11(4), 0.12, 0.13(3), 0.14(3), 0.15, 0.16, 0.18 (2), 0.21(3), 0.22(2), 0.23(2), 0.26(2), 0.28, 0.29, 0.30, 0.34, 0.42 and 0.58 mg/kg.

In the USA cyromazine may be applied to peppers at up to 6 applications at a rate of 0.14 kg ai/ha with a PHI of 0 days. Data from 12 US trials on chilli and bell pepper in 1984/1985 did not comply with GAP as 12 applications were made at 0.14 or 0.28 kg ai/ha, residues found at 0 day ranged from 0.10 to 0.95 mg/kg. Although these trials were conducted with a higher number of applications, residues found at 0 days PHI were within the same range as residues found in tomato and eggplants. The Meeting decided that data from trials on tomato and eggplants, conducted according to GAP, supported the residues found in peppers.

Based on the residues found in tomato and eggplant, the Meeting estimated a maximum residue level of 1 mg/kg, an STMR of 0.16 mg/kg and an HR of 0.58 mg/kg for cyromazine in fruiting vegetables, other than cucurbits, except sweet corn (on-the-cob) and mushrooms.

The Meeting recommends withdrawing the previous recommendations of 0.5 mg/kg for cyromazine in tomato and of 1 mg/kg for cyromazine in peppers.

Mushrooms

Spanish GAP allows cyromazine application to mushrooms at rates up to 0.75 g ai/m^2; Swiss GAP allows treatment at 1 g/m^2 to the casing layer or compost with a PHI of 14/15 days. In France, the application rate is 0.4 g/m^2 with a 14 day PHI. In the USA, cyromazine can be used as a coarse drenching spray at a maximum rate of 0.57 g ai/ m^2, with no specified PHI. Nine mushroom-house trials were conducted in France, Italy and Switzerland from 1986 to 2001 using 1 or 2 applications of cyromazine at 0.4 to 0.8 g ai/m^2. In four trials conducted according to French GAP, residues of cyromazine were 0.37, 1.3, 2.4 and 4.2 mg/kg. Samples collected at a higher PHI in three other trials giving residues of 0.75, 2.2 and 2.8 mg/kg were also considered for MRL estimation. Two trials

conducted at double rate gave residues in the same range. Residues considered for the estimation of an MRL and STMR level were: 0.37, 0.75, 1.3, 2.2, 2.4, 2.8 and 4.2 mg/kg.

The Meeting estimated a maximum residue level of 7 mg/kg, an STMR of 2.2 mg/kg and an HR of 4.2 mg/kg for cyromazine in mushrooms.

The Meeting recommends withdrawing of the previous recommendations of 5 mg/kg for cyromazine in mushroom.

Lettuce

Cyromazine is approved for use on lettuce in a number of European countries. French and Italian GAP for field grown lettuce allows a maximum rate of 0.3 kg ai/ha with a PHI of 21 days and 14 days, respectively. In Spain and Switzerland, GAP comprises a maximum rate of 0.03 kg ai/hL or 0.3 kg ai/ha with a PHI of 7 days in the production of either field grown or protected lettuce. Between 1993 and 2002, 40 trials were conducted in Europe in head and leaf lettuce in both field and greenhouse situations using 3 applications at 0.19 to 0.30 kg ai/ha (0.03 to 0.1 kg ai/hL). These trials were evaluated against either the GAP of Italy (PHI of 14 days) or of Spain/Switzerland (PHI of 7 days).

In three field trials conducted in France in head lettuce complying with the Spanish GAP rate, residues at 14 days PHI were: < 0.03, 0.34 and 1.7 mg/kg. In four protected cropping trials (plastic tunnels), residues were: 2.2, 2.9, 3.0 and 4.9 mg/kg.

In 14 field trials conducted in France, Italy, Spain and Switzerland in Cos lettuce (leaf) complying with the Italian GAP rate, residues at 7 days PHI were: 0.15, 0.18, 0.19, 0.22, 0.24, 0.27, 0.28, 0.34, 0.45, 1.3, 1.5, 1.8(2) and 2.0 mg/kg. Residues in trials according to Spanish or Italian GAP with PHIs of 7 or 14 days in 17 protected trials were: 0.13, 0.55, 1.5, 2.4, 2.8, 3.3, 4.7, 5.2(2), 5.8(2), 6.2, 6.5, 7.9, 11, 14, 15 and 18 mg/kg.

On the basis of the European trials, the Meeting concluded that residues conducted with head and Cos lettuce using the same rate gave residues in the same range. Residues from 17 field trials conducted in lettuce in Europe in ranked order (median underlined), were: < 0.03, 0.15, 0.18, 0.19, 0.22, 0.24, 0.27, 0.28, 0.34(2), 0.45, 1.3, 1.5, 1.7, 1.8(2) and 2.0 mg/kg. Residues from 22 protected trials were: 0.13, 0.55, 1.5, 2.2, 2.4, 2.8, 2.9, 3.0, 3.3, 4.7, 4.9, 5.2(2), 5.8(2), 6.2, 6.5, 7.9, 11, 14, 15 and 18 mg/kg.

In the USA, GAP for leafy vegetables, including brassica leafy vegetables, is a maximum of 5 or 6 applications (6 for head lettuce 5 for all other leafy vegetables) at 0.14 kg ai/ha with a 7 days PHI. In nine trials conducted with head lettuce using 8 applications at 0.14 or 0.28 kg ai/ha rate, residues 7 days after the final application ranged from < 0.05 to 3.8 mg/kg. In nine field trials conducted with leaf lettuce using 5 applications at 0.14 kg ai/ha, residues at 7 days after the final application were: 0.58, 1.5, 1.6, 2.0, 2.8(2), 3.9, 4.4, 5.2 mg/kg.

The Meeting considered the field and protected cropping trials conducted in Europe and the field trials conducted in USA were from different populations and could not be combined. The Meeting considered that the 22 protected trials, conducted in Europe, reflected the most critical use in lettuce.

The Meeting estimated a maximum residue level of 25 mg/kg, an STMR of 2.8 mg/kg and an HR of 18 mg/kg for cyromazine in head lettuce and leaf lettuce.

The IESTI calculation indicates that the consumption of lettuce, at the HR level of 18 mg/kg coming from protected trials, would lead to an exceedance of the ARfD. Consequently, the Meeting used the prospective alternative GAP approach and selected the USA residue data for the maximum residue level estimation.

The Meeting estimated a maximum residue level of 10 mg/kg, an STMR of 2.8 mg/kg and an HR of 5.2 mg/kg for cyromazine in head lettuce and leaf lettuce.

The IESTI calculation indicates that the consumption of lettuce at the HR level of 5.2 mg/kg, coming from the USA field trials, would lead to an exceedance of the ARfD for children. The Meeting once again used the prospective alternative GAP approach and selected the EU residue data population, coming from field trials, for the recommendations.

The Meeting estimated a maximum residue level of 4 mg/kg, an STMR of 0.34 mg/kg and an HR of 2 mg/kg for cyromazine in head lettuce and leaf lettuce.

Mustard greens

Five trials were conducted in the USA according to the GAP for brassicas leafy vegetables (maximum of 5 applications at 0.14 kg ai/ha with a 7 days PHI). Residues in mustard greens (leaves) were: 1.1, 1.6, 2.7, 6.5 and 7.4 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for cyromazine in mustard greens of 10, 2.7 and 7.4 mg/kg.

Spinach

From 16 trials conducted with spinach in the USA, eight were conducted according to GAP for leafy vegetables. Residues at 7 days PHI were: 0.4, 1.1, 1.2, 1.8, 2.3, 4.2, 5.4 and 6.1 mg/kg. The Meeting estimated a maximum residue level of 10 mg/kg, an STMR value of 2.0 mg/kg and an HR value of 6.1 mg/kg for cyromazine in spinach.

The IEST calculation indicates that the consumption of spinach at the HR level of 6.1 mg/kg will lead to an exceedance of the ARfD, however no data was available for an alternative GAP review to estimate a lower maximum residue level.

Beans

US GAP allow 6 applications of cyromazine in lima bean and dry beans at a rate of 0.14 kg ai/ha with a PHI of 7 days. In nine trials conducted in lima beans complying with GAP from the USA, residues found in ranked order (median underlined), were: < 0.05, 0.11, 0.17, 0.19, 0.23(2), 0.32, 0.38 and 0.58 mg/kg. Trials conducted with 8 applications at 0.14 kg ai/ha or 6 applications at 0.28 kg ai/ha gave residues in the range of 0.23 to 1.0 mg/kg.

The Meeting estimated a maximum residue level of 1 mg/kg, an STMR of 0.23 mg/kg and an HR of 0.58 mg/kg for cyromazine in lima beans.

In nine trials in dry beans from the USA complying with that countries GAP, residues found in ranked order (median underlined), were: 0.23, 0.68, 0.84, 0.97, 1.0, 1.1(2), 1.2 and 1.8 mg/kg.

The Meeting estimated a maximum residue level of 3 mg/kg and an STMR of 1 mg/kg for cyromazine in beans (dry).

Potato

In Spain cyromazine may be applied to potatoes at a maximum rate of 0.24 kg ai/ha (0.02 kg ai/hL) with a PHI of 21 days. In Italy, field and greenhouse GAP consists of an application rate of 0.3 kg ai/ha with a PHI of 35 days. In eight potato trials conducted in Spain using 3 applications at 0.17 to 0.33 kg ai/ha with samples harvested at 21 or 35 days post application. Four trials could be evaluated against Spanish or Italian GAP, with residues of < 0.05, 0.06, 0.11, and 0.12 mg/kg.

The Meeting decided that there were insufficient trials submitted, complying with GAP, and did not estimate a maximum residue level.

Stalk and stem vegetables

In Spain, cyromazine can be used in artichoke at 0.03 kg ai/hL with a PHI of 7 days. In four Spanish trials conducted complying with that countries GAP, residues were: 0.85, 0.95, 1.1 and 1.3 mg/kg.

The Meeting estimated a maximum residue level of 3 mg/kg, an STMR of 1 mg/kg and an HR of 1.3 mg/kg for cyromazine in artichoke.

In France, cyromazine can be applied to celery in the field or in greenhouses at an application rate of 0.3 kg ai/ha with a PHI of 14 days. In 11 trials conducted in France and Spain from 1998 to 2003 using 3 or 4 applications at 0.3–0.36 kg ai/ha, residues, in ranked order (median underlined), were: 0.27(3), 0.36, 0.57, 0.58, 0.60, 0.68, 1.6, 1.8 and 2.3 mg/kg. The commodity description in the trials specified whole plant or stems and was interpreted by the Meeting as matching the Codex description for celery (whole commodity).

Fourteen trials were conducted in the USA in celery at a greater than GAP application frequency (maximum of 6 applications at 0.14 kg ai/ha with a 7 days PHI). Residues 7 days after the last application ranged from 0.05 to 13 mg/kg.

Based on the European trials, the Meeting estimated a maximum residue level of 4 mg/kg, an STMR value of 0.58 mg/kg and an HR value of 2.3 mg/kg for cyromazine in celery.

Fate of residues in processing

Hydrolysis studies representing food processing procedures of pasteurization, baking, boiling, brewing and sterilization were conducted with [^{14}C]cyromazine in buffer solution at pH 4, 5 and 6, incubated for 20 or 60 minutes at 90–120 ˚C, showed that cyromazine was the only compound found at the end of the incubation period.

In a tomato processing study in the USA, tomatoes were harvested 7 days after the last of 6 applications at 0.140 or 0.250 kg ai/ha. Treated samples were pooled and subject to treatment simulating normal commercial processing. Residues decreased after washing, in canned tomato, tomato juice and in ketchup, with mean processing factors (PF) of 0.71, 0.53, 0.75 and 0.84. Residues in wet pomace remained unchanged, but increased in dry pomace (PF=2.8), puree (PF=1.2) and paste (PF=2.1).

Based on the estimated PFs and STMR for tomato of 0.16 mg/kg, the Meeting estimated an STMR-P of 0.11 mg/kg for washed tomato, 0.09 mg/kg for canned tomato, 0.12 for tomato juice, 0.13 mg/kg for ketchup, 0.19 mg/kg for puree and 0.34 mg/kg for tomato paste.

In one study conducted with potatoes, samples from six trials conducted in USA in 1996 were processed according to commercial practices. Mean cyromazine residues in the raw potato was 0.71 mg/kg, which decreased in peeled/rinsed potatoes with a mean PF of 0.9, but increased in potato chips (PF=1.3) and potato granules (PF=2.8). As no recommendation was made for the raw commodity potato, the Meeting did not make a recommendation for processed potato products.

Residues in animal commodities

Direct treatment of poultry (in-feed use)

In four feeding trials, conducted in Australia, hens were fed at rates of 1.5 mg ai/kg for 35 days, 3 mg ai/kg for 4 days, 5 mg ai/kg for 7 days and 9 mg ai/kg for 4 days, samples were taken of muscle, liver and/or eggs. Muscle and liver samples from hens, treated at the GAP rate of 5 mg ai/kg feed, were taken immediately after treatment and up to 2 days post-treatment. Cyromazine residues in muscle were found to decrease from 0.03 to < 0.02 mg/kg in muscle and from 0.12 to < 0.05 mg/kg in liver.

In two trials conducted in France in 1985/1986, hens were fed cyromazine at 5 mg ai/kg feed for up to 38 days. Residues in eggs (egg white/yolk) sampled from 0 to 22 days, following 15 to 38

days of feeding were: 0.15/0.16, 0.15/0.11, 0.12/0.05, 0.08/0.11, 0.12/0.05, 0.04/0.08, 0.08/0.06, 0.08/0.04, < 0.02/0.04, < 0.02/0.03(3) and < 0.02/0.02(9) mg/kg. As the egg white comprises approximately 66% and the yolk 33% of a typical poultry egg, the levels found in egg white/yolk can be expressed on a whole egg basis, in ranked order, as: < 0.02(12), 0.04, 0.05, 0.07(2), 0.09, 0.10(2), 0.14 and 0.15 mg/kg.

In a trial conducted in Israel in 1987, hens were fed cyromazine at 5 and 50 mg/kg feed for 31 days with the animals sacrificed 4 h after removal of the feed. Residues of cyromazine in muscle and liver ranged from 0.04 to 0.10 mg/kg at the 5 mg/kg treatment level and from 0.36 to 0.76 mg/kg at the higher feeding level. Eggs were not analysed.

In a study conducted in the Philippines in 1982 hens were fed for 60 days, at a rate of 1.6 mg ai/kg of feed, no residues were detected in muscle (< 0.025 mg/kg) and liver (< 0.04 mg/kg) in animals slaughtered 2 to 9 days after cessation of feeding. Residues in eggs collected from animals fed cyromazine from 29 to 60 days, 0 to 9 days after feeding ceased were 0.02, < 0.02 and 0.04 mg/kg.

In ten studies conducted in the USA from 1979 to 1986, hens were fed cyromazine for up to 56 days at levels of 2.5, 5.0, 25 and 50 mg ai/kg of feed. In one trial where hens were fed cyromazine at 5 mg/kg from 14 to 27 days, residues in egg white/yolk at day 0 were: 0.09/0.08, 0.11/0.06 and 0.11/0.07 mg/kg, or 0.09 (2) and 0.10 mg/kg in the whole egg. In three trials conducted at 5.0 mg ai/kg feed, egg samples were collected 0 to 7 days after feeding from animals fed 14 to 56 days. Residues in eggs in ranked order, were: < 0.05(4), 0.11(2), 0.07, 0.09(3), 0.10(7), 0.12(4) and 0.16 mg/kg. In one feeding study conducted at a 2.5 mg/kg feeding level for 14 days, residues at 0 days were < 0.05 mg/kg in muscle, skin and fat and 0.08 mg/kg in liver. The levels found after the animals had been fed for 27 days were 0.05 mg/kg in meat and < 0.05 mg/kg in the other tissues. In all cases, residues in fat were < 0.05 mg/kg.

In one study conducted in Japan in 2000, hens were fed cyromazine for 28 days at the level of 5 mg ai/kg. Residues in egg white/yolk collected from 0 to 2 days after treatment were < 0.02/0.03, < 0.02/0.05 and 0.04/0.07 mg/kg, or < 0.02, 0.04 and 0.05 mg/kg expressed on a whole egg basis. Residues at 0 day were 0.05 mg/kg in muscle, 0.07 mg/kg in liver and 0.09 mg/kg in kidney. Cyromazine levels in all tissues after 1 to 3 days were < 0.02 mg/kg.

In summary, residues of cyromazine in eggs from trials conducted according to GAP were: < 0.02 (13), 0.02, 0.04 (3), < 0.05 (4), 0.05 (2), 0.07(3), 0.09 (4), 0.10(9), 0.11(2), 0.12(4), 0.14, 0.15 and 0.16 mg/kg. Residues at 0 day at 2.5 mg/kg level were < 0.05 and 0.05 mg/kg in muscle, < 0.05 and 0.08 mg/kg in liver and < 0.05 mg/kg in fat.

Lactating dairy cows

In two feeding studies conducted in the USA in 1983 and 1992, Holstein dairy cows were dosed at 5.0, 10, 25, 50 or 100 mg ai/kg diet for up to 28 days. Animals were sacrificed on test days 14, 21 and 28 with tissue samples taken. Milk samples consisted of pooled aliquots from the evening and the following morning's milk. Residues in milk plateaued rapidly on the commencement of dosing with the mean levels, after 28 days treatment, increasing proportionally with the dose, ranging from 0.02 mg/kg at the 5 mg/kg to 0.42 mg/kg at the 100 mg/kg level. In one study, the highest residues in tissues, at the lower dose, were found in the animals sacrificed following 14 days of feeding with 0.13 mg/kg in kidney and 0.12 mg/kg in meat; these levels increased to 1.9 and 0.59 mg/kg, respectively in the animals dosed at 50 mg/kg. In the second study, no residues (< 0.05 mg/kg) were found in tissues from animals dosed at 10 mg/kg level. No residues were found in fat samples from any animal at any dosing level in either study.

Livestock Dietary burden

Dietary burden calculations for beef and dairy cattle and broilers and laying poultry are provided in Annex 6. The calculations were made according to the animal diets from US-Canada, EU and Australia in the OECD Table (Annex 6 of the 2006 JMPR Report). A summary of the results are shown on the Table below.

Animal (feed items)	Livestock dietary burden, cyromazine, ppm of dry matter diet					
	US-Canada		EU		Australia	
	max	mean	max	mean	max	mean
Beef cattle	0.31	0.17	8.54	0.57	1.02	0.57
Dairy cattle	0.31	0.17	8.54	0.57	0.31	0.17
Poultry - broiler and layer	0.41	0.06	2.4	0.14	1.4	0.21

Residues in animal commodities

The high and the mean estimated dietary burden for cattle were 8.5 and 0.57 ppm. The estimations were done by interpolation of residues at the 5 ppm feeding level.

Dietary burden (mg/kg)[1] Feeding level [ppm][2]		Cyromazine residues, mg/kg[3]				
		Milk Mean	Muscle High	Liver High	Kidney High	Fat High
MRL cattle beef and dairy	(8.5) [5] high		*(0.204)* 0.12	*(0.153)* 0.09	*(0.221)* 0.13	*(< 0.05)* 0
STMR cattle beef and dairy	(0.57) [5] av		*(0.01)* 0.06	*(0.01)* 0.06	*(0.01)* 0.08	*(< 0.05)* *0*
STMR cattle beef and dairy	0.57) [5] av	*(0.005)* 0.045				

[1] Values in parentheses are the estimated dietary burdens

[2] Values in square brackets are the actual feeding levels in the transfer study

[3] Residue values in parentheses in italics are interpolated from the dietary burden, feeding levels in the transfer study and the residues found in the transfer study. High is the highest individual animal tissue residue in the relevant feeding group. Mean is mean animal tissue (or milk) residue in the relevant feeding group.

The Meeting estimated a maximum residue level of 0.3 mg/kg, an STMR of 0.01 and an HR of 0.20 mg/kg for cyromazine in meat (from mammals other than marine mammals).

The Meeting estimated a maximum residue level of 0.3 mg/kg, an STMR of 0.01 and an HR of 0.187 mg/kg for cyromazine in edible offal (mammalian).

The Meeting estimated a maximum residue level of 0.01 mg/kg and an STMR of 0.005 mg/kg for cyromazine in milks. The Meeting also estimated a median and a highest residue level of 0 mg/kg in mammalian fat.

The high and the mean estimated dietary burden for poultry were 2.4 and 0.14 ppm. The direct treatment for poultry (in-feed use) conducted at 2.5 mg/kg feeding level can be used for estimating residues in poultry tissues.

The Meeting estimated a maximum residue level of 0.1 mg/kg, an STMR of 0.05 mg/kg and an HR of 0.05 mg/kg for cyromazine in poultry meat.

The Meeting estimated a maximum residue level of 0.2 mg/kg, an STMR of 0.065 mg/kg and an HR of 0.08 mg/kg for cyromazine in poultry edible offal. The Meeting also estimated a median and a highest residue level of 0 mg/kg in poultry fat.

The Meeting agreed that for the residue estimation in eggs, the residues coming from the direct use of cyromazine in the feed at 5 mg/kg level, according to GAP (0 day withholding period) represents a better estimation of the likely residues.

The Meeting estimated a maximum residue level of 0.2 mg/kg and an STMR of 0.07 mg/kg and an HR of 0.16 mg/kg for cyromazine in eggs.

The Meeting recommends the withdrawal of the current recommendation of 0.2* mg/kg for cyromazine in eggs, of 0.01* mg/kg in milks, and of 0.05* mg/kg in poultry meat and sheep meat.

DIETARY RISK ASSESSMENT

Long-term intake

The ADI for cyromazine is 0-0.06 mg/kg bw. The International Estimated Daily Intakes (IEDI) for cyromazine was estimated for the 13 GEMS/Food cluster diets using the STMR or STMR-P values estimated by the current Meeting for 35 commodities. The results are shown in Annex 3. The IEDI ranged from 0–2% of the maximum ADI. The Meeting concluded that the long-term intake of residues of cyromazine from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The ARfD for cyromazine is 0.1 mg/kg bw. The International Estimated Short Term Intake (IESTI) for cyromazine was calculated for the plant commodities for which STMRs and HRs were estimated and for which consumption data were available. The results are shown in Annex 4. For the general population, the IESTI was higher than the ARfD for cabbage (120%) and spinach (130% ARfD). For children, the IESTI was higher than the ARfD for cabbage (280%) and spinach (390%). For all the other commodities, the intakes ranged from 0–40%.

The Meeting concluded that the short-term intake of residues of cyromazine from uses other than cabbage and spinach that had been considered by the JMPR is unlikely to present a public concern. The information provided to the JMPR precludes an estimate that the short-term intake of residues of cyromazine from the consumption of cabbage and spinach will be below the ARfD.

The ARfD established by the Meeting in 2006 was based on body-weight loss and decrease in food consumption in dams in developmental toxicity studies. The reason for these effects was unknown and there is a rapid recovery on cessation of administration. The Meeting noted that this ARfD may be conservative. Furthermore, it is possible that the short-term risk assessment conducted by the Meeting may also be conservative.

The Meeting noted that no residue data was available from an alternative GAP to estimate a lower maximum residue level for cyromazine in cabbage and spinach.

5.10 DIFENOCONAZOLE (224)

TOXICOLOGY

Difenoconazole (CAS name, 1-[[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl]methyl]-1*H*-1,2,4-triazole, CAS No. 119446-68-3) is a systemic triazole fungicide that controls a broad spectrum of foliar, seed and soil-borne diseases caused by *Ascomycetes*, *Basidiomycetes* and

Deuteromycetes in cereals, soya, rice, grapes, pome fruit, stone fruit, potatoes, sugar beet and several vegetable and ornamental crops. It is applied by foliar spray or seed treatment and acts by interference with the synthesis of ergosterol in the target fungi by inhibition of the 14α-demethylation of sterols, which leads to morphological and functional changes in the fungal cell membrane. Difenoconazole is being reviewed for the first time by the present Meeting at the request of the CCPR. All critical studies complied with GLP.

Biochemical aspects

In rats given [^{14}C]difenoconazole labelled in either the triazole or phenyl rings as a single oral dose at 0.5 or 300 mg/kg bw, the radiolabel was rapidly and almost completely absorbed from the gastrointestinal tract, widely distributed, and eliminated from the body with excretion half-lives of about 20 h at the lower dose and about 33–48 h at the higher dose. At doses of 0.5 and 300 mg/kg bw, approximately 13–22% and 8–15%, respectively, of the applied radioactivity was excreted via the urine in rats. Excretion via the faeces accounted for 81–87% (lower dose) to 85–95% (higher dose) of the radiolabel; however, approximately 73% (males) to 76% (females) of the lower dose and approximately 39% (females) to 56% (males) of the higher dose was eliminated from the body via the bile in bile-duct cannulated rats. Thus, bioavailability decreased with increasing dose. When bile from rats given difenoconazole was introduced into the duodenum of other bile-cannulated rats, 80% of the radioactivity was re-eliminated in the bile and 4% in the urine, indicating that there was extensive enterohepatic recirculation. The greater quantities of radioactivity were distributed to the gastrointestinal tract, liver and kidneys. The initial plasma half-life was approximately 4–6 h at the lower dose and 22–24 h at the higher dose and the terminal half-life was approximately 3–4 days at both doses. In spite of these long terminal half-lives, there was no evidence for bioaccumulation of difenoconazole.

After oral administration to male and female rats, the systemically available portion of [^{14}C-phenyl]difenoconazole was rapidly and extensively metabolized to a number of biotransformation products. Three main metabolites isolated from the faeces accounted for approximately 68% of the administered doses. These were: the hydroxylated product of cleavage of the dioxolane ring; its further metabolite resulting from hydroxylation of the chlorophenoxy ring; and the product of the hydroxylation of difenoconazole, occurring directly in the chlorophenoxy ring. A minor metabolic pathway involves cleavage of the alkyl chain between the triazole and the inner phenyl ring, resulting in a hydroxy acetic acid, 2-chloro-4-(4-chlorophenoxy)-benzoic acid and free 1,2,4-triazole. Sulfate conjugates were identified for some hydroxylated metabolites.

Toxicological data

The acute toxicity of difenoconazole was low, with values for the oral LD_{50} being 1453 mg/kg bw in rats and > 2000 mg/kg bw in mice. The dermal LD_{50} in rabbits was > 2010 mg/kg bw and the inhalation LC_{50} in rats was > 3.3 mg/L. Difenoconazole is very slightly and transiently irritating to the skin and moderately and transiently irritating to the eyes of rabbits and is non-sensitizing in a modified Buehler test in guinea-pigs.

Overall, in short-term studies with orally-administered difenoconazole, the signs of toxicity observed in mice, rats and dogs were similar, with reduced body-weight gain and increased liver weights being common features. Histopathology confirmed the liver as a target organ with observation of diffuse or centrilobular hypertrophy of hepatocytes in rats and mice, although this can also be indicative of an adaptive response. Cataracts were found in dogs fed diets containing difenoconazole at a concentration of ≥ 3000 ppm, equal to 96.6 mg/kg bw per day, for 6 months, with an NOAEL of 1000 ppm, equal to 31.3 mg/kg bw per day; however, cataracts were not induced in a second study in dogs given diets containing difenoconazole at up to 1500 ppm, equal to 51.2 mg/kg bw per day, for 1 year. Increased activity of alkaline phosphatase was observed in two studies in rats and in one in dogs. No other blood chemistry changes were consistently observed, although reduced

concentrations of blood protein were observed in dogs given diets containing difenoconazole at 6000 ppm, equal to 157.8 mg/kg bw per day. Also in dogs, a reduction in erythrocyte count of almost 20% was observed in females at this high level of exposure.

For the short-term dietary studies, the NOAELs were: in studies of up to 90 days in rats, 200 ppm (equal to 17 mg/kg bw per day) on the basis of increased hepatocellular hypertrophy and liver weight; in a 90-day dietary study in mice, 200 ppm (equal to 34.2 mg/kg bw per day) on the basis of clinical signs of toxicity and changes in liver weight and increased incidence of centrilobular hepatocellular hypertrophy; in a 28-week study in dogs, 1000 ppm (equal to 31.3 mg/kg bw per day) on the basis of cataracts and liver-weight changes; in a 12-month study in dogs, 100 ppm (equal to 3.6 mg/kg bw per day) on the basis of reduced body-weight gain; in a 4-week study of dermal toxicity with difenoconazole in rats, 100 mg/kg bw per day, on the basis of minimal centrilobular hepatocellular hypertrophy, minimal to moderate thyroid follicular cell hypertrophy and skin lesions at the site of application.

Long-term feeding studies in rats and mice fed with difenoconazole confirmed that the primary target organ was the liver. There was no evidence for any carcinogenic potential in rats, in which hepatic effects were increases in liver weight and hepatocellular hypertrophy in male and female rats. In addition, there were reductions in erythrocyte parameters in female rats at the highest dose, 2500 ppm, equal to 170 mg/kg bw per day.

In mice, there was very high, treatment-related mortality at the beginning of the 18-month study. In groups of 70 mice, there were 52 deaths among females receiving difenoconazole at 4500 ppm and 16 deaths among females at 3000 ppm (reduced to 2500 ppm after 1 week) within the first 2 weeks, while, among the male mice there were 11 deaths in the group at 4500 ppm within the first 3 weeks of the study. There was an increased incidence of hepatocellular adenomas and carcinomas in the group of male and female mice fed diet containing difenoconazole at 2500 ppm, equal to 423 and 513 mg/kg bw per day, respectively, and males at 4500 ppm, equal to 819 mg/kg bw per day. No increase in the incidence of tumours was observed at 300 ppm, equal to 46.3 and 57.8 mg/kg bw per day in males and females, respectively. However, the neoplastic responses occurred at highly toxic doses that also caused the death of substantial proportions of the groups of mice. Among the survivors, biliary stasis and hepatic single-cell necrosis as well as hepatocellular hypertrophy were significantly increased in male and female mice at the tumorigenic doses. On the basis of a study of enzyme activities in male mice, difenoconazole is considered to be a reversible barbiturate-type inducer of metabolizing enzymes in the mouse liver. No peroxisome proliferation was observed. The NOEL was 10 mg/kg, there being no inductive effect on metabolizing enzymes and other parameters in the mouse liver.

The NOAEL in long-term studies in rats was 20 ppm, equal to 1.0 mg/kg bw per day, on the basis of reduced body-weight gains during the first year in males and females, reduced platelet counts in males and hepatic centrilobular hypertrophy in males and females at 500 ppm, equal to 24 mg/kg bw per day. In long-term studies in mice, the NOAEL was 30 ppm, equal to 4.7 mg/kg bw per day, on the basis of decreased body-weight gain in males, increased liver weight in females and hepatocellular hypertrophy in males at 300 ppm, equal to 46.3 mg/kg bw per day.

Difenoconazole was tested for genotoxicity in an adequate range of assays, both in vitro and in vivo. No evidence for genotoxicity was observed in any test.

The Meeting concluded that difenoconazole is unlikely to be genotoxic.

The Meeting concluded that difenoconazole caused an increase in the incidence of hepatocellular adenomas and carcinomas in mice (but not in rats) by a non-genotoxic mode of action, the nature of which has not been established but which resembles that for phenobarbital in its liver enzyme-inducing characteristics. It is therefore unlikely to pose a carcinogenic risk to humans at exposure levels that do not cause changes in the liver.

The reproductive toxicity of difenoconazole was investigated in a two-generation study of reproduction in rats and in studies of developmental toxicity in rats and rabbits.

Reproductive function was not affected in rats in the two-generation study and the NOAEL for reproductive function was 2500 ppm, equal to 132.1 mg/kg bw per day, the highest dose tested. The NOAEL for systemic toxicity in the parental animals was 250 ppm, equal to 11.5 mg/kg bw per day on the basis of reduced body-weight gain during the pre-mating period in F_0 and F_1 generations at 2500 ppm, equal to 122.7 mg/kg bw per day during these periods. In pups, lower birth weight and subsequent decreased body-weight gain at 2500 ppm, equal to 158.0 mg/kg bw per day, were the effects that defined the NOAEL for offspring toxicity at 250 ppm, equal to 14.1 mg/kg bw per day in the females.

In a study of developmental toxicity in which rats were given difenoconazole by gavage on days 6–15 of gestation, the NOAEL for maternal toxicity was 20 mg/kg bw per day on the basis of reduced body-weight gain and excess salivation first observed on day 2 of dosing in 14 out of 23 dams at 100 mg/kg bw per day. There was a statistically significant, but small increased incidence of changes in thoracic vertebral ossification centres in foetuses at 200 mg/kg bw. The NOAEL for foetal toxicity was 100 mg/kg bw per day on the basis of these skeletal anomalies.

In a study of developmental toxicity in which rabbits were given difenoconazole by gavage on days 7–19 of gestation, the NOAEL for maternal toxicity was 25 mg/kg bw per day on the basis of reduced body-weight gain in the first few days of dosing at 75 mg/kg bw per day. Examination of the foetuses did not reveal any treatment-related effects in soft or ossified tissues. The NOAEL for developmental toxicity was 75 mg/kg bw per day, the highest dose tested.

In a single-dose study of neurotoxicity in rats treated by gavage, the NOAEL was 25 mg/kg bw based on reduced forelimb-grip strength interpreted as a non-specific response at 200 mg/kg bw. In a 90-day study of neurotoxicity in rats given diets containing difenoconazole, the NOAEL was 40 ppm, equal to 2.8 mg/kg bw per day, on the basis of reduced hind limb-grip strength in males during the final week of the study at 250 ppm, equal to 17.3 mg/kg bw per day. These responses were considered to be non-specific effects of difenoconazole because of the absence of any changes in the multiple end-points of neurotoxicity that were measured and the absence of neuropathological findings.

The Meeting concluded that difenoconazole is unlikely to cause neurotoxicity in humans.

There were no indications of immunotoxicity in general studies of toxicity in dogs, rats and mice.

Some aspects of the toxicology of three plant metabolites of difenoconazole that are also found in rats given difenoconazole were investigated. These metabolites were: 1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-(1,2,4-triazol)-1-yl-ethanone, 1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-(1,2,4-triazol)-1-yl-ethanol and 2-chloro-4-(4-chlorophenoxy)-benzoic acid. The LD_{50} value for each of these metabolites was > 2000 mg/kg bw and none of them showed any alerts for mutagenic activity. In addition, there are three metabolites which are common to all parent triazoles: 1, 2, 4-triazole, triazole alanine and triazole acetic acid. 1,2,4-Triazole is a soil metabolite that also appears to a small extent (< 10%) in some studies in plants and is found as at least 10% of the total metabolites in rats administered difenoconazole. Triazole alanine and triazole acetic acid are plant-specific metabolites. The acute toxicity (LD_{50}) values for 1,2,4-triazole, triazole alanine and triazole acetic acid were similar to or higher than the LD_{50} values for difenoconazole. Some recent studies conducted with 1,2,4-triazole have shown certain effects at high doses, i.e., testicular atrophy in mice at $\geq$ 487 mg/kg bw per day; effects on the central nervous system and pathology in rats at $\geq$ 183 mg/kg bw per day; and a reduction in fertility in a two-generation study of reproduction in rats at 218 mg/kg bw per day. The NOAELs for 1,2,4-triazole for these effects were 90 mg/kg bw per day for testicular atrophy in mice, 33 mg/kg bw per day for neurotoxicity in rats and 16 mg/kg bw per day for effects on fertility in rats.

Repeat-dose studies in which triazole alanine was administered for up to 90 days did not show any significant effects other than reduced body-weight gains at 20 000 ppm, equivalent to 2000 mg/kg bw per day in rats and 500 mg/kg bw per day in dogs. The NOAELs in these studies were 5000 ppm,

equivalent to 500 mg/kg bw per day, in rats and 8000 ppm, equivalent to 200 mg/kg bw per day, in dogs. In a two-generation study with triazole alanine in rats, the NOAEL for parental toxicity was 10 000 ppm, equivalent to 500 mg/kg bw per day, the highest dose tested, and the NOAEL for reproductive toxicity was 2000 ppm, equivalent to 100 mg/kg bw per day, on the basis of reduced birth weights at 10 000 ppm. In a study of teratogenicity in rats, the NOAEL for maternal toxicity was 1000 mg/kg bw per day, the highest dose tested, and the NOAEL for developmental toxicity was 100 mg/kg bw per day on the basis of retarded ossification at 1000 mg/kg bw per day.

Triazole acetic acid has been tested in a 14-day dietary study in which the NOAEL was 8000 ppm, equal to 704 mg/kg bw per day, respectively, the highest dose tested.

None of these metabolites has been tested for carcinogenicity. The extent to which 1,2,4-triazole, triazole alanine and triazole acetic acid had been tested for mutagenicity varied, but no significant responses were obtained in any of the studies.

Medical surveillance of personnel has been conducted since the early 1990s at sites in several countries where difenoconazole is manufactured. Reports were available up to the end of 2002. There have been no reports of toxicity in workers during manufacture and there was only one case of allergic reaction to a formulated product. There were no reports of poisoning and no reports of sensitization during use of the formulated product.

The Meeting concluded that the existing database was adequate to characterize the potential hazards to foetuses, infants and children.

Toxicological evaluation

An ADI of 0–0.01 mg/kg bw was established for difenoconazole based on the NOAEL of 1.0 mg/kg bw per day in rats, identified on the basis of reduced body-weight gains, reduced platelet counts and hepatic hypertrophy in a 24-month long-term dietary study of toxicity and carcinogenicity. A safety factor of 100 was applied. The increased incidence of hepatocellular adenomas and carcinomas observed in mice at 423 mg/kg bw per day, the NOAEL being 4.7 mg/kg bw per day, in an 18-month long-term dietary study of toxicity and carcinogenicity, was likely to be due to a mode of action without human relevance at exposure levels that do not cause changes in the liver.

An ARfD of 0.3 mg/kg bw was established for difenoconazole. This was based on the NOAEL of 25.0 mg/kg bw in rats, identified on the basis of clinical signs in a single-dose study of neurotoxicity and using a safety factor of 100. This ARfD is supported by the NOAEL of 25 mg/kg bw per day for maternal toxicity in a study of developmental toxicity in rats and rabbits on the basis of excess salivation in rats at 100 mg/kg bw per day and body-weight loss in rabbits during the first few days of treatment at 75 mg/kg bw per day.

A toxicological monograph was prepared.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Mouse	Eighteen-month study of toxicity and carcinogenicity	Toxicity	30 ppm, equal to 4.7 mg/kg bw per day	300 ppm, equal to 46.3 mg/kg bw per day
		Carcinogenicity	300 ppm, equal to 46.3 mg/kg bw per day	2500 ppm[a], equal to 423 mg/kg bw per day

Rat	Twenty-four-month studies of toxicity and carcinogenicity	Toxicity	20 ppm, equal to 1.0 mg/kg bw per day	500 ppm, equal to 24 mg/kg bw per day
		Carcinogenicity	2500 ppm[a] equal to 124 mg/kg bw per day	—
	Two-generation study of reproductive toxicity[b]	Reproductive toxicity	2500 ppm[a] equal to 132.1 mg/kg bw per day	—
		Parental toxicity	250 ppm, equal to 11.5 mg/kg bw per day	2500 ppm[a] equal to 122.7 mg/kg bw per day
		Offspring toxicity	250 ppm, equal to 14.1 mg/kg bw per day	2500 ppm[a] equivalent to 158 mg/kg bw per day
	Developmental toxicity[c]	Maternal toxicity	20 mg/kg bw per day	100 mg/kg bw per day
		Embryo and foetal toxicity	100 mg/kg bw per day	200 mg/kg bw per day[a]
	Acute neurotoxicity	Toxicity	25 mg/kg bw	200 mg/kg bw per day[a]
Rabbit	Developmental toxicity[c]	Maternal toxicity	25 mg/kg bw per day	75 mg/kg bw per day[a]
		Embryo and foetal toxicity	75 mg/kg bw per day[a]	—
Dog	One-year study of toxicity	Toxicity	100 ppm, equal to 3.6 mg/kg bw per day	500 ppm, equal to 16.4 mg/kg bw per day

[a] Highest dose tested.

[b] Measurements of intake of the compound are the mean for the pre-mating phases for females.

[c] Gavage administration.

Estimate of acceptable daily intake for humans

0–0.01 mg/kg bw

Estimate of acute reference dose

0.3 mg/kg bw

Information that would be useful for the continued evaluation of the compound

Results from epidemiological, occupational health and other such observational studies of human exposure

Critical end-points for setting guidance values for exposure to difenoconazole

Absorption, distribution, excretion and metabolism	
Rate and extent of oral absorption	High, but incomplete (rats)
Dermal absorption	Approximately 8% (rats)
Distribution	Distributed throughout the body; higher concentrations in liver and gastrointestinal tract

Potential for accumulation	Low, no evidence of accumulation
Rate and extent of excretion	High; essentially 100% excretion in bile and urine within 7 days
Metabolism in animals	Extensive; a small number (< 10) of metabolites; little parent compound remaining
Toxicologically significant compounds in animals, plants and environment	Parent, 1,2,4-triazole
Acute toxicity	
Rat, LD_{50}, oral	1453 mg/kg bw
Rat, LC_{50}, inhalation	3.3 mg/L (4 h)
Rabbit, LD_{50}, dermal	2010 mg/kg bw
Rabbit, skin irritation	Very slightly and transiently irritating
Rabbit, eye irritation	Moderately and transiently irritating
Guinea-pig, skin sensitization	Not sensitizing (modified Buehler test)
Short-term studies of toxicity	
Target/critical effect	Liver; body weight
Lowest relevant oral NOAEL	3.6 mg/kg bw per day (12-month study in dogs)
Lowest relevant dermal NOAEL	100 mg/kg bw per day (4-week study in rats)
Lowest relevant inhalation NOAEC	No data
Genotoxicity	
	Not genotoxic
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	Liver; body weight
Lowest relevant NOAEL	1.0 mg/kg bw per day (24-month study in rats)
Carcinogenicity	Not carcinogenic at levels below those causing changes in the liver
Reproductive toxicity	
Reproductive target/critical effect	None
Lowest relevant reproductive NOAEL	132 mg/kg bw per day
Developmental target/critical effect	Not teratogenic; reduced foetal body weight, delayed ossifications in rats, but not in rabbits
Lowest relevant developmental NOAEL	100 mg/kg bw per day (rats)
Neurotoxicity/delayed neurotoxicity	
Single-dose study of neurotoxicity	No signs of neurotoxicity, NOAEL was 25 mg/kg bw (rats)
Ninety-day study of neurotoxicity	No signs of neurotoxicity, NOAEL was 2.3 mg/kg bw (rats)
Other toxicological studies	
	Induction of liver xenobiotic metabolizing enzymes
	Studies of mammalian and plant metabolites
Medical data	
	No reports of toxicity in workers exposed during

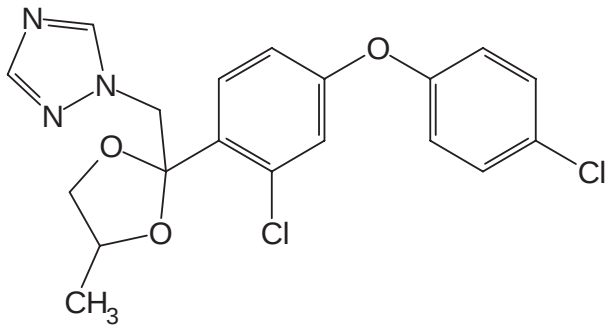
manufacture or use

Summary			
	Value	**Study**	**Safety factor**
ADI	0–0.01 mg/kg bw	Rat, 2-year study of toxicity and carcinogenicity	100
ARfD	0.3 mg/kg bw	Rat, single-dose study of neurotoxicity study, supported by maternal effects in a study of developmental toxicity studying rabbits	100

RESIDUE AND ANALYTICAL ASPECTS

Difenoconazole was considered for the first time by the present meeting. It is a broad-spectrum fungicide used for disease control in many fruits, vegetables, cereals and other field crops. It has preventive and curative action. Difenoconazole acts by inhibition of demethylation during ergosterol synthesis.

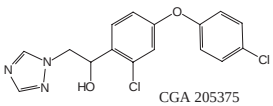
1-[2-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-4-methyl[1,3]dioxolan-2-ylmethyl]-1H-1,2,4-triazole



Animal metabolism

The Meeting received animal metabolism studies with difenoconazole in rats, lactating goats and laying hens. Difenoconazole [^{14}C] labelled in the central phenyl ring or the triazole ring was used in most of the metabolism studies. Difenoconazole [^{14}C] labelled in the chlorophenoxy ring was used in some of the studies.

Difenoconazole is rapidly metabolized, initially to 1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-(1,2,4-triazol)-1-yl-ethanol (CGA 205375) and then with cleavage of the triazole moiety from the chlorophenoxyphenyl moiety. Conjugates are formed from hydroxylated metabolites. TRR levels are higher in the liver than in other tissues. Most of the TRR is rapidly excreted.



CGA 205375

Parent difenoconazole has a tendency to fat-solubility, but it is always a minor component of the residue. The major component of the residue in most animal commodities is CGA 205375, which appears to be fat-soluble because residue concentrations in fat are approximately 3 times as high as those in muscle. However, it is not strong fat-solubility because residue concentrations in fat are less than those in kidney and much less than those in liver (typically residues in liver are 6–8 times as high as in the fat).

When rats were orally dosed with labelled difenoconazole it was readily absorbed followed by extensive metabolism and excretion. The following metabolites were identified in excreta: CGA 205375, 1,2,4-triazole, 2-chloro-4-(4-chlorophenoxy)-benzoic acid, 2-chloro-4-(4-

chlorophenoxy)-phenyl-hydroxyacetic acid, hydroxylated difenoconazole and hydroxylated CGA 205375. Sulphate conjugates of the hydroxylated metabolites were identified in urine. (See the toxicology report for more details of laboratory animal metabolism)

When two lactating goats were orally dosed with labelled ([^{14}C]triazole and [^{14}C]phenyl) difenoconazole for 10 consecutive days at 7.5 mg/animal/day, equivalent to 4.7 and 5.6 ppm in the feed, most of the administered [^{14}C] was excreted in the faeces (75% and 67%) and urine (31% and 21%). Residues in milk reached a plateau by day 2 (phenyl) and days 4–7 (triazole). Of the [^{14}C] in milk, 19% and 32% were distributed into the fat portion for the triazole and phenyl labels respectively (metabolite 1,2,4-triazole is water soluble). Residues of [^{14}C] were higher in liver (0.28 and 0.26 mg/kg) than in other tissues. Metabolite CGA 205375 constituted 57–58% of the TRR in liver, with parent difenoconazole at 1% or less. Triazole was the major component identified in milk, constituting 47% TRR.

When four lactating goats were orally dosed with labelled ([^{14}C]triazole and [^{14}C]phenyl) difenoconazole for 4 consecutive days at 150 mg/animal/day, equivalent to 100 ppm in the feed, [^{14}C] recovery was marginal at 40–64%. The TRR in liver (7.5 and 6.0 mg/kg) was much higher than other tissues. CGA 205375 was the major residue in each tissue, accounting for approximately 30–70% of the TRR. Difenoconazole residues in liver (0.62 and 0.40 mg/kg) were higher than in other tissues. Difenoconazole accounted for 1.5–8.3% of the TRR in each of the tissues. In milk, CGA 205375 accounted for 21% and 34% of the TRR (0.38 and 0.14 mg/kg), while difenoconazole (6–9% TRR) and triazole (6% TRR) were minor parts of the residue.

Two lactating goats were dosed orally once daily for 4 consecutive days by gelatin capsule with 150 mg/animal/day of [^{14}C-phenyl]difenoconazole, equivalent to 100 ppm in the feed and were slaughtered approximately 6 h after the final dose for tissue collection. CGA 205375 was the major component of the residue in all tissues and milk. Parent difenoconazole was present in all tissues and milk, but never exceeding 10% of the TRR. A number of metabolites resulted from hydroxylation and conjugation with glucuronic acid, sulphate and glycine. The concentration of the main component, CGA 205375, in fat was 2.3 times its concentration in muscle, but much below its concentration in liver and similar to that in kidney, suggesting borderline fat solubility.

When 4 laying hens were orally dosed with labelled ([^{14}C]triazole and [^{14}C]phenyl) difenoconazole for 14 consecutive days at 0.55 mg/bird/day, equivalent to 5 ppm in the feed, most of the administered [^{14}C] was excreted in the faeces (> 89%). Highest TRR appeared in the kidney (0.43 and 0.49 mg/kg) and liver (0.13 and 0.13 mg/kg). Apparent plateaus for TRR in egg whites and yolks were reached after approximately 4 and 7 days of dosing respectively. The plateau TRR values in egg whites were quite different for the two labels: 0.14 mg/kg for [^{14}C]triazole label and 0.011 mg/kg for [^{14}C]phenyl label, whereas the plateau levels in the yolks were essentially the same (0.28 and 0.29 mg/kg).

When 20 laying hens were orally dosed with labelled ([^{14}C]triazole and [^{14}C]phenyl) difenoconazole for 3 consecutive days at 7.5 mg/bird/day, equivalent to 68 ppm in the feed, most of the administered [^{14}C] was excreted in the faeces (76%). Highest TRR occurred in the liver (4.3 and 4.7 mg/kg) and kidney (1.9 and 2.2 mg/kg). CGA 205375 was the major identified component in each tissue: liver (30% and 34% TRR), kidney (20% and 22%), muscle (8.8% and 35%) and fat (46% and 64%). Parent difenoconazole accounted for less than 5% TRR in each tissue. For eggs from the phenyl label treatment, CGA 205375 was the main component of the residue (73–83% TRR). For the triazole label, triazole accounted for 67% of TRR in egg white and 33% TRR in egg yolk, while CGA 205375 accounted for 7.8% TRR in egg white and 36% TRR in egg yolk. Approximately 4-5% of the TRR in egg yolks was identified as parent difenoconazole.

Five laying hens were dosed orally once daily for 4 consecutive days by gelatin capsule with 12.5 mg/bird/day of [^{14}C-triazole]difenoconazole, equivalent to 121 ppm in the feed and were slaughtered approximately 6 h after the final dose for tissue collection. Significant [^{14}C] levels appeared in all tissues (liver 13 mg/kg, muscle 4.9 mg/kg, fat 10.4 mg/kg) and eggs (whites 4.0 mg/kg, yolks 4.5 mg/kg). CGA 205375 was a major component of the residue in tissues (liver 56%

TRR, muscle 24% TRR, fat 61% TRR) and egg yolk (53% TRR). Triazole was also a significant component of the residue in tissues (liver 18% TRR, muscle 55% TRR, fat 4.6% TRR) and eggs (whites 75% TRR, yolks 31% TRR). Parent difenoconazole was a minor component of the residue in liver, muscle and egg yolk (< 5%TRR) but accounted for 18% of the TRR in fat.

The metabolism of difenoconazole in rats, goats and hens is qualitatively similar.

Plant metabolism

The Meeting received plant metabolism studies with difenoconazole in tomatoes, wheat, potatoes, grapes and oilseed rape. Difenoconazole [^{14}C] labelled in the central phenyl ring, in the triazole ring or in the chlorophenoxy ring was used in the metabolism studies.

Difenoconazole is generally slowly absorbed and metabolized. In most cases, particularly for parts of the plant directly exposed to the treatment, the parent difenoconazole is the dominant part of the residue. Parts of the plant not directly exposed are more likely to contain a residue dominated by a mobile water-soluble metabolite such as triazolylalanine.

The following plant metabolites apparently do not occur as animal metabolites of difenoconazole: triazolylalanine (2-amino-3-(1,2,4]triazol)-1-yl-propionic acid), triazolyl acetic acid (1,2,4-triazol-1-yl-acetic acid) and triazolyl-lactic acid (1,2,4-triazol-1-yl-lactic acid). At least some of these metabolites are common to other fungicides containing the 1,2,4-triazole moiety.

In a tomato metabolism study in USA, tomato plants in pots in a greenhouse were foliar sprayed 6 times at 7-day intervals with [^{14}C]phenyl and [^{14}C]triazole labelled difenoconazole at the equivalent of 0.12 kg ai/ha. Parent difenoconazole was the major part of the residue on foliage. Residue levels on tomato fruits sampled 7 days after the final treatment were insufficient for identification. A field-grown tomato metabolism study produced similar results.

In another tomato metabolism study in USA, tomato plants in pots in a greenhouse were foliar sprayed 6 times at 7-day intervals with [^{14}C]triazole labelled difenoconazole at the equivalent of 0.12 kg ai/ha. In tomato fruits sampled 33 days after the final treatment, parent difenoconazole (12–51% TRR) and metabolite triazolylalanine (19–42% TRR) were major components of the residue (TRR 0.13–0.20 mg/kg). In a parallel study with phenyl labelled difenoconazole, tomato fruits, sampled 33 days after the final treatment, contained parent difenoconazole (66% TRR) as the major part of the residue (TRR 0.17 mg/kg). In both of these studies low concentrations (< 2% TRR) of metabolite CGA 205375 and its ketone (1-(2-chloro-4-(4-chloro-phenoxy)-phenyl)-2-(1,2,4-triazol)-1-yl-ethanone) occurred in the fruits.

In a wheat metabolism study, triazole and triazolylacetic acid were identified in the mature stalks and grain produced from [^{14}C]triazole labelled difenoconazole treated seed. Metabolite CGA 205375 was identified in wheat tops from a parallel wheat metabolism study with [^{14}C]phenyl labelled difenoconazole.

In a greenhouse wheat metabolism study in USA, spring wheat seeds were treated with [^{14}C]phenyl and [^{14}C]triazole labelled difenoconazole at 0.25 and 0.30 g ai/kg seed and grown to maturity. Parent difenoconazole and metabolite CGA 205375 were identified at low levels in wheat tops at 25 % maturity (40 days post sowing).

In a greenhouse wheat metabolism study in USA, spring wheat was foliar sprayed 4 times with [^{14}C]phenyl and [^{14}C]triazole labelled difenoconazole at a rate equivalent to 0.25 kg ai/ha. Mature samples of grain were harvested 29 days after the final application. In grain from the [^{14}C-triazole]difenoconazole treated crop, triazolylacetic acid and triazole accounted for 20% and 10% of the TRR (1.4 mg/kg) respectively. In grain from the [^{14}C-phenyl]difenoconazole treated crop, the TRR (0.064 mg/kg) was much lower, demonstrating that metabolic cleavage of the compound occurred before translocation to the grain. In the mature stalks, difenoconazole accounted for 50% of the TRR (54 and 47 mg/kg) for both labels.

Parent difenoconazole was not identified in mature grain from the wheat metabolism studies.

In a greenhouse potato metabolism study in USA, potato plants were foliar sprayed 6 times with [^{14}C]chlorophenoxy labelled difenoconazole at the equivalent of 0.12 kg ai/ha per application. Very little of the [^{14}C] translocated to the tubers (TRR 0.012 mg/kg) with parent difenoconazole and two primary metabolites identified as low-level components of the residue (< 10% TRR). Parent difenoconazole was the major component (76% TRR) of the foliage residue.

In a parallel study on potatoes with [^{14}C]triazole labelled difenoconazole, triazolylalanine (79% TRR) was the major part of the residue in tubers (TRR 0.087 mg/kg). Parent difenoconazole was again the major component (71% TRR) of the foliage residue.

In a field plot grape metabolism study in USA, grape vines were foliar sprayed 5 times with [^{14}C]phenyl and [^{14}C]triazole labelled difenoconazole. Parent difenoconazole was the major component (51% and 45% TRR) of the residue (TRR 0.13 and 0.12 mg/kg) in grapes harvested 20 days after 3 and 5 sprays. None of the identified metabolites exceeded 10% of the TRR in grapes. Parent difenoconazole was also the major identified component (17% TRR) of the residue (TRR 0.047 mg/kg) in grapes harvested 77 days after the second treatment.

In a field plot oilseed rape metabolism study in Switzerland, spring rape received two foliar sprays with [^{14}C]chlorophenoxy labelled difenoconazole at the equivalent of 0.13 kg ai/ha. Parent difenoconazole was the major identified component of the residue in stalks (17% TRR), seeds (15% TRR) and pods (17% TRR) taken at mature harvest 39 days after the second application and in oil (26% TRR) produced from the seed. Metabolite CGA 205375 exceeded 10% of TRR in the stalks (14%) and pods (11%).

In a parallel oilseed rape study with [^{14}C]triazole labelled difenoconazole, parent difenoconazole was a major identified component of the residue in stalks (17% TRR), pods (14% TRR) from samples taken at mature harvest, 39 days after the second application, and in oil (84% TRR) produced from the seed. Metabolite CGA 205375 exceeded 10% of TRR in the stalks (17%) and pods (13%). Triazolylalanine, the major residue component in the seed (56% TRR) also exceeded 10 % in pods (12%). Triazolylalanine was also the major residue component in the meal (56% TRR). Other identified components of the residue in the meal were triazolylacetic acid, CGA 205375 and difenoconazole.

Parent difenoconazole is the main component of the residues in those parts of the crop directly exposed to treatment. For other parts of the crop, e.g., the grain of cereals and the tubers of potatoes, the main components of the residue are translocatable metabolites, e.g., triazolylalanine, which are common to other fungicides containing the 1,2,4-triazole moiety.

Environmental fate in soil

The Meeting received information on soil aerobic metabolism and soil photolysis properties of difenoconazole as well as studies on the behaviour of difenoconazole residues in crop rotations. Difenoconazole residues are reasonably persistent in soils and are expected to be present in the soil at harvest time for treated root and tuber crops. Difenoconazole residues are also expected to persist in the soil until the sowing of rotational crops. The confined rotational crops studies demonstrate that difenoconazole itself does not appear as a residue in the rotational crop. The water-soluble and mobile metabolites triazolylalanine, triazolylacetic acid and triazolyl-lactic acid have been identified in the rotational crops.

Aerobic soil degradation rates were influenced by the nature of the soil, temperature, moisture status of the soil and dose when [^{14}C]difenoconazole was subjected to laboratory soil incubation. Estimated aerobic soil metabolism half-lives for difenoconazole at 20 °C ranged from 63 to 700 days (n=12) with a median of 181 days. After 220–300 days, mineralization and unextractable residues (20–54% of dose) were major sinks for the [^{14}C] label. The degree of mineralization was different for

the phenyl and triazole label positions, e.g., 0.8–4.6 % of the dose for the triazole label and 3.4–33 % for the phenyl label.

CGA 205375 and 1,2,4-triazole were identified as soil metabolites. Metabolite CGA 205375 consistently reached a maximum (expressed as parent) of 5–10% of the dose and had begun to decline by the end of the observation period. Metabolite 1,2,4-triazole typically reached a maximum (expressed as parent) around 20% of the dose during the observation period. The aerobic soil metabolism of the metabolites, CGA 205375 and 1,2,4-triazole, was studied separately. The major metabolite of CGA 205375 was 1,2,4-Triazole.

Difenoconazole on a soil surface was stable to photolysis during the test period of 30 days.

In rotational crops with the [^{14}C] label in the phenyl moiety, the level of carry-over residues in rotational crops was too low for characterization or identification. With the [^{14}C] label in the triazole moiety and application to bare ground at 0.13 kg ai/ha, metabolites triazolylalanine, triazolylacetic acid and triazolyl-lactic acid were identified in rotational crops: maize grain TRR 0.21 mg/kg (66% triazolylalanine 66%); wheat grain 0.34 mg/kg (44% triazolylalanine, 26% triazolylacetic acid); lettuce heads 0.017 mg/kg (31% triazolylalanine, 43% triazolyl-lactic acid; and sugar beet tops 0.029 mg/kg (25% triazolylalanine, 54% triazolyl-lactic acid).

In outdoor non-confined rotational crop studies in Germany, bare ground was treated directly with difenoconazole at a rate equivalent to 0.75 kg ai/ha and the upper 10 cm soil layer was turned over to mix in the applied material. Carrots or spinach were sown 30–31 days after the difenoconazole application and harvested for analysis 97–136 days (carrots) and 62–77 days (spinach) after the application. Residues of difenoconazole (LOQ 0.02 mg/kg) and triazolylalanine (LOQ 0.05 mg/kg) in the carrots and spinach did not exceed the LOQs. Difenoconazole residue levels in the soil were in the range 0.15-0.23 mg/kg during rotational crop samplings.

Methods of residue analysis

The Meeting received descriptions and validation data for analytical methods for residues of parent difenoconazole in raw agricultural commodities, processed commodities, feed commodities, animal tissues, milk and eggs. Methods were provided also for metabolite CGA 205375 in animal tissues, milk and eggs.

In the methods for plant commodities, macerated samples are typically extracted with methanol or acetonitrile and the extract is cleaned up by solvent partitions and solid phase column chromatography. The final residue may be determined by GLC with ECD or NPD or alternatively by LC-MS-MS. LOQs are typically in the 0.01–0.05 mg/kg range. The analytical methods for animal commodities are similar, but with extraction methods tailored for milk, eggs or animal tissues. The LOQ for milk is 0.005 mg/kg and eggs and tissues 0.01–0.05 mg/kg.

Analytical recovery data were satisfactory for difenoconazole and CGA 205375 (in animal commodities) for numerous commodities.

Residue methods were tested by independent laboratories unfamiliar with the analysis and were found to have satisfactory recoveries and no background interferences.

DFG Method S19 (revision) was demonstrated to be suitable for analysis of difenoconazole residues in a number of crop commodities.

The acetonitrile-water extraction of poultry tissues and eggs, as in the analytical method, was applied to liver, fat, muscle and egg yolk samples from a [^{14}C-triazole]difenoconazole metabolism study and was shown to provide comparable extraction for difenoconazole, CGA 205375 and 1,2,4-triazole with the exhaustive extraction of the metabolism study.

Stability of residues in stored analytical samples

Information was received on the freezer storage stability of parent difenoconazole residues in plant and animal commodities, and of residues of CGA 205375 in animal commodities.

Difenoconazole residues were stable in the following crop commodities for the intervals tested, some for 1 year, but most for 2 years: banana, cotton seed, cotton seed meal, cotton seed oil, lettuce, potatoes, soya beans, tomatoes, wheat forage, wheat grain and wheat straw.

Difenoconazole and metabolite CGA 205375 spiked into animal tissues (0.2 mg/kg) and milk (0.05 mg/kg) were stable when stored at or below -18 °C for approximately 10 months.

Definition of the residue

Parent difenoconazole is the dominant component of the residue in crop commodities and is a suitable analyte for enforcement purposes.

Parent difenoconazole is generally no more than a minor component in animal commodities. The major component of the residue in most animal commodities is metabolite CGA 205375 (1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-(1,2,4-triazol)-1-yl-ethanol).

In the goat metabolism studies, the concentration of CGA 205375 in the fat was approximately 3 times as high as in the muscle, but much lower than in the liver. In the dairy cow feeding studies, the concentration of CGA 205375 in the fat was approximately 3 times as high as in the muscle, but much lower than in the liver. In the laying hen metabolism studies, the concentration of CGA 205375 in the fat was approximately 5–8 times as high as in the muscle, but also much lower than in the liver. The octanol-water partition coefficient of CGA 205375 (log P_{OW}=3.8) suggests fat-solubility.

The Meeting decided the residue would be defined as fat-soluble.

The Meeting recommended a residue definition for difenoconazole.

Definition of the residue (for compliance with the MRL and for estimation of dietary intake) for plant commodities: difenoconazole.

Definition of the residue (for compliance with the MRL and for estimation of dietary intake) for animal commodities: sum of difenoconazole and 1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-(1,2,4-triazol)-1-yl-ethanol), expressed as difenoconazole.

The residue is fat soluble.

Results of supervised residue trial on crops

The Meeting received supervised trials data for difenoconazole uses on oranges, pome fruits (apple, pear), stone fruits (cherries, peach, plum), grapes, olives, tropical fruits (banana, mango, papaya), bulb vegetables (garlic, leek), Brassica vegetables (broccoli, Brussels sprouts, cabbages, cauliflower), watermelon, fruiting vegetables (chilli peppers, tomatoes), lettuce, soya beans, root and tuber vegetables (carrot, potato, sugar beet), stalk and stem vegetables (asparagus, celeriac, celery), cereal grains (rice, wheat) and oilseeds (rape seed, sunflower seed). Residue data were also provided on wheat straw and fodder, rice straw and fodder, sugar beet leaves and tops, oilseed rape fodder and sunflower plant and stubble.

In trials where duplicate field samples from an unreplicated plot were taken at each sampling time and analysed separately, the mean of the two results was taken as the best estimate of the residue from the plot.

Labels (or translations of labels) were available from Australia, Belgium, Brazil, Central America (Belize, Costa Rica, Dominican Republic, El Salvador, Guatemala, Honduras, Nicaragua,

Panama), France, Germany, Indonesia, Italy, Poland, Spain, Switzerland and UK describing the registered uses of difenoconazole.

Citrus fruits

In Brazil, difenoconazole may be applied to citrus trees twice at a spray concentration of 0.005 kg ai/hL with a 30 days PHI. In two trials in Brazil matching GAP and two others with a spray concentration of 0.01 kg ai/ha, difenoconazole residue levels were < 0.05 mg/kg.

The number of trials was insufficient for an orange MRL recommendation.

Pome fruit

Spanish GAP allows five applications of difenoconazole to apple or pear trees at 0.075 kg ai/ha with a PHI of 14 days. In three trials from Spain, matching GAP, difenoconazole residues in apples were 0.10, 0.14 and 0.15 mg/kg.

In two apple trials from France with application parameters matching Spanish GAP, difenoconazole residues were 0.11 and 0.28 mg/kg.

In two trials from Greece, also with application parameters matching Spanish GAP, difenoconazole residues were 0.05 and 0.13 mg/kg.

In two trials from Italy also with application conditions matching Spanish GAP, difenoconazole residues were 0.06 and 0.08 mg/kg.

In one pear trial from France and one from Greece, matching Spanish GAP, difenoconazole residues in pears were 0.07 and 0.16 mg/kg, respectively.

The Meeting decided to combine the apple and pear data to support a pome fruit MRL. Residues in the 11 trials in ranked order (median underlined) were: 0.05, 0.06, 0.07, 0.08, 0.10, <u>0.11</u>, 0.13, 0.14, 0.15, 0.16 and 0.28 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in pome fruit of 0.5, 0.11 and 0.28 mg/kg respectively.

Stone fruits

Polish GAP allows 3 applications of difenoconazole to cherry trees at 0.05 kg ai/ha with a PHI of 14 days.

In a cherry trial from France and two from Germany, with application conditions matching Polish GAP, difenoconazole residues in cherries were 0.08, 0.06 and 0.10 mg/kg, respectively.

Italian GAP allows 3 applications of difenoconazole to peach trees with a spray concentration of 0.0075 kg ai/hL with a PHI of 7 days. In five Italian trials matching Italian GAP, difenoconazole residues on peaches were 0.07, 0.11, 0.14, 0.14 and 0.19 mg/kg.

In a peach trial from France and two from Greece with application conditions matching Italian GAP, difenoconazole residues in peaches were 0.18, 0.16 and 0.26 mg/kg, respectively.

In summary, the difenoconazole residues on peaches from eight trials (in ranked order, median underlined) were: 0.07, 0.11, 0.14, <u>0.14</u>, <u>0.16</u>, 0.18, 0.19 and 0.26 mg/kg.

French GAP allows 3 applications of difenoconazole to plum trees with a spray concentration of 0.005 kg ai/hL with a PHI of 14 days. In four French trials matching GAP (accepted variation on spray concentration 0.0035–0.0065 kg ai/hL) difenoconazole residues on plums were 0.02, 0.03, 0.07 and 0.10 mg/kg.

In four German trials on plums with application conditions matching French GAP (accepted variation on spray concentration 0.0035–0.0065 kg ai/hL), difenoconazole residues were < 0.01, 0.01, 0.02 and 0.04 mg/kg.

In two Spanish trials on plums with application parameters matched French GAP, difenoconazole residues were 0.03 and 0.08 mg/kg.

In summary, the difenoconazole residues on plums from 10 trials were: < 0.01, 0.01, 0.02, 0.02, 0.03, 0.03, 0.04, 0.07, 0.08 and 0.10 mg/kg.

The data from the peaches and plums were apparently of different populations and could not be combined.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in peaches of 0.5, 0.15 and 0.26 mg/kg respectively. These values may also be used for nectarines.

The data from plums and cherries were combined for mutual support, residues in 13 trials in ranked order (median underlined) were: < 0.01, 0.01, 0.02, 0.02, 0.03, 0.03, 0.04, 0.06, 0.07, 0.08, 0.08, 0.10 and 0.10 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in plums and cherries of 0.2, 0.04 and 0.10 mg/kg respectively.

Grapes

Italian GAP allows 4 applications of difenoconazole to grape vines with a spray concentration of 0.005 kg ai/hL with a PHI of 21 days. In six Italian trials from 2003–2004 matching GAP, difenoconazole residues on grapes were 0.01, 0.02, 0.02, 0.03, 0.03 and 0.04 mg/kg. In two French trials matching Italian GAP, residues in grapes were 0.04 and 0.07 mg/kg.

In summary, the difenoconazole residues on grapes from eight trials in ranked order (median underlined) were: 0.01, 0.02, 0.02, 0.03, 0.03, 0.04, 0.04 and 0.07 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in grapes of 0.1, 0.03 and 0.07 mg/kg respectively.

Olives

In Spain, difenoconazole may be applied to olive trees three times at a spray concentration of 0.015 kg ai/hL with a 30 days PHI. In seven trials in Spain in 2003–2005 matching GAP, difenoconazole residue levels were 0.22, 0.29, 0.40, 0.42, 0.51, 0.90 and 1.2 mg/kg.

In an olive trial in France with application conditions matching Spanish GAP, difenoconazole residues on olives were 0.76 mg/kg.

In summary, difenoconazole residues in olives from eight trials in ranked order (median underlined) were: 0.22, 0.29, 0.40, 0.42, 0.51, 0.76, 0.90 and 1.2 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in olives of 2, 0.465 and 1.2 mg/kg respectively.

Bananas

In Costa Rica, Guatemala and Honduras difenoconazole may be applied 8 times to bananas at 0.1 kg ai/ha with harvest permitted on the day of application. The use pattern includes aerial application.

In the banana trials in 1997 in Ecuador, Colombia and Honduras, unbagged fruit were chosen for study although these cropping conditions, approved as GAP, rarely occur in commercial banana

production. The trials of 1993 in Costa Rica and Guatemala included both bagged and unbagged fruits. For the purposes of estimating an MRL, only data from unbagged fruit are considered in this case.

In three banana trials in Colombia with conditions matching the GAP of Costa Rica, residues of difenoconazole in whole fruit were < 0.02, 0.02 and 0.04 mg/kg, with residues in pulp all at < 0.02 mg/kg.

In two banana trials in Costa Rica with conditions matching GAP, difenoconazole in whole fruit were 0.03 and 0.04 mg/kg, with residues in pulp both at < 0.02 mg/kg.

In three banana trials in Ecuador with conditions matching the GAP of Costa Rica, difenoconazole in whole fruit were all < 0.02 mg/kg, with residues in pulp also all at < 0.02 mg/kg.

In one banana trial from Guatemala with conditions matching the GAP of Costa Rica, difenoconazole in whole fruit were 0.07 mg/kg, with residues in pulp at < 0.02 mg/kg.

In three banana trials in Honduras with conditions matching the GAP of Costa Rica, difenoconazole in whole fruit were < 0.02, < 0.02 and 0.03 mg/kg, with residues in pulp also all at < 0.02 mg/kg.

In summary, difenoconazole residues in whole bananas from the 12 unbagged trials were: < 0.02 (5), 0.02, 0.02, 0.03, 0.03, 0.04, 0.04 and 0.07 mg/kg. Residues in banana pulp were all < 0.02 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in bananas of 0.1, 0.02 and 0.02 mg/kg respectively.

Mango

In Brazil, difenoconazole may be applied to mango trees three times at a spray concentration of 0.0125 kg ai/hL with a 7 days PHI. In four trials in Brazil in 2003 matching GAP, difenoconazole residues in mango whole fruits were 0.025, 0.025, 0.035 and 0.04 mg/kg. No data were available for residues in edible portion.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in mangos of 0.07, 0.03 and 0.04 mg/kg respectively.

Papaya

In Brazil, difenoconazole may be applied to papayas four times at a spray concentration of 0.0075 kg ai/hL with a 14 days PHI. In four trials in Brazil in 2002 matching GAP, difenoconazole residues in papaya whole fruits were 0.02, 0.03, 0.07 and 0.10 mg/kg and residues in edible portion were all < 0.01 mg/kg. In four trials where the spray concentration was 0.015 kg ai/hL (2 × label) residues in whole papaya fruit were 0.09, 0.09 0.12 and 0.20 mg/kg and residues in edible portion were < 0.01 (3) and 0.02 mg/kg, suggesting residues could occur in the edible portion, i.e., not a nil residue.

The double rate trials provided additional support, particularly in cases such as this for difenoconazole where the residue is generally external and essentially non-systemic.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in papaya of 0.2, 0.01 and 0.02 mg/kg respectively.

Garlic

In Brazil, difenoconazole may be applied to garlic crops six times at a rate of 0.13 kg ai/ha with a 14 days PHI. In four trials in Brazil in 1995 with 6 applications of 0.19 or 0.38 kg ai/ha (1.5 × and 3 ×

label rates), difenoconazole residues in bulbs of garlic were all < 0.02 mg/kg at PHIs of approximately 0, 7, 14 and 21 days.

Data from the exaggerated rates and various sampling intervals suggest that difenoconazole residues do not reach garlic bulbs.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in garlic of 0.02*, 0 and 0 mg/kg respectively.

Leeks

In Germany, difenoconazole may be applied to leek crops 3 times at a rate of 0.1 kg ai/ha with a 21 days PHI. In four trials in Germany with application in line with GAP, difenoconazole residues in whole plants with roots removed were 0.02, 0.07, 0.09 and 0.12 mg/kg.

In four leek trials in France with conditions matching German GAP, difenoconazole residues in whole plants were 0.03, 0.05, 0.13 and 0.21 mg/kg.

In two leek trials from Italy with conditions matching German GAP, difenoconazole residues in whole plants were 0.14 and 0.17 mg/kg.

In two leek trials from Switzerland with conditions matching German GAP, difenoconazole residues in edible portions were 0.02 and 0.04 mg/kg.

The Meeting accepted that the three descriptions of the commodity analysed, i.e., (1) whole plants with roots removed, (2) whole plants and (3) edible parts, were all intended to agree with the Codex description of the commodity for analysis: *Whole vegetable after removal of roots and adhering soil*.

In summary, difenoconazole residue in leeks from the 12 trials, in rank order (median underlined), were: 0.02, 0.02, 0.03, 0.04, 0.05, <u>0.07</u>, <u>0.09</u>, 0.12, 0.13, 0.14, 0.17 and 0.21 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in leeks of 0.3, 0.08 and 0.21 mg/kg respectively.

Broccoli

In Belgium, difenoconazole may be applied twice to broccoli at a rate of 0.13 kg ai/ha with a 14 days PHI. In trials in France, Netherlands and Spain, difenoconazole was applied 3 times rather than twice. Difenoconazole is a reasonably persistent residue as found in the decline trials with residue remaining on the whole plant just prior to the final application. However, carryover on the flower heads is not expected as they were unlikely to be formed at the time of the first application.

In four broccoli trials in France with conditions matching Belgian GAP, except for 3 applications instead of 2, difenoconazole residues in flower heads on days 13–15 after the final application were 0.02, 0.05, 0.08 and 0.10 mg/kg.

In two broccoli trials from The Netherlands, with conditions matching Belgian GAP except for 3 applications instead of 2, difenoconazole residues in flower heads on day 14 after the final application were < 0.02 and 0.03 mg/kg.

In two broccoli trials in Spain, with conditions matching Belgian GAP except for 3 applications instead of 2, difenoconazole residues in flower heads on day 14 and day 21 (higher residues than on day 14) after the final application were 0.41 and 0.15 mg/kg.

In summary, difenoconazole residue in broccoli flower heads from the eight trials, in ranked order (median underlined), were: 0.02, 0.02, 0.03, <u>0.05</u>, <u>0.08</u>, 0.10, 0.15 and 0.41 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in broccoli of 0.5, 0.065 and 0.41 mg/kg respectively.

Brussels sprouts

In France, difenoconazole may be applied to Brussels sprouts 3 times at a rate of 0.13 kg ai/ha with a 21 days PHI.

In four Brussels sprouts trials from Belgium in 1999, with conditions in line with French GAP, difenoconazole residues in buttons on days 20–21 and 28 (higher residues than on day 21) after the final application were 0.02, 0.05, 0.07 and 0.09 mg/kg.

In eight Brussels sprouts trials in the UK, with conditions matching French GAP, difenoconazole residues in buttons on days 21–22 after the final application were 0.04, 0.05, 0.05, 0.06, 0.07, 0.08, 0.10 and 0.14 mg/kg.

In summary, difenoconazole residues in Brussels sprouts buttons from the 12 trials, in ranked order (median underlined), were: 0.02, 0.04, 0.05, 0.05, 0.05, 0.06, 0.07, 0.07, 0.08, 0.09, 0.10 and 0.14 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in Brussels sprouts of 0.2, 0.065 and 0.14 mg/kg respectively.

Cabbage

In France, difenoconazole may be applied to cabbage 3 times at a rate of 0.13 kg ai/ha with a 21 days PHI. In six trials from France, with application parameters in line with GAP, difenoconazole residues in cabbage heads were < 0.01 (2), 0.01, < 0.02 and < 0.05 (2) mg/kg.

In Germany, difenoconazole may be applied to cabbage 3 times at a rate of 0.1 kg ai/ha with a 21 days PHI. In two trials in Germany, with trial parameters in line with GAP, difenoconazole residues in cabbage heads were < 0.02 (2) mg/kg.

In five cabbage trials in Belgium in 1999, with conditions in line with French GAP, difenoconazole residues in cabbage heads on day 21 after the final application were < 0.02 (5) mg/kg.

In two cabbage trials in Germany in 2003, with conditions in line with French GAP, difenoconazole residues in cabbage heads on day 21 after the final application were < 0.02 and 0.19 mg/kg.

In two cabbage trials in The Netherlands in 2002, with conditions in line with French GAP, difenoconazole residues in cabbage heads on day 21 after the final application were < 0.02 (2) mg/kg.

In three cabbage trials in UK in 1990 with conditions in line with French GAP, difenoconazole residues in cabbage hearts on day 21 after the final application were 0.06, 0.10 and 0.13 mg/kg. The Meeting accepted that cabbage “hearts” meant the same as cabbage “heads”.

In summary, difenoconazole residues in cabbages from the 20 trials, in rank order (median underlined), were: < 0.01 (3), 0.01, < 0.02 (10), < 0.05 (2), 0.06, 0.10, 0.13 and 0.19 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in head cabbage of 0.2, 0.035 and 0.19 mg/kg respectively.

Cauliflowers

In France, difenoconazole may be applied to cauliflowers 3 times at a rate of 0.13 kg ai/ha with a 14 days PHI. In 12 trials from France matching GAP, difenoconazole residues in the flower heads were 0.01, < 0.02 (9), 0.03 and 0.10 mg/kg.

In a cauliflower trial in Switzerland in 2005, with conditions in line with French GAP, difenoconazole residues in flower heads on day 14 after the final application were < 0.01 mg/kg.

In two cauliflower trials in the UK in 1999 and 2005, with conditions matching French GAP, difenoconazole residues in flower heads on day 14 after the final application were < 0.02 and 0.02 mg/kg.

In summary, difenoconazole residues in cauliflowers from the 15 trials, in ranked order (median underlined), were: < 0.01, 0.01, < 0.02 (10), 0.02, 0.03 and 0.10 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in cauliflowers of 0.2, 0.02 and 0.10 mg/kg respectively.

Watermelons

Residue data were available only on the edible portion of the watermelons in the four trials provided, so estimation of an MRL was not possible.

Chilli peppers

In Indonesia, difenoconazole may be applied at 7 day intervals to chilli pepper crops at a spray concentration of 0.0063–0.013 kg ai/hL with no required PHI.

One trial from Indonesia matched GAP for maximum spray concentration with harvest on day 6 after treatment. A second Indonesian trial used a spray concentration of 0.025 kg ai/hL (2 × label rate). One trial from Malaysia matched Indonesian GAP for maximum spray concentration and harvest on the day of treatment. A second Malaysian trial used a spray concentration of 0.025 kg ai/hL (2 × label rate).

The Meeting agreed that, for a minor use, a minimum of three trials matching GAP conditions is needed. The Meeting was not able to recommend a maximum residue level for difenoconazole residues in chilli peppers.

Tomatoes

In Italy, difenoconazole may be applied to tomato crops 4 times at a rate of 0.13 kg ai/ha with a 7 days PHI.

In two tomato trials (glasshouse and polytunnel) in France in 2005, with conditions in line with Italian GAP, difenoconazole residues in tomatoes on day 7 after the final application were 0.04 and 0.05 mg/kg.

In five tomato trials (field) in Greece in 2001–2003, with conditions in line with Italian GAP, difenoconazole residues in tomatoes on day 7 and 10 (higher residues than on day 10) after the final application were 0.10, 0.13, 0.18, 0.28 and 0.36 mg/kg.

In a tomato trial (glasshouse) in UK in 2005, with conditions in line with Italian GAP, difenoconazole residues in tomatoes on day 7 after the final application were 0.10 mg/kg.

In two tomato trials (field) in Spain in 2003, with conditions in line with Italian GAP, difenoconazole residues in tomatoes on day 7 after the final application were 0.03 and 0.09 mg/kg.

In a tomato trial (polytunnel) in Spain in 2005, with conditions in line with Italian GAP, difenoconazole residues in tomatoes on day 7 after the final application were 0.12 mg/kg.

In summary, difenoconazole residues in tomatoes from the field trials were: 0.03, 0.09, 0.10, 0.13, 0.18, 0.28 and 0.36 mg/kg; and from protected trials were: 0.04, 0.05, 0.10, and 0.12 mg/kg. The data appear to be from similar populations and can be combined.

In summary, difenoconazole residues in tomatoes from the 11 trials, in ranked order (median underlined), were: 0.03, 0.04, 0.05, 0.09, 0.10, 0.10, 0.12, 0.13, 0.18, 0.28 and 0.36 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in tomatoes of 0.5, 0.10 and 0.36 mg/kg respectively.

Lettuce

In Spain, the registration document states that difenoconazole is registered for use on lettuce at a rate of 0.13–0.20 kg ai/ha with a 14 days PHI. The maximum application rate on the available label was 0.13 kg ai/ha. The Meeting agreed to use the GAP from the registration document.

In eight lettuce trials from Spain in 1991 and 2003 with application rates of 0.17–0.18 kg ai/ha (within 30% of GAP rate) the residues 13–14 days after the final application, in ranked order (median underlined), were: 0.07, 0.08, 0.29, 0.31, 0.51, 0.56, 0.65 and 1.0 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in head lettuce and leaf lettuce of 2, 0.41 and 1.0 mg/kg respectively.

Soya beans

In Brazil, difenoconazole may be applied to soya bean crops once at a rate of 0.075 kg ai/ha with a 30 days PHI. In six soya bean trials in 2000 and 2003 in Brazil with conditions in line with GAP, except that there were 2 applications in place of 1, difenoconazole residues in the dry beans on day 30 and 31 after the final application were < 0.01 (3) and < 0.02 (3) mg/kg.

The Meeting estimated a maximum residue level and an STMR value for difenoconazole in soya beans of 0.02* and 0.02 mg/kg respectively.

Carrots

In France, difenoconazole may be applied to carrot crops 3 times at a rate of 0.13 kg ai/ha with a 14 days PHI. In nine carrot trials in 1991–1993, 1996 and 2000 in France, with conditions in line with GAP, difenoconazole residues in the carrots on days 14 or 15 after the final application were 0.02, 0.02, 0.03, 0.03, 0.04, 0.05, 0.07, 0.11 and 0.13 mg/kg.

In two carrot trials in 1987 in Switzerland, with conditions in line with French GAP, difenoconazole residues in carrots on day 14 after the final application were 0.07 and 0.12 mg/kg.

In summary, difenoconazole residues in carrots from the 11 trials, in rank order (median underlined), were: 0.02, 0.02, 0.03, 0.03, 0.04, 0.05, 0.07, 0.07, 0.11, 0.12 and 0.13 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in carrots of 0.2, 0.05 and 0.13 mg/kg respectively.

Potatoes

In Spain, difenoconazole may be applied to potato crops 4 times at a rate of 0.2 kg ai/ha with a 30 days PHI. In seven potato trials in 2003 and 2005 in Spain with conditions in line with GAP except that only 2 applications were made, difenoconazole residues in the potato tubers on days 27–31 after the second and final application were < 0.01 (6) and 0.01 mg/kg.

In a trial in 2005 in Italy with the application rate in line with Spanish GAP, difenoconazole residues in potato tubers on day 29 after the second application were < 0.01 mg/kg.

The potato metabolism studies suggest that parent difenoconazole residues in tubers should be below LOQ. However, residues might be occasionally expected in tubers with surface exposure to spray application.

In summary, difenoconazole residues in potatoes from the eight trials, in rank order (median underlined), were: < 0.01 (7), 0.01 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in potatoes of 0.02, 0.01 and 0.01 mg/kg respectively.

Sugar beet

In Germany, difenoconazole may be applied to sugar beet crops twice at a rate of 0.1 kg ai/ha with a 28 days PHI. In 14 sugar beet trials in 1987–88 and 1995-96 in Germany with conditions in line with GAP except that in some trials 3 applications were made, difenoconazole residues in the sugar beet roots on days 27–30, or later if higher residues, after the second application were < 0.02 (4), 0.02 (4), 0.03, 0.03, 0.06, 0.08, 0.08 and 0.10 mg/kg.

In three sugar beet trials in 1985 and 1991 in France, with conditions in line with German GAP, difenoconazole residues in sugar beet tubers on days 25, 29 and 33 after the second application were all < 0.02 mg/kg.

In a sugar beet trial in Denmark with conditions matching German GAP, difenoconazole residue in sugar beet root 37 days after the second application was 0.08 mg/kg.

In a sugar beet trial in the UK with conditions matching German GAP, difenoconazole residue in sugar beet root 35 days after the second application was 0.08 mg/kg.

In summary, difenoconazole residues in sugar beet from the 19 trials, in ranked order (median underlined), were: 0.01, < 0.02 (7), <u>0.02</u> (4), 0.03, 0.033, 0.06, 0.08, 0.08, 0.08 and 0.10 mg/kg.

The Meeting estimated a maximum residue level and an STMR value for difenoconazole in sugar beet of 0.2 and 0.02 mg/kg respectively.

Asparagus

In France, difenoconazole may be applied to asparagus crops 3 times at 0.13 kg ai/ha. In asparagus crops protected by 6 to 8 applications of fungicide per year, the difenoconazole product should be used for the first three treatments and other products that act in a different way should be used to complete the season.

In four asparagus trials in France, two in Italy and two in Switzerland where difenoconazole was applied 4–8 times at 0.13 kg ai/ha and asparagus shoots were harvested for analysis 179–290 days later (approximating French GAP), the resulting difenoconazole residues were < 0.02 (7) and 0.02 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in asparagus of 0.03, 0.02 and 0.02 mg/kg respectively.

Celeriac

In Belgium, difenoconazole may be applied to celeriac 4 times at a rate of 0.13 kg ai/ha with a 14 days PHI. In three Belgian trials matching GAP, difenoconazole residues in celeriac roots 15 days after the final treatment were 0.08, 0.12 and 0.22 mg/kg.

The Meeting acknowledged that celeriac is a minor crop and decided to estimate an MRL based on the three trials. The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in celeriac of 0.5, 0.12 and 0.22 mg/kg respectively.

Celery

In France, difenoconazole may be applied to celery crops 4 times at a rate of 0.13 kg ai/ha with a 14 days PHI.

The Codex description of the sample to be analysed is: "*Whole commodity as marketed after removal of obviously decomposed or withered leaves.*" For celery, the commodity marketed is usually

trimmed celery, i.e., most foliage removed. In a number of the celery trials, leaf and stems had been detached and analysed separately. The Meeting agreed to use the stem data where stems and leaf were analysed separately.

In four celery trials in 2003–04 in France, with conditions in line with GAP, difenoconazole residues in celery stems on day 14 after the final application were 0.03, 0.04, 0.14 and 0.26 mg/kg.

In two celery trials in 1990 in Italy, with conditions in line with French GAP, difenoconazole residues in celery edible parts and celery stems on day 14 after the final application were 1.2 and 2.0 mg/kg respectively.

In two celery trials in 2004 in Spain and one in Switzerland in 1988, with conditions in line with French GAP, difenoconazole residues in celery stems on day 14 after the final application were 0.04, 0.05 and 0.17 mg/kg. Data from a second trial in Switzerland were not used because difenoconazole residues (0.02 mg/kg) in a sample from the control plot were significant with respect to the residue (0.058 mg/kg) in the treated plot.

In summary, difenoconazole residues in celery from the nine trials, in ranked order (median underlined), were: 0.03, 0.04, 0.04, 0.05, <u>0.14</u>, 0.17, 0.26, 1.2 and 2.0 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in celery of 3, 0.14 and 2.0 mg/kg respectively.

Rice

In Indonesia, difenoconazole may be applied to rice at 0.050 to 0.10 kg ai/ha, with one application at the mid booting stage (45 days after sowing) and one at the 75% flowering stage (approximately 60 days after sowing). These growth stages are interpreted as equivalent to BBCH 43–45 and BBCH 63–67 growth stages.

In two rice trials in Indonesia with application rates of 0.063 kg ai/ha (37% below maximum GAP) and with timing to match GAP, residues in rice grain were 1.3 and 0.75 mg/kg.

In three rice trials in Malaysia with application rates of 0.064–0.075 kg ai/ha and timing to match Indonesian GAP, difenoconazole residues in rice grain harvested 28–30 days after the second application were 0.15, 0.16 and 0.37 mg/kg. In another trial in Malaysia at 0.12 kg ai/ha and with similar timing, residues of difenoconazole in rice grain were 0.76 mg/kg.

In summary, difenoconazole residues in rice grain from the six trials were: 0.15, 0.16, 0.37, 0.75, 0.76 and 1.3 mg/kg.

The Meeting decided that six trials (some at application rates not close enough to maximum GAP) were insufficient for a major commodity such as rice and did not estimate a maximum residue level.

Wheat

In Switzerland, difenoconazole may be applied once to wheat crops at a rate of 0.13 kg ai/ha up to growth stage BBCH 61.

In three wheat trials in Denmark, three in France and one in Switzerland where the difenoconazole was applied at 0.13 kg ai/ha up to growth stage BBCH 61, residues of difenoconazole in wheat grain were all < 0.02 mg/kg.

In nine wheat trials in France and seven in the UK, where the difenoconazole was applied at 0.12–0.15 kg ai/ha from growth stages BBCH 61 to 87, residues of difenoconazole in wheat grain were also all < 0.02 mg/kg.

In summary, difenoconazole residues in wheat grain from the 23 trials were all < 0.02 mg/kg.

The metabolism studies suggest that parent difenoconazole residues should not occur in the grain. The Meeting agreed that the evidence supported an STMR of nil residues in wheat.

The Meeting estimated a maximum residue level and an STMR value for difenoconazole in wheat of 0.02* and 0 mg/kg respectively.

Rapeseed

In the UK, difenoconazole may be applied twice to oilseed rape crops at a rate of 0.13 kg ai/ha up to the end of flowering (growth stage BBCH 69).

In four oilseed rape trials in 1996 in Germany, with conditions in line with GAP of the UK, difenoconazole residues in rape seed on days 56–80 after the second application were all < 0.02 mg/kg.

In three oilseed rape trials in 1997 in Germany with the second of two applications of difenoconazole of 0.13 kg ai/ha at growth stages BBCH 69–75, i.e., later than approved in UK GAP, difenoconazole residues in rape seed on days 55–56 after the second application were all < 0.02 mg/kg.

In two oilseed rape trials in 1988 in France with two applications of difenoconazole of 0.13 kg ai/ha and harvest 83 days after the second application (probably before end of flowering), i.e., within the conditions of UK GAP, difenoconazole residues in rape seed were both 0.04 mg/kg.

In summary, difenoconazole residues in rape seed from the nine trials, in ranked order (median underlined), were: < 0.<u>02</u> (7), 0.04 and 0.04 mg/kg.

The Meeting estimated a maximum residue level and an STMR value for difenoconazole in rape seed of 0.05 and 0.02 mg/kg respectively.

Sunflower seed

In Switzerland, difenoconazole may be applied once to sunflower crops at a rate of 0.13 kg ai/ha up to growth stage BBCH 51. In three trials on sunflower in 2004–2005 in Switzerland according to the conditions of GAP, except that 2 applications were made instead of 1, difenoconazole residues in sunflower seed, harvested 68–73 days after the second application were all < 0.01 mg/kg.

In six sunflower trials in 2004–05 in France, with conditions matching Swiss GAP, except for 2 applications instead of 1, difenoconazole residues in sunflower seed harvested 59–101 days after the second application were < 0.01 (5) and 0.01 mg/kg.

In two sunflower trials in 2005 in Spain with conditions matching Swiss GAP, except for 2 applications instead of 1, difenoconazole residues in sunflower seed harvested 74 and 87 days after the second application were both < 0.01 mg/kg.

In summary, difenoconazole residues in sunflower seed from the 11 trials, in ranked order (median underlined), were: < 0.<u>01</u> (10), 0.01 mg/kg.

The Meeting estimated a maximum residue level and an STMR value for difenoconazole in sunflower seed of 0.02 and 0.01 mg/kg respectively.

Wheat straw and fodder

In Switzerland, difenoconazole may be applied once to wheat crops at a rate of 0.13 kg ai/ha up to growth stage BBCH 61. In a Swiss trial on wheat in 1989 with conditions matching GAP, difenoconazole residues in wheat straw harvested 45 days after the single application were 1.2 mg/kg.

In three wheat trials in 1989–1990 in Denmark with conditions in line with Swiss GAP, difenoconazole residues in wheat straw on days 57, 58 and 75 after the single application were 0.26, 0.64 and 0.31 mg/kg.

In two wheat trials in 1989 in France, with conditions in line with Swiss GAP, difenoconazole residues in wheat straw on days 57 and 63 after the single application were 0.73 and 0.82 mg/kg.

In summary, difenoconazole residues in wheat straw from the six trials, in ranked order (median underlined), were: 0.26, 0.31, 0.64, 0.73, 0.82 and 1.2 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and a highest residue value for difenoconazole in wheat straw and fodder of 3, 0.685 and 1.2 mg/kg respectively.

Sugar beet leaves or tops

In Germany, difenoconazole may be applied to sugar beet crops twice at a rate of 0.1 kg ai/ha with a 28 days PHI. In 14 sugar beet trials in 1987–1988 and 1995–1996 in Germany with conditions in line with GAP except that in some trials 3 applications were made, difenoconazole residues in the sugar beet leaves or tops on days 27–30 after the second application were 0.084, 0.087, 0.09, 0.11, 0.20, 0.25, 0.25, 0.26, 0.43, 0.43, 0.47, 0.53, 0.62 and 0.95 mg/kg.

In a sugar beet trial in 1985 in France, with conditions in line with German GAP, difenoconazole residues in sugar beet leaves 24 days after the second application were 0.17 mg/kg.

In a sugar beet trial in Denmark with conditions matching German GAP, difenoconazole residues in sugar beet leaves 37 days after the second application were 0.45 mg/kg.

In a sugar beet trial in the UK, with conditions matching German GAP, difenoconazole residues in sugar beet leaves 27 days after the second application were 0.09 mg/kg.

In summary, difenoconazole residues in sugar beet leaves or tops from the 17 trials in ranked order (median underlined), were: 0.084, 0.087, 0.09, 0.09, 0.11, 0.17, 0.20, 0.25, 0.25, 0.26, 0.43, 0.43, 0.45, 0.47, 0.53, 0.62 and 0.95 mg/kg.

The Meeting estimated an STMR value and a highest residue value for difenoconazole in sugar beet leaves or tops of 0.25 and 0.95 mg/kg (fresh weight), respectively.

Fate of residues during processing

The Meeting received information on the fate of difenoconazole residues during the processing of apples for juice, carrots for juice and canning, grapes for wine and dried grapes, olives for oil, rape seed for oil, sugar beet for sugar and molasses, and tomatoes for juice and puree. Also information was provided on hydrolysis studies of difenoconazole to assist with identification of the nature of the residue during processing.

Processing factors have been calculated for difenoconazole residues in apples, carrots, grapes, olives and tomatoes. The data for rape seed and sugar beet could not be used as residue levels in the raw commodity did not exceed the LOQ.

Difenoconazole was stable under the hydrolysis conditions (pH, temperature, time) representing the food processes pasteurisation, baking, brewing and boiling and sterilisation.

Apples from difenoconazole field trials at exaggerated application rates were washed, sliced and pressed to separate pomace from juice. The juice was pasteurised at 80–82 °C for 30 minutes. Puree was produced by boiling washed apples until the puree passed through a sieve. Sugar, citric acid and ascorbic acid were added until the puree reached a pH of 3.0–4.5 and then was heated at 95 °C for 20 minutes.

In a grape drying trial in Chile, grapes were harvested 63 days after the third of 3 applications of difenoconazole at 1 × and 5 × the label rate. The grapes were washed for about one minute and then placed in wooden trays with mesh bottoms and subjected to sulphur dioxide fumigation for 12 h. The trays of grapes were then dried in ovens at 65 °C for about 36–40 h losing approximately two-thirds of their weight, 30 kg grapes producing 10 kg dried grapes.

Wine was produced from grapes in a series of supervised field trials in France and Spain. Difenoconazole residues appeared in the pomace, but not in the wine. In grape trials in Chile, difenoconazole residues appeared in the pomace, but not in the juice.

Olives from a difenoconazole field trial at an exaggerated rate (2 ×) were processed into virgin oil and refined oil. The virgin oil was separated by centrifuging the mixture of olive pulp (from milling) and added water. The oil was refined by a sodium hydroxide process to produce soap from free acids. Residue levels in virgin and refined oil were essentially the same.

In a tomato processing trial in France, tomatoes were harvested 7 days after the final of 3 applications of difenoconazole at 0.37 kg ai/ha. In processing to juice, unwashed tomatoes were crushed and sieved to produce juice and pomace. Finished juice was produced by pasteurization for 1 minute at 82–85 °C after citric acid and salt were added to raw juice. In the production of puree, unwashed tomatoes were crushed and concentrated in a saucepan and then sieved. Salt and citric acid were added and the puree, in glass jars, was sterilised for 10 minutes at 115 °C. In the simulation of canning, unwashed tomatoes were blanched and then immediately plunged into cold water to split and loosen the peel which was removed with a knife. The peeled tomatoes, in glass jars, were covered with tomato juice and sterilised for 10 minutes at 115–120 °C.

In a carrot processing trial in France, carrots were harvested 7 days after the final of 3 difenoconazole applications at 0.50 kg ai/ha. In the simulation of canning, carrots were sorted and peeled with both ends removed. The peeled carrots were washed thoroughly and blanched in boiling water for 1 minute and placed in jars with brine and added citric acid to produce a pH of 3.5 and then sealed and sterilized for 10 minutes at 115–120 °C. For cooked carrots, the washed carrots were cooked in boiling water for 15 minutes and packaged in plastic bags under vacuum. For juicing, carrots were washed thoroughly after sorting, peeling and end removal and were then processed in a juice extractor which separated juice from pulp in a centrifugal filter. After the pH of the juice was adjusted to 3.5 with citric acid, the juice was pasteurized at approximately 85 °C and packaged in glass jars.

Calculated processing factors and the median or best estimate are summarized in the following table.

Raw agricultural commodity (RAC)	Processed commodity	Calculated processing factors.	Median or best estimate
Apple	juice	< 0.02, < 1.0. < 1.0	< 0.02
Apple	dry pomace	15.4	15
Apple	puree	0.14	0.14
Carrot	canned	0.02, 0.03, 0.05, 0.12	0.04
Carrot	juice	0.02, 0.05, 0.06, 0.12	0.055
Grapes	juice	< 0.5	< 0.5
Grapes	dry pomace	9.3, 10.3, 14.0, 15.4	12
Grapes	dried grapes	1.01, 1.4	1.2
Grapes	wine	< 0.18, < 0.20, < 0.20, < 0.29, < 0.33, < 0.33, < 0.33, < 0.50, < 0.50, < 0.50, < 0.50	< 0.18
Olives	refined oil	1.19, 1.40, 1.50, 1.51	1.4
Olives	virgin oil	1.47, 1.50, 1.50, 1.63	1.5
Tomatoes	canned tomato	< 0.05, 0.06, 0.07, 0.08	0.065
Tomatoes	juice	0.14, 0.15, 0.28, 0.32	0.22
Tomatoes	puree	0.54, 0.58, 0.74, 1.00	0.66

The processing factors for dry apple pomace (15), apple juice (< 0.02) and apple puree (0.14) were applied to the estimated STMR for pome fruits (0.11 mg/kg) to produce STMR-P values for dry apple pomace (1.65 mg/kg), apple juice (0.0022 mg/kg) and apple puree (0.015 mg/kg).

The processing factors for dry grape pomace (12), grape juice (< 0.5) and wine (< 0.18) were applied to the estimated STMR for grapes (0.03 mg/kg) to produce STMR-P values for dry grape pomace (0.36 mg/kg), grape juice (0.015 mg/kg) and wine (0.0054 mg/kg).

The processing factor for dried grapes (1.2) was applied to the estimated STMR and HR for grapes (0.03 and 0.07 mg/kg) to produce STMR-P and HR-P values for dried grapes (raisins) of 0.036 and 0.084 mg/kg respectively.

The Meeting estimated a maximum residue level for difenoconazole in dried grapes (= currants, raisins, sultanas) of 0.1 mg/kg. The estimated maximum residue level is the same as for grapes, so no separate MRL recommendation is necessary.

The processing factors for canned carrots (0.04) and carrot juice (0.055) were applied to the estimated STMR for carrots (0.05 mg/kg) to produce STMR-P values for canned carrots (0.002 mg/kg) and carrot juice (0.0028 mg/kg).

The processing factors for tomato puree (0.66), tomato juice (0.22) and canned tomato (0.065) were applied to the estimated STMR for tomatoes (0.10 mg/kg) to produce STMR-P values for tomato puree (0.066 mg/kg), tomato juice (0.022 mg/kg) and canned tomato (0.0065 mg/kg).

The processing factors for virgin olive oil (1.5) and refined olive oil (1.4) were applied to the estimated STMR for olives (0.465 mg/kg) to produce STMR-P values for virgin olive oil (0.70 mg/kg) and refined olive oil (0.65 mg/kg)

Residues in animal commodities

Livestock feeding

The meeting received lactating dairy cow feeding studies and a laying hen feeding study, which provided information on likely residues resulting in animal commodities, milk and eggs from difenoconazole residues in the animal diet.

Lactating dairy cows

Groups of 3 lactating Holstein dairy cows were dosed once daily via gelatin capsule with difenoconazole at 1 ppm (1 ×), 3 ppm (3 ×) and 10 ppm (10 ×) in the dry-weight diet for 29–30 consecutive days. Parent difenoconazole residues did not occur above LOQ in muscle, kidney or fat tissues or milk for any of the test doses, but were present in liver from the 10 ppm feeding-level group. Metabolite CGA 205375 was present in each of the tissues from the 3 and 10 ppm feeding-level groups and in the liver and fat from the 1 ppm feeding-level animals. The concentration of metabolite CGA 205375 in fat was approximately 3.3 times its concentration in muscle. The average concentrations of metabolite CGA 205375 in the tissues from the 10 ppm feeding-level animals were: muscle 0.020 mg/kg; liver 0.30 mg/kg; kidney 0.044 mg/kg; fat 0.072 mg/kg. For metabolite CGA 205375 in liver, the transfer factors for the 3 feeding levels were reasonably consistent. For fat, the transfer factors for metabolite CGA 205375 apparently decreased as the feeding level increased. For the 10 ppm feeding-level animals, metabolite CGA 205375 was consistently present in the milk from day 2 onwards at 0.005–0.009 mg/kg.

In a second study, groups of 3 lactating Holstein dairy cows were dosed once daily via gelatin capsule with difenoconazole at 1 ppm (1 ×), 5 ppm (5 ×) and 15 ppm (15 ×) in the dry-weight diet for 29–30 consecutive days. Parent difenoconazole residues did not occur above LOQ in muscle, kidney or fat tissues or milk for any of the test doses. Parent difenoconazole residues were present in liver from the 5 and 15 ppm feeding-level groups. Metabolite CGA 205375, the major part of the residue, was present in each of the tissues from the 5 and 15 ppm feeding-level animals and in the liver, kidney and fat from the 1 ppm feeding-level group. In the 15 ppm feeding-level group, the concentration of metabolite CGA 205375 in fat was approximately 3.1 times its concentration in muscle. The average concentrations of metabolite CGA 205375 in the tissues from the 15 ppm feeding-level animals were: muscle 0.04 mg/kg; liver 0.57 mg/kg; kidney 0.11 mg/kg; fat 0.12 mg/kg. For metabolite CGA 205375 in liver, the transfer factors for the 5 ppm and 15ppm feeding levels were close. For fat, the transfer factors for metabolite CGA 205375 were also consistent for the 5 ppm and

15 ppm feeding levels. Metabolite CGA 205375 reached a plateau level in milk of approximately 0.012 mg/kg within 2 days from the 15 ppm feeding-level animals. Metabolite 1,2,4-triazole (not included in the difenoconazole residue definition) was consistently present in the milk from the 5 and 15 ppm feeding levels groups where plateau concentrations in milk of approximately 0.017 mg/kg and 0.04 mg/kg respectively were quickly reached.

The two feeding studies were generally in good agreement of transfer factors. The Meeting decided to use the study with the 1 and 3 ppm feeding levels as most closely bracketing the dietary burdens.

Laying hens

Laying white leghorn hens were fed rations treated with difenoconazole at 0.3 ppm, 1 ppm, 3 ppm and 10 ppm for 28 consecutive days. Parent difenoconazole residues did not occur above LOQ (0.01 mg/kg) in muscle, fat, liver or eggs for any of the test doses. Metabolite CGA 205375 also was not present in the tissues above LOQ (0.01 mg/kg). Average levels of 1,2,4-triazole in the tissues from the 10 ppm feeding-level birds were: skin plus attached fat 0.012 mg/kg; peritoneal fat < 0.005 mg/kg; liver 0.02 mg/kg; muscle 0.022 mg/kg. Metabolite CGA 205375 occurred in eggs from the 1, 3 and 10 ppm feeding-level groups reaching a plateau after approximately 9 days with levels of 0.037 mg/kg and 0.13 mg/kg in eggs from the 3 and 10 ppm feeding-level groups respectively. At the 1 ppm feeding level, CGA 205375 was present in eggs at close to the LOQ (0.01 mg/kg). Metabolite 1,2,4-triazole occurred in eggs from the 1, 3 and 10 ppm feeding-level birds. It reached a plateau after approximately 6 days with plateau levels of 0.007, 0.020 and 0.060 mg/kg in eggs from the 1, 3 and 10 ppm feeding-level birds respectively.

Livestock dietary burden

The Meeting estimated the dietary burden of difenoconazole in livestock on the basis of the diets listed in Annex 6 of the 2006 JMPR Report (OECD Feedstuffs Derived from Field Crops). Calculation from highest residue, STMR (some bulk commodities) and STMR-P values provides the levels in feed suitable for estimating MRLs, while calculation from STMR and STMR-P values for feed is suitable for estimating STMR values for animal commodities. The percentage dry matter is taken as 100% when the highest residue levels and STMRs are already expressed as dry weight.

Estimated maximum and mean dietary burdens of livestock

Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are provided in Annex 6. The calculations were made according to the livestock diets from US-Canada, EU and Australia in the OECD Table (Annex 6 of the 2006 JMPR Report).

	Livestock dietary burden, difenoconazole, ppm of dry matter diet					
	US-Canada		EU		Australia	
	max	mean	max	mean	max	mean
Beef cattle	0.62	0.48	1.85	0.81	1.42	0.9 [2]
Dairy cattle	0.44	0.30	2.10 [1]	0.76 [3]	0.59	0.44
Poultry - broiler	0.01	0.01	0.12	0.05	0.01	0.01
Poultry - layer	0.01	0.01	0.54 [4]	0.20 [5]	0.01	0.01

[1] Highest maximum beef or dairy cattle dietary burden suitable for MRL estimates for mammalian meat and milk.

[2] Highest mean beef or dairy cattle dietary burden suitable for STMR estimates for mammalian meat.

[3] Highest mean dairy cattle dietary burden suitable for STMR estimates for milk.

[4] Highest maximum poultry dietary burden suitable for MRL estimates for poultry meat and eggs.

[5] Highest mean poultry dietary burden suitable for STMR estimates for poultry meat and eggs.

Animal commodities, MRL estimation

For MRL estimation, the residues in the animal commodities are the sum of difenoconazole and CGA 205375 (1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-(1,2,4-triazol)-1-yl-ethanol)) expressed as difenoconazole.

Cattle

For MRL estimation, the high residues in the tissues were calculated by interpolating the maximum dietary burden (2.10 ppm) between the relevant feeding levels (1 and 3 ppm) from the dairy cow feeding study and using the highest tissue concentrations from individual animals within those feeding groups.

The STMR values for the tissues were calculated by taking the STMR dietary burden (0.95 ppm) as a proportion of the lowest feeding level (1 ppm) multiplied by the feeding-level residue (mean of the 3 animals).

Residues in the milk were below LOQ (0.005 mg/kg) for all samples from the 1 ppm and 3 ppm feeding groups, so the dietary burdens (2.10 and 0.95 ppm) were taken as a proportion of the 3 ppm to calculate the residues resulting from the dietary burdens.

In the table below, dietary burdens are shown in round brackets (), feeding levels and residue concentrations from the feeding study are shown in square brackets [] and estimated concentrations related to the dietary burdens are shown without brackets.

Dietary burden (ppm) Feeding level [ppm]	Milk	Muscle	Liver	Kidney	Fat
MRL					
	mean	highest	highest	highest	highest
MRL dairy cattle (2.10) [1, 3]	< 0.004 [< 0.005, < 0.005]	0.019 [< 0.01, 0.026]	0.11 [0.051, 0.15]	0.016 [< 0.01, 0.021]	0.028 [0.015, 0.038]
STMR					
	mean	mean	mean	mean	mean
STMR beef cattle (0.95) [0, 1]		< 0.01 [0, < 0.01]	0.043 [0, 0.045]	< 0.01 [0, < 0.01]	0.012 [0, 0.013]
STMR dairy cattle (0.76) [0, 1, 3]	< 0.001 [0, < 0.005, < 0.005)]				

The data from the cattle feeding studies were used to support mammalian meat and milk MRLs.

The Meeting estimated a maximum residue level and an STMR value for difenoconazole in milks of 0.005* and 0.001 mg/kg, respectively. No information was available on the distribution of residue between the fat and non-fat milk fractions.

For muscle, the residue arising from a dietary burden of 2.10 ppm was 0.019 mg/kg, while the residue resulting from a dietary burden of 0.95 ppm was < 0.01 mg/kg. For fat, the residue arising from a dietary burden of 2.10 ppm was 0.028 mg/kg, while the residue resulting from a dietary burden of 0.95 ppm was 0.012 mg/kg.

The Meeting estimated a maximum residue level for difenoconazole in mammalian meat (fat) of 0.05 mg/kg. The Meeting estimated STMR and HR values for meat (fat) of 0.012 and 0.028 mg/kg respectively. The Meeting estimated STMR and HR values for meat (muscle) of 0.01 and 0.019 mg/kg respectively.

For liver, the residue arising from a dietary burden of 2.10 ppm was 0.11 mg/kg, while the residue resulting from a dietary burden of 0.95 ppm was 0.043 mg/kg. The Meeting estimated a

maximum residue level, an STMR value and an HR value for difenoconazole in liver of 0.2, 0.043 and 0.11 mg/kg, respectively.

For kidney, the residue arising from a dietary burden of 2.10 ppm was 0.016 mg/kg, while the residue resulting from a dietary burden of 0.95 ppm was < 0.01 mg/kg. Although the residue levels in kidney were somewhat below those in liver, the Meeting decided that it was preferable to have an offal MRL which would be supported by the liver data.

The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in mammalian edible offal of 0.2, 0.043 and 0.11 mg/kg, respectively.

Poultry

In the table, dietary burdens are shown in round brackets (), feeding levels and residue concentrations from the feeding study are shown in square brackets [] and estimated concentrations related to the dietary burdens are shown without brackets.

Dietary burden (ppm) Feeding level [ppm]	Eggs	Muscle	Liver	Fat	Skin + attached fat
MRL					
	highest	highest	highest	highest	highest
MRL laying hens (0.54) [0, 1]	0.0054 [0, 0.01]				
MRL laying hens (0.54) [0, 3, 10]		< 0.00054 [0, < 0.01, < 0.01]	< 0.00054 [0, < 0.01, < 0.01]	< 0.00054 [0, < 0.01, < 0.01]	< 0.00054 [0, < 0.01, < 0.01]
STMR					
	mean	mean	mean	mean	mean
STMR laying hens (0.20) [0, 1]	< 0.0020 [0, < 0.01]				
STMR laying hens (0.20) [0, 3, 10]		< 0.0002 [0, < 0.01, < 0.01]	< 0.0002 [0, < 0.01, < 0.01]	< 0.0002 [0, < 0.01, < 0.01]	< 0.0002 [0, < 0.01, < 0.01]

The data from the laying hen feeding studies were used to support poultry meat and egg MRLs.

The residue levels of difenoconazole + CGA 205375, expressed as difenoconazole, in poultry tissues and eggs arising from the dietary burdens (0.54 and 0.20 ppm difenoconazole in feed, dry weight) were all less than the analytical method LOQ (0.01 mg/kg).

For poultry tissues, residues were below LOQ (0.01 mg/kg) even at the 10 ppm feeding level, so an estimate of the STMRs was made by dividing the dietary burden (0.20 ppm) by 10 ppm and multiplying by the LOQ (0.01 mg/kg) to produce a value of 0.00020 mg/kg. An estimate of the HRs was made by dividing the dietary burden (0.54 ppm) by 10 ppm and multiplying by the LOQ (0.01 mg/kg) to produce a value of 0.00054 mg/kg.

For eggs, residues were below LOQ (0.01 mg/kg) at the 1 ppm feeding level, so an estimate of the STMR was made by dividing the dietary burden (0.20 ppm) by 1 ppm and multiplying by the LOQ (0.01 mg/kg) to produce a value of 0.0020 mg/kg. Similarly, a calculation for the HR for eggs produced a value of 0.0054 mg/kg.

The Meeting estimated maximum residue levels of 0.01* mg/kg for poultry eggs, poultry meat (fat) and poultry edible offal.

The Meeting estimated STMRs of 0.0020 mg/kg for eggs and 0.00020 mg/kg for poultry meat and poultry edible offal.

The Meeting estimated HRs of 0.0054 mg/kg for eggs and 0.00054 mg/kg for poultry meat and poultry edible offal.

DIETARY RISK ASSESSMENT

Also see the General Report on triazoles.

Long-term intake

The evaluation of difenoconazole resulted in recommendations for MRLs and STMR values for raw and processed commodities. Where data on consumption were available for the listed food commodities, dietary intakes were calculated for the 13 GEMS/Food Consumption Cluster Diets. The results are shown in Annex 3.

The IEDIs in the thirteen Cluster Diets, based on estimated STMRs were 1–10% of the maximum ADI (0.01 mg/kg bw). The Meeting concluded that the long-term intake of residues of difenoconazole from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The IESTI of difenoconazole calculated on the basis of the recommendations made by the JMPR represented 0–10% of the ARfD (0.3 mg/kg bw) for children and 0–7% for the general population.

The Meeting concluded that the short-term intake of residues of difenoconazole resulting from uses that have been considered by the JMPR is unlikely to present a public health concern.

5.11 DIMETHOMORPH (225)

TOXICOLOGY

Dimethomorph is a cinnamic acid derivative for which the chemical name is (*E*,*Z*)-4-[3-(4-chlorophenyl)-3-(3,4-dimethoxyphenyl)acryloyl]morpholine or (*EZ*)-4-[3-(4-chlorophenyl)-3-(3,4-dimethoxyphenyl)-1-oxo-2-propenyl]morpholine, according to IUPAC and CAS nomenclatures respectively (CAS No. 110488-70-5). Dimethomorph is a mixture of *E*- and *Z*-isomers in the ratio of approximately 1 : 1.

Dimethomorph is a fungicide that disrupts fungal cell-wall formation. Fungicidal activity is primarily associated with the *Z*- isomer.

Dimethomorph has not been evaluated previously by the JMPR and was reviewed at the present Meeting at the request of the CCPR. All pivotal studies with dimethomorph were certified as complying with GLP.

Biochemical aspects

In most studies, the batch of dimethomorph used consisted of mixtures of the *E*- and *Z*- isomers in approximately equal amounts. It was reported that the two isomers can interconvert on exposure to light.

In several studies, the absorption, distribution, metabolism and excretion of dimethomorph were investigated in rats treated orally. After single oral doses of 10 or 500 mg/kg bw administered by gavage to male and female rats, more than 90% of the lower dose was absorbed and excreted via bile and 7% via urine. At 500 mg/kg bw, absorption decreased to 65% in males and 40% in females. Pre-treatment of the animals with nonlabelled dimethomorph at the lower dose did not influence the pattern of excretion. At 10 mg/kg bw, t_{max} for total radioactivity was reached after 1.4–2.8 h and excretion was virtually complete after 48 h. After 24 h, up to 10% of the administered dose was found in the gastrointestinal tract (including contents, 0.4–1% in the gastrointestinal tract only). Less than 1% of the administered dose was found in the carcass and in liver, and 0.2% or less of the

administered dose was found in the kidneys, plasma and erythrocytes. In all other organs, concentrations of radioactivity were no longer quantifiable. At 500 mg/kg bw, some delay in depletion from organs was observed; residual radioactivity in tissues as a percentage of administered dose was approximately threefold that at 10 mg/kg bw. After 168 h, the pattern of distribution was very similar. Dimethomorph is extensively metabolized by demethylation of one of the methoxy groups and formation of *O*-conjugate and degradation products of morpholine ring-opening were found.

Toxicological data

Dimethomorph is of low acute toxicity in rats; the oral LD_{50} was 350 mg/kg bw in females and 4300 mg/kg bw in males. The oral LD_{50}s for the *E*- and *Z*- isomers were similar. In studies with dimethomorph administered dermally or by inhalation, the LD_{50} was > 2000 mg/kg bw and the LC_{50} was > 4.24 mg/L, respectively. Dimethomorph was not a skin irritant and was not a skin sensitizer in the Magnusson & Kligman test. In a test for ocular irritation, all animals showed reddened conjunctivae and slight chemosis. These effects had resolved within 4 h after dosing.

In short- and long-term studies, the liver was consistently a target organ; increased organ weights were often accompanied by hepatocyte hypertrophy.

In short-term studies of toxicity in mice fed diets containing dimethomorph at up to 10 000 ppm, equal to 1145 mg/kg bw per day, dimethomorph was generally well tolerated, but increased liver weights were observed at all doses. In 4-week studies in rats given doses of 220 mg/kg bw per day and greater, decreased body-weight gains, liver-weight increases with increased hepatocyte hypertrophy and, at higher doses, histological changes in the intestine were observed. Generally, the same effects were also seen in two 4-week studies in rats given isolated *E*- and Z- isomers; NOAELs were 10 mg/kg bw per day. In a 13-week feeding study in rats allowed a recovery period after dosing, the NOAEL was 14 mg/kg bw per day on the basis of increased liver weights in females at higher doses; in males, an increase in vacuolation in adrenals was found and slightly changed haematology parameters at higher doses. In both sexes, vascular congestion of the ileum mucosa was also observed. The severity of most effects was reduced in the recovery period. In a later re-examination of histology slides, findings in the ileum of mice and rats, dilatation, mucosal hyperplasia and fibre separation in muscle layers were identified with rats being more sensitive than mice. In a 13-week feeding study in dogs, lip-licking and subdued behaviour were seen usually shortly after feeding at the highest dose of 43 mg/kg bw per day. At this dose, alkaline phosphatase activity in both sexes had nearly doubled, and males showed an increase in relative thymus weight and decreased prostate weight with increased fibrosis, while females showed an increase in liver weight. The NOAEL was 450 ppm, equal to 15 mg/kg bw per day. In the 52-week feeding study in dogs, liver weights in both sexes were increased at a dietary concentration of 450 ppm, equal to 15.2 mg/kg bw per day, and greater. At 1350 ppm, equal to 44.8 mg/kg bw per day, the highest dose, alkaline phosphatase activity was increased in males and females and, as in the 13-week study, prostate weights were decreased, with a very slightly increased severity of fibrosis. Testes weights were statistically significantly increased at the intermediate dose of 450 ppm and greater, but without a histological correlate and therefore this was not considered toxicologically relevant. The NOAEL was 450 ppm, equal to 15.2 mg/kg bw per day, on the basis of weight changes in the liver and prostate, and prostate fibrosis at 1350 ppm.

In a 24-month feeding study in mice, dimethomorph was well tolerated. Treatment-related findings were reduced absolute terminal body weight in males at 1000 mg/kg bw per day without decreased feed intake. In an interim sacrifice of animals at the highest dose at week 52, liver-weight increases and dilatations in the ileum were found; both effects were more pronounced in females. At study termination, more animals (males and females) with enlarged spleens were recorded, without a histological correlate. In females at the highest dose, an increase in the incidence of mammary adenocarcinomas was found that was within the range for historical controls. The Meeting concluded that the increased incidence in mammary adenocarcinoma was not due to a tumorigenic potential of

dimethomorph. The NOAEL was 100 mg/kg bw per day on the basis of body-weight gain decreases at the highest dose.

There were two 24 month feeding studies in rats, one of toxicity and another one of carcinogenicity. In the long-term feeding study in rats, feed intake was not affected in any group. At the highest dose (2000 ppm, equal to 99.9 mg/kg bw per day), body weight was decreased in females and an increase in relative kidney weights in females and a statistically non-significant increase in liver weights were observed in both sexes. Incidences of histological changes in the liver included ground-glass foci, periacinar hypertrophy and pigmentation, and were increased statistically significantly at the highest dose of 2000 ppm. The NOAEL was 750 ppm, equal to 36.3 mg/kg bw per day in males and 57.7 mg/kg bw per day in females, on the basis of body-weight decreases and histological changes in the liver of females at 2000 ppm. Effects observed in the study of carcinogenicity in rats were similar to those seen in the study of toxicity. Feed intake was decreased only decreased by 6% in females at the highest dose only. At the lowest dose of 200 ppm, equal to 8.8 mg/kg bw per day, body-weight gain among females was reduced by 9%, with reductions of 23% and 38% at the next higher doses. Although body-weight gain in females at 750 ppm was statistically significantly decreased, the effect was not considered to be treatment-related because there was high variability in body-weight development in the control and the dosed groups between the two 2-year studies. In males, body-weight gain was only impaired in the group at the highest dose of 2000 ppm, equal to 94.6 mg/kg bw per day. In animals at the highest dose, an increase in swollen hind feet/limbs was seen, with unknown etiology. In males, the frequency of findings of lymph node cysts and dilated blood vessels was also increased. At dietary concentrations of 2000 ppm, statistically significantly increased incidences of histological changes in the liver of males and females were seen, increased pancreatitis being observed in males at the highest dose. As in the study of toxicity, males receiving dimethomorph showed more interstitial-cell hyperplasia and adenoma of the testes than did the controls. In both studies, the incidence of adenoma at 2000 ppm, equal to 94.6 mg/kg bw per day, the highest dose, were close to the upper limit of the range for historical controls. However, there was no clear dose–response relationship and therefore adenoma was considered as part of a continuum with interstitial-cell hyperplasia. Additionally, this type of tumour is usually secondary to hormonal perturbation, an effect that is not suggested by the current toxicology database for any species. In males at the highest dose, there was also an increase in the incidence of benign medulla tumours of the adrenals when compared with concurrent controls, but this was within the range for historical controls. The Meeting concluded that dimethomorph was not tumorigenic in rats. When evaluating the two 2-year studies together, the overall NOAEL was 750 ppm, equal to 36.3 mg/kg bw per day, on the basis of reduced body-weight gain in both sexes and histological changes in the liver of females at 2000 ppm.

Dimethomorph was not carcinogenic in mice or rats.

With the exception of three assays for chromosomal aberration in V79 cells and in human lymphocytes, dimethomorph gave negative results in a battery of appropriate tests for genotoxicity. A slight increase in the frequency of aberrant cells was found in V79 cells and in human lymphocytes at high doses, with reduced mitotic indices and slight precipitation of the compound.

The Meeting concluded that dimethomorph was unlikely to be genotoxic in vivo.

On the basis of the absence of carcinogenicity and genotoxicity, the Meeting concluded that dimethomorph is unlikely to pose a carcinogenic risk to humans.

In a two-generation study of reproductive toxicity studying rats, there was a reduction in body-weight gain in dams at the highest concentration of 1000 ppm, equal to 80 mg/kg bw per day, in the pre-mating period; this was compensated for thereafter and had no impact on reproductive performance. In F_1, F_{2a} and F_{2b} pups, the only finding was a slight delay in incisor eruption, which did not affect feeding capacity. Overall, pups developed normally; no other developmental markers, such as eye-opening, pinna unfolding or hair growth, were affected. Therefore, the NOAEL for maternal and reproductive toxicity was 1000 ppm, equal to 80 mg/kg bw per day, the highest dose tested.

In studies of developmental toxicity in rats, reduced feed consumption and reduced body-weight gain were recorded at the highest dose of 160 mg/kg bw per day on days 6–10 of gestation, but not thereafter. On day 20 of gestation, the difference in absolute body weight compared with that in control animals was marginal. At the highest dose, an increase in total litter losses and an increase in post-implantation losses in females with live foetuses at terminal sacrifice were observed. There were no other effects on foetal development. The NOAEL for developmental toxicity was 160 mg/kg bw per day, the highest dose tested. The NOAEL for maternal toxicity and embryotoxicity was 60 mg/kg bw per day, on the basis of intermittent decreases in body-weight gain in dams and post-implantation losses.

In two studies of developmental toxicity in rabbits, dams lost weight or did not show an increase in body weight during days 6–12 of gestation at 600 and 650 mg/kg bw per day, respectively. At this dose, the incidence of total litter losses was increased, but there were no increases in malformations or variations. The NOAEL for maternal and developmental toxicity was 300 mg/kg bw per day.

The Meeting concluded that dimethomorph is not teratogenic.

The Meeting considered that dimethomorph is not neurotoxic on the basis of the available data.

The Meeting concluded that the existing database on dimethomorph was adequate to characterize the potential hazards to foetuses, infants and children.

No health effects related to exposure to dimethomorph were reported in personnel working in a production plant.

Toxicological evaluation

The Meeting established an ADI of 0–0.2 mg/kg bw based on a NOAEL of 15.2 mg/kg bw per day identified on the basis of the liver weight and clinical chemistry changes and prostate weight changes and prostate fibrosis observed at higher doses in the 13-week and the1-year studies in dogs. A safety factor of 100 was applied.

The Meeting established an ARfD of 0.6 mg/kg bw based on a NOAEL of 60 mg/kg bw per day identified on the basis of post-implantation losses at higher doses in the study of developmental toxicity in rats. A safety factor of 100 was applied.

A toxicological monograph was prepared.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Mouse	Two-year study of toxicity and carcinogenicity[a]	Toxicity	100 mg/kg bw per day	1000 mg/kg bw per day
		Carcinogenicity	1000 mg/kg bw per day[c]	—
Rat	Two-year studies[d]	Toxicity	750 ppm, equal to 36.3 mg/kg bw per day	2000 ppm, equal to 99.9 mg/kg bw per day
		Carcinogenicity	2000 ppm, equal to 99.9 mg/kg bw per day[c]	—
	Two-generation study of reproductive toxicity[a]	Parental toxicity	1000 ppm, equal to 80 mg/kg bw per day[c]	—

		Offspring toxicity	1000 ppm, equal to 80 mg/kg bw per day[c]	—
	Developmental toxicity[b]	Maternal toxicity	60 mg/kg bw per day	160 mg/kg bw per day
		Embryo/fetotoxicity	60 mg/kg bw per day	160 mg/kg bw per day
Rabbit	Developmental toxicity[b]	Maternal toxicity	300 mg/kg bw per day	650 mg/kg bw per day
		Embryo/fetotoxicity	300 mg/kg bw per day	650 mg/kg bw per day
Dog	Thirteen-week and 1-year studies of toxicity[ad]	Toxicity	450 ppm, equal to 15.2 mg/kg bw per day	1350 ppm, equal to 44.8 mg/kg bw per day

[a] Dietary administration.
[b] Gavage administration.
[c] Highest dose tested.
[d] The results for two studies were combined.

Estimate of acceptable daily intake for humans

0–0.2 mg/kg bw

Estimate of acute reference dose

0.6 mg/kg bw

Information that would be useful for the continued evaluation of the compound

Results from epidemiological, occupational health and other such observational studies of human exposures.

Critical end-points for setting guidance values for exposure to dimethomorph

Absorption, distribution, excretion and metabolism in mammals	
Rate and extent of oral absorption	Rapid, > 90% within 24 h
Dermal absorption	4.75% after application of single dose of 7.7 mg/kg bw for 8 h
Distribution	Extensive
Potential for accumulation	Low, no evidence of accumulation
Rate and extent of excretion	Rapid, close to 100% within 48 h, mainly via faeces
Metabolism in animals	Extensive, demethylation and morpholine ring-opening
Toxicologically significant compounds in animals, plants and the environment	Dimethomorph
Acute toxicity	
Rat, LD_{50}, oral	3900 mg/kg bw > 5000 mg/kg bw (*Z*-isomer) 4715 mg/kg bw (*E*-isomer)
Rat, LD_{50}, dermal	> 2000 mg/kg bw; > 5000 mg/kg bw (*Z*-isomer)
Rat, LC_{50}, inhalation	> 4.24 mg/L

Rabbit, skin irritation	Not irritating
Rabbit, eye irritation	Initially slightly irritating
Guinea-pig, skin sensitization (test method used)	Not a sensitizer (Magnusson & Kligman)
Short-term studies of toxicity	
Target/critical effect	Prostate and liver and clinical chemistry (dogs)
Lowest relevant oral NOAEL	15.2 mg/kg bw per day (dog)
Lowest relevant dermal NOAEL	No data
Lowest relevant inhalation NOAEC	No data
Genotoxicity	
	Unlikely to be genotoxic in vivo
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	Liver histology and body-weight decrease (rats)
Lowest relevant NOAEL	36.3 mg/kg bw per day
Carcinogenicity	Not carcinogenic
Reproductive toxicity	
Reproduction target/critical effect	No reproductive effects
Lowest relevant reproductive NOAEL	80 mg/kg bw per day, the highest dose tested
Developmental target/critical effect	Increased incidence of total litter losses (rats and rabbits)
Lowest relevant developmental NOAEL	60 mg/kg bw per day (rats)
Neurotoxicity/delayed neurotoxicity	
	No evidence in conventional studies
Other toxicological studies	
	In pharmacological studies, evidence for an increase in phenobarbital sleeping time
Medical data	
	Medical surveillance of workers in a plant producing dimethomorph did not reveal any adverse health effects.

Summary

	Value	Study	Safety factor
ADI	0–0.2 mg/kg bw	Dog, 13-week and 1-year study	100
ARfD	0.6 mg/kg bw	Rat, study of developmental toxicity	100

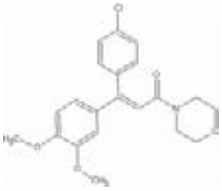
RESIDUE AND ANALYTICAL ASPECTS

Dimethomorph is a morpholine fungicide with protective action against plant pathogenic Phytophthora species and a number of downy mildew diseases of fruit, vegetables and potatoes. It was included on the schedule of new compounds for consideration by the 2007 JMPR. The Meeting received a full data package including animal and plant metabolism studies (goats, hens, grapes, potato, lettuce, tomato), soil metabolism, dissipation and photodegradation, crop rotational studies, information on analytical methods, freezer storage stability, supervised residue trial data from use as a

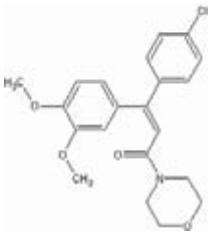
foliar spray on a range of fruit, vegetable, cereal and oil seed crops, processing studies and livestock feeding studies. GAP information was also submitted by Australia.

Chemical name and structure

(E,Z) 4-[3-(4-chlorophenyl)-3-(3,4-dimethoxy-phenyl)-1-oxo-2-propenyl]-morpholine



E- isomer



Z- isomer

The following abbreviations are used for the metabolites discussed below:

*Z*7	4-Chloro-3',4'-dimethoxy-benzophenone
*Z*67	(*E/Z*)-4-(3-(4-Chlorophenyl)-3-(3'-methoxy-4'-hydroxyphenyl)-1-oxo-2-prophenyl)-morpholine
*Z*69	(*E/Z*)-4-(3-(4-Chlorophenyl)-3-(3'-hydroxy-4'-methoxyphenyl)1-oxo-2-prophenyl)-morpholine
*Z*89	N-[3-(4-chlorophenyl)-3-3,4-dimethoxyphenyl)-1-oxo-2-propenyl-glycine
CL 411266	4-[(1Z)-1-(4-chlorophenyl)-3-(4-morpholinyl)-3-oxo-1-propenyl]-2-methoxyphenyl

Animal metabolism

The Meeting received information on the fate of orally dosed dimethomorph in the lactating goat and in laying hens. Experiments were carried out with dimethomorph with the chlorophenyl ring uniformly labelled with [^{14}C]. Metabolism in laboratory animals (rats) was summarized and evaluated by the WHO panel of this JMPR Meeting.

In rats, after oral gavage with a single dose of 10 mg/kg bw per day, dimethomorph is quantitatively absorbed and excreted to more than 90% via bile and to 7% via urine in both sexes. Following a single dose of 500 mg/kg bw per day, absorption was decreased to 65% in males and to 40% in females. At the low dose rate, excretion virtually is complete after 48 h with less than 1% of dose found in carcass and in liver and less or equal to 0.2% in kidneys. Dimethomorph is extensively metabolized by demethylation of one of the methoxy groups and formation of O-conjugate and degradation products of morpholine ring opening were found.

Two lactating goats orally treated twice daily with [^{14}C] labelled dimethomorph at 0.55 mg/kg bw per day (equivalent to 25 ppm in feed for a day). Each animal received 15 doses over 7.5 days, the last being the morning of the 8th day, 4 h before slaughter.

Most of the applied radioactivity was excreted in urine (about 15%) and faeces (about 72%). Total Radioactive Residues (TRR) in edible tissues averaged 7.1 mg/kg in liver, 0.28 mg/kg in kidney, 0.07 mg/kg in fat and 0.03 mg/kg in muscle. In milk, residues reached a plateau of about 0.06 mg/kg after 2 days, with residues generally ranging from 0.03–0.1 mg/kg (average 0.06 mg/kg). About 80% of the TRR in milk was present in whey. The overall recovery of the radioactivity was 88–92%.

The unchanged parent was the primary residue, comprising 72% of the liver TRR, 10% of the kidney TRR, 7.5% of the muscle TRR and 75% of the fat TRR. In milk, the major identified residue

was the polar Z89 metabolite, making up approximately 48% of the milk TRR. Metabolites Z67 and Z69 were also detected in liver at levels of 3–4% of the liver TRR.

The proposed metabolic pathway for dimethomorph in the lactating goat is similar to that suggested for rats, involving the demethylation of one of the phenolic methoxy-groups, with an alternative pathway being the cleavage of the morpholine-ring.

Groups of 6–9 laying hens were orally dosed twice daily for seven consecutive days with 1 mg [^{14}C] labelled dimethomorph/kg bw per day, equivalent to 40 ppm in the feed. The hens were sacrificed 8 h, 7 days and 12 days after the last administration. Most of the administered radioactivity (85%) was found in the excreta, with edible tissues (liver, kidney, muscle and fat) containing about 0.4% and < 0.1% found in eggs. The highest radioactive residues were in liver (1.1 mg/kg dimethomorph equivalents) with lower levels found in kidney (0.3 mg/kg), fat/skin (0.04 mg/kg) and muscle (0.02 mg/kg). In egg whites, TRR reached a maximum of 0.056 mg/kg after 4 days, while in yolks, highest TRR (0.51 mg/kg) was found at day 7. At the end of the depuration period (12 days) the radioactivity levels had decreased to about the background level of 0.01 mg/kg (egg whites) and 0.02 mg/kg (yolks). The overall recovery of the radioactivity (including residues in the cage wash) was around 88%.

Dimethomorph (unchanged parent) was only found in fat and skin, at levels of < 0.02 mg/kg. Metabolites Z67 and Z69 were the major residue components identified in liver (0.13 mg/kg), egg yolks (0.07 mg/kg), kidney (0.03 mg/kg) and muscle (0.003 mg/kg). Low levels (0.02–0.05 mg/kg) of the Z43 and Z95 metabolites were reported in kidney and/or egg yolks.

In general, the metabolism of dimethomorph in farm animals is similar to that in laboratory animals, and is mostly (85–87%) excreted in urine or faeces. Most of the remaining radioactive residues are found in liver and to a much lesser extent in kidney and egg yolk, with other edible tissues and milk containing less than 0.1 mg/kg TRR. Unchanged parent is the predominant residue identified in goat liver (about 5 mg/kg) and is also present in fat, kidney (goats), poultry skin and muscle (goats), but at levels below 0.06 mg/kg. In milk, the major residue is the Z89 metabolite (0.05 mg/kg). The metabolites Z67 and Z69 are the major residue components present in poultry, mostly in liver and kidney but also at low levels in muscle (0.003 mg/kg) and in egg yolks (0.07 mg/kg).

The Meeting concluded that the major residue component in ruminant animal commodities, from the oral administration of dimethomorph, is the parent compound, with the metabolite Z89 being the major residue in milk and that the metabolites Z67 and Z69 are the predominant residues in poultry commodities.

Plant metabolism

The Meeting received information on the fate of dimethomorph in grapes, potato, lettuce and tomato, following treatment with [p-chlorophenyl-U-^{14}C]dimethomorph and also on potato following treatment with [morpholine-U-^{14}C]dimethomorph.

Grape vines grown outdoors under shelter in Germany were treated by syringe with an EC formulation of [^{14}C] labelled dimethomorph at a rate equivalent to 0.09 kg ai/hL or 0.9 kg ai/ha with four applications being made at 9–10 day intervals up to 35 days before harvest. Grapes and leaves were washed with acetone to remove surface residues and the washed samples were then homogenised and remaining residues were further extracted with acetone and methanol. Radioactive residues in the surface washes (leaves and grapes) accounted for 70–72% of the applied radioactivity with about 26% of the TRR in grapes (3.8 mg/kg) being found in the homogenised samples. The majority of the extractable residue was the unchanged parent (83–86% TRR).

Potato plants grown in pots in a glasshouse in Germany were sprayed with [^{14}C]-[chlorophenyl]-dimethomorph (EC) at a rate equivalent to 0.06 kg ai/hL or 0.6 kg ai/ha with four applications at 10 day intervals with the last up to 7 days before harvest. Stems, leaves and tubers

were washed with acetone to remove surface residues and the washed samples were then homogenised and remaining residues extracted with methanol. About 61% of the recovered radioactivity was present as a surface residue. The majority of the extractable residue in foliage was the unchanged parent dimethomorph (68% of the TRR). Only trace amounts of radioactivity (0.01–0.02 mg/kg) were found in tubers.

In a complimentary potato metabolism study, dimethomorph (EC) labelled with [^{14}C] in the morpholine ring was applied to greenhouse potato plants at a rate equivalent to 0.06 kg ai/hL (0.6 kg ai/ha) with four applications at 10 day intervals up to 7 days before harvest. Surface residues were removed in acetone, after which the samples were homogenised and the remaining residues extracted in methanol. In treated foliage the acetone surface wash contained about 72% of the TRR. Small amounts of radioactivity were measured in tubers from treated plants predominantly in peel where radioactive residues of < 0.03 mg/kg were found. The majority of the foliage residue was the unchanged parent (76% of the foliage TRR or 13.8 mg/kg) with the remaining extractable residue consisting of several unknown (mainly polar) metabolites at levels too low to identify.

In an additional study on potato plants grown in a lysimeter, [^{14}C]-[chlorophenyl]-dimethomorph (DC) was applied at a rate equivalent to 0.3 kg ai/ha as a foliar spray three times, 10 days apart, up to 28 days before harvest. About 98% of the recovered radioactivity was found in the foliage, with about 1.5% TRR being found in the tubers, 0.8% (0.12 mg/kg) in the peel and 0.7% (0.025 mg/kg) in the peeled potatoes. Further investigation of the tuber residues identified the unchanged parent compound to be the major residue, predominantly in the peel (about 46% or 0.06 mg/kg), with the metabolites Z67 and Z69 comprising < 10% of the peel TRR.

In field grown lettuce, chlorophenyl ring labelled [^{14}C]dimethomorph (DC) was applied in four successive foliar applications at a rate equivalent to 1.14 kg ai/ha. Applications were made 8 days after transplanting and at intervals of 9, 10 and 11 days, with plants (without roots) being sampled four days after the final application. Close to 99% of the TRR was extracted from macerated samples with acetone or acetone:water with most of this (93%) being the unchanged parent. Trace levels of the metabolites Z7 and Z67 were also reported, each accounting for 0.5% TRR (0.5 mg/kg). The remaining extractable residue (4.5% TRR) consisted of several minor unknown polar components, which were not further characterized.

Tomatoes (young plants) were treated with [^{14}C]-[chlorophenyl]-dimethomorph by the addition of 8 mg ai/L to the hydroponic nutrient solution for 7 days. Plant samples (without roots) were taken 0, 14 and 28 days after termination of the application. Total radioactive residues in leaves and stems, at the end of the 7 day exposure period were 24.5 mg/kg dimethomorph equivalents, reducing to 12.5 mg/kg after 14 days and to 7 mg/kg after 28 days. Dimethomorph was the predominant residue, initially comprising 66% of the TRR and reducing to 28% after 14 days and to 16% after 28 days. The calculated half-life of the parent compound was about 13 days. The demethylated metabolite Z69 (including conjugates) was the major metabolite found (13–34% TRR), with metabolites Z93 (8–17% TRR), Z95 (4–8% TRR) and Z98 (1–7% TRR) also being found.

The Meeting concluded that the metabolic pathways of dimethomorph in plants show a common pattern, with the unchanged parent being the only significant residue in plant commodities. Residues are mostly found on the plant surface, i.e., negligible systemic translocation, with only low residues being found in potato tubers (almost all in the peel). However, when young tomato plants are exposed to dimethomorph in a hydroponic nutrient solution, residues can be taken up by the roots and translocated to leaves and stems. The primary metabolic pathway involves the demethylation of the dimethoxyphenyl ring to produce the metabolites Z67 and Z69, with the probable formation of the associated glucose conjugates. A secondary pathway involves the hydrolysis of dimethomorph to form the Z7 metabolite.

Environmental fate in soil

The Meeting received information on the environmental fate of dimethomorph in soil, including aerobic soil metabolism, soil photodegradation and also confined and field rotational crop studies.

Aerobic soil metabolism

In six laboratory studies the degradation of dimethomorph in soil under aerobic conditions was investigated in sand, loamy sand, sandy loam and silty clay loam, using [^{14}C] labelled dimethomorph (labelled in either the chlorophenyl or the morpholine ring). Under sterile conditions, dimethomorph was stable, with about 90% of the applied radioactivity identified as the parent compound after four months (compared with 36% remaining in a comparable unsterile soil), indicating microbial action was the major source of degradation. As the levels of extractable dimethomorph decreased over time, there was a corresponding increase in unextracted residues, the nature of which was not investigated. The shift in the ratio of *E*- and *Z*-isomers of dimethomorph was investigated in most of these studies, with the initial *E:Z* ratio of about 50:50 shifting to about 40:60 after 60–90 days and 30:70 after 180 days. Half-lives in the laboratory studies ranged from 47 days to 90 days except in one atypical acidic sandy soil (pH 3.5, 99% sand), where 86% of the applied dimethomorph remained after 120 days.

In field studies, where dimethomorph was applied at rates of 0.43–0.6 kg ai/ha to a range of different soil types (sand, loamy sand, sandy loam, clay), dimethomorph residues were only detected in the top 10 cm, with trace amounts of the metabolites Z67 and Z69 being found in the top 20 cm, but only within the first two months after treatment. Half-lives for dimethomorph in these studies ranged from 10–61 days.

Photodegradation in soil

In a soil photolysis study where [^{14}C] labelled dimethomorph was added to sterile sandy-loam soil and exposed to light continuously for 15 days, less than a 10% decrease in dimethomorph residues was observed, with two minor (unidentified) metabolites found at levels up to 4.2% of the applied radioactivity. During the study period, the *E/Z*-isomer ratio shifted from about 40:60 to 34:66.

Residues in rotational crops

In two confined rotational crop studies, [^{14}C] labelled dimethomorph was applied to bare soil at rates equivalent to 4 kg ai/ha and 1.7 kg ai/ha.

In the first study, lettuce, carrots and wheat were planted in soil treated with dimethomorph to simulate the application of 4 kg ai/ha followed by incorporation to a depth of 15 cm and aged for 29, 120 and 361 days. Total radioactive residues of 4.8 mg/kg were found in wheat straw, 1 mg/kg in wheat forage and 0.14–0.2 mg/kg in carrot tops and lettuce planted in the 29 day aged soil. Dimethomorph residues in soil at the time of planting were about 0.8 mg/kg. In the soil aged for 120 days, dimethomorph residues at planting were about 0.05 mg/kg and total radioactive residues in all subsequent crops were < 0.1 mg/kg except wheat foliage (0.24 mg/kg) and wheat straw (0.78 mg/kg).

In the second study, wheat, lettuce, soya beans and radish were planted in soil treated with the equivalent of 1.7 kg ai/ha and aged for 30–394 days. In soil aged for 30 days, total radioactive residues were < 0.1 mg/kg in all crops except wheat straw (0.15 mg/kg). Dimethomorph residues were 0.01 mg/kg or less in all crops and the only metabolite found was CL 411266, at 0.04 mg/kg in wheat straw and 0.01 mg/kg in radish tops and wheat forage. In soil aged for 60 days, total radioactive residues were < 0.05 mg/kg in all crops except wheat straw (0.13 mg/kg). Dimethomorph residues were not found in any crops and the metabolite CL 411266 was measured in wheat straw (0.03 mg/kg) and lettuce (0.02 mg/kg). Radioactive residues did not exceed 0.05 mg/kg in any samples from crops grown in soil aged for 394 days.

Rotational crop field studies were conducted Germany, where carrots, spinach and beans were planted immediately after harvest of a potato crop treated with 3 applications of 0.18 kg ai/ha dimethomorph (PHIs of 2–6 weeks). At the time of planting the rotational crops, dimethomorph residues in soil were 0.08–0.14 mg/kg. Dimethomorph residues in subsequent crops were all 0.02 mg/kg or less, except in spinach sampled 72–76 days after the last soil treatment, where residues of 0.09 mg/kg and 0.21 mg/kg were found. Residues were below the limit of quantification in all three crops at maturity.

The Meeting concluded that dimethomorph is stable to hydrolysis and photolysis and is moderately persistent in soil with field half-lives of 10–61 days. In rotational crops, dimethomorph can be taken up by the roots and dimethomorph residues may occur in early harvest crops (e.g., spinach) planted within 44 days of the last application.

Methods of analysis

The Meeting received data on analytical methods for enforcement and monitoring of dimethomorph and its major metabolites in plant and animal commodities. A number of these methods are capable of determining the individual dimethomorph isomers but in most cases these residues have been combined in the supervised field trial reports, as to minimise isomerization reactions during preparation and analysis, the analytical work needs to be conducted in the absence of light. However these isomerization reactions do not influence the measurement of total residues.

Analytical methods for enforcement and monitoring

The multi-residue analytical method DFG S19, with a modification to use ethyl acetate:cyclohexane instead of dichloromethane in the partition clean-up step, has been validated in a range of commodities as an enforcement-monitoring method for the determination of dimethomorph in plant commodities. With an alternative extraction procedure for fat (DFG Method 5), this method can be used to measure dimethomorph residues in animal matrices. Reported LoQs are 0.01 mg/kg for animal matrices and 0.02 mg/kg for plant matrices.

Analytical methods used in study reports

Analytical methods used in the supervised residue trials and in the animal residue studies generally involve extraction with acetone, acetonitrile or acidified methanol with residues being partitioned into dichloromethane, ethyl acetate or cyclohexane and cleaned-up by gel permeation chromatography prior to analysis. An additional silica gel column clean-up step is included in some methods, and for some matrices, an additional partition step with hexane (to remove fatty constituents) is included. Analysis can be by HPLC-UV, GC-NPD, GC-MS or HPLC-MS/MS. In most of the commonly used methods, LOQs of 0.01 mg/kg or 0.02 mg/kg have been reported. The methods used in the animal studies were capable of measuring the parent compound, the Z89 metabolite and the sum of the Z67 and Z69 metabolite residues.

Validation studies on the more commonly used analytical methods generally reported mean recovery rates of 73–116% when a wide range of plant and animal matrices were fortified with dimethomorph at concentrations of 0.01–5 mg/kg and with 0.1 mg/kg of the metabolites Z89, Z67 and Z69 in the case of cattle matrices.

The Meeting concluded that adequate analytical methods exist for the determination of dimethomorph in crops and livestock commodities both for data collection and MRL enforcement purposes.

Stability of residues in stored analytical samples

The Meeting received information on the frozen storage stability of residues in cattle milk and edible tissues, grapes, rape seed, hops, tomato, broccoli, spinach, potato and processed grape, hops, tomato

and potato matrices. In all cases, residues were stable in the macerated matrices under conditions of frozen storage for an interval at least as great as the storage interval of supervised field trial or livestock feeding samples.

Dimethomorph residues were stable under conditions of frozen storage for the intervals tested: 24 months in broccoli, grapes, spinach, tomato, 21 months in processed tomato matrices, 18 months in soil, rape seed, hops, beer, spent hops and brewer's yeast, 16 months in processed grape commodities, 14 months in raisins and 6 months in potatoes and processed potato commodities. In cattle meat, milk, liver and kidney, residues of dimethomorph and its metabolites Z67 and Z69 were stable for the 16 month frozen storage interval. The predominant residue in milk (the Z89 metabolite) was also stable over the 16 month test interval.

The Meeting concluded that dimethomorph is stable (less than 10% loss of residues) in most crop, processed commodity, and livestock commodity samples under frozen storage conditions.

Definition of the residue

In plants, dimethomorph is stable to hydrolysis and occurs mostly as surface residue with no significant metabolism. The major residue resulting from foliar applications of dimethomorph is the parent compound, present as a mixture of the *E*- and *Z*-isomers, the ratio of which can change over time as a result of isomerisation reactions stimulated by light.

In animals, while metabolism studies indicate that the parent compound is the major residue in cattle liver and fat, residues of the metabolites Z67 and Z69 are also present in significant amounts and metabolite Z89 is the largest single component in milk. In poultry commodities, the parent compound is only found in fat and skin, with metabolites Z67 and Z69 being the major residues. However the Meeting noted that these results were from feeding studies involving exaggerated dosing regimes, and that under practical conditions, residues are not expected in animal commodities.

A validated multi-residue method is available to measure dimethomorph, as the sum of the *E*- and *Z*-isomers in both plant and animal matrices.

Based on the above, the Meeting agreed:

Definition of the residue in plant commodities for estimation of dietary intake and for compliance with MRLs: dimethomorph (sum of isomers).

Definition of the residue in animal commodities for estimation of dietary intake and for compliance with MRLs: dimethomorph (sum of isomers).

The results of the animal metabolism studies indicate that dimethomorph is not fat-soluble.

Results of supervised trials on crops

Supervised trials were available for the use of dimethomorph as a foliar spray on citrus (oranges), strawberries, grapes, pineapples, onions, green onions, brassica vegetables (cabbage, broccoli, kohlrabi), cucumber, courgettes (zucchini), melons, tomatoes, peppers (sweet), lettuce, spinach and hops.

Supervised trials involving dimethomorph seed-piece treatment on pineapples and as a seed treatment on oil seed rape were also made available.

In many countries, dimethomorph is available in formulations with and without other complimentary fungicides such as mancozeb, chlorothalonil, copper and folpet. For the purpose of this evaluation, the PHIs defined as GAP for each crop are those established for dimethomorph when formulated without other active ingredients. Where dimethomorph is available only as combination products with different PHIs, the shortest PHI has been selected when defining GAP.

Oranges, sweet, sour

The results of residue trials in Spain involving foliar applications on oranges were made available to the Meeting.

The only GAP provided to the Meeting was for stem paint treatments in Thailand and Vietnam.

The Meeting agreed the data was not sufficient to estimate a maximum residue limit for oranges.

Strawberries

In Belgium, GAP is for three root drench applications of 0.05 g ai/plant, just after planting, one month later and again at the start of spring growth (about 2 months before harvest). In trials from Belgium, matching this GAP, residues found were 0.01, 0.01, 0.02 and 0.02 mg/kg.

In Netherlands, GAP for protected strawberries is to apply 0.05 g ai/plant with the nutrient solution as a root drench up to 35 days before harvest. In three outdoor trials match Netherlands GAP, residues found were 0.01, 0.01 and 0.02 mg/kg.

GAP for outdoor strawberries in Netherlands is for a single foliar spray (0.15 kg ai/ha) just after planting and in four trials in Netherlands matching this GAP, residues were all < 0.01 mg/kg.

The Meeting agreed to use the data from the root drench trials in Belgium and Netherlands to give a combined data set of: 0.01 (4), 0.02 and 0.02 mg/kg.

The Meeting estimated a maximum residue level of 0.05 mg/kg for dimethomorph in strawberries and estimated an STMR of 0.01 mg/kg and an HR of 0.02 mg/kg.

Grapes

The results of residue trials in grapes from France, Germany, Greece, Italy, Spain, Australia, New Zealand and Brazil were made available to the Meeting.

Residues in trials in Brazil matching the GAP in Columbia (0.3–0.4 kg ai/ha, PHI 19 days) were: 0.24, 0.31, 0.99 and 1.1 mg/kg.

Residues in trials from Germany matching the GAP of Belgium (0.3 kg ai/ha, up to 3 applications per season, with a PHI of 28 days) were: 0.26, 0.36, 0.6, 0.71, 1.2 and 1.3 mg/kg.

Residues in trials from Spain matching the GAP of Spain (0.03 kg ai/hL, with a PHI of 28 days) were: 0.09, 0.11, 0.14, 0.24 and 0.25 mg/kg.

Residues in trials from France, matching the GAP of Spain (0.03 kg ai/hL, PHI 28 days), were: 0.16, 0.20, 0.27, 0.38, 0.38, 0.39, 0.39, 0.46, 0.47, 0.51, 0.51, 0.61, 0.62, and 1.7 mg/kg.

Residues in trials from Italy, matching the GAP of Spain (0.03 kg ai/hL, PHI 28 days), were: 0.1, 0.18, 0.19, 0.21, 0.42, 0.85, 0.94, and 1.2 mg/kg.

Residues from a single trial from Greece, matching the GAP of Spain (0.03 kg ai/hL, PHI 28 days), were: 0.39 mg/kg.

The Meeting agreed to use the trials in Spain, France, Italy and Greece matching the GAP of Spain. Residues in ranked order (median underlined) were: 0.09, 0.1, 0.11, 0.14, 0.16, 0.18, 0.19, 0.20, 0.21, 0.24, 0.25, 0.27, 0.38, 0.38, 0.39, 0.39, 0.39, 0.42, 0.46, 0.47, 0.51, 0.51, 0.61, 0.62, 0.85, 0.94, 1.2 and 1.7 mg/kg (n=27).

The Meeting estimated a maximum residue level of 2 mg/kg for dimethomorph in grapes and estimated an STMR of 0.39 mg/kg and an HR of 1.7 mg/kg.

Pineapple

GAP for pineapples in Philippines is for pre-plant dip treatments of seed-pieces (0.19 kg ai/hL dipping solution) and up to 3 post-planting foliar spray applications (1.8 kg ai/ha), 4, 7 and 10 months after planting. Pineapples are commonly harvested about 16–17 months after planting, about 6 months after the last foliar spray.

In a set of trials in Philippines, residues in pineapples following pre-plant seed-piece dipping treatments at 2 × and 4 × the recommended rate were < 0.01 (2) mg/kg in both flesh and peel. Residues were also < 0.01 (2) mg/kg in flesh and peel of pineapples following the pre-plant seed-piece dip treatments (2 × and 4 ×) combined with three foliar sprays matching the recommended application rate and timing. Similarly, pineapples treated with a combination of pre-plant seed-piece dipping (2 × and 4 ×) and three foliar sprays (2 ×), residues were also < 0.01 (2) mg/kg in both flesh and peel.

Since residues were all < 0.01 mg/kg in all four trials involving exaggerated (2 × and 4 ×) pre-plant dipping treatment combined with foliar treatments (1 × and 2 ×), the Meeting agreed to use the results of these trials to give a combined data set of < 0.01, < 0.01, < 0.01 and < 0.01 mg/kg.

The Meeting estimated a maximum residue level of 0.01* mg/kg for dimethomorph in pineapple and estimated an STMR of 0 mg/kg and an HR of 0 mg/kg.

Onions, bulb

In Australia, GAP for onions is up to 0.18 kg ai/ha (maximum 3–4 applications per season), with a PHI of 7 days and in one trial in Australia matching this GAP (but with 7 applications), residues were < 0.02 mg/kg.

Residues in two trials from Germany, matching the German GAP of 4 × 0.3 kg ai/ha, with a PHI of 14 days for bulb vegetables, were < 0.01 and < 0.01 mg/kg.

In one trial in France, matching the German GAP, residues were 0.02 mg/kg.

The Meeting agreed the data was not sufficient to estimate a maximum residue limit for onions, bulb.

Green onions

The Meeting received results of residue trials in Australia on green onions (spring onions).

GAP for bulb vegetables in USA is 0.22 kg ai/ha, PHI 0 days, in Australia GAP for onions is 0.18 kg ai/ha, PHI 7 days, maximum 4 applications/season and in Germany, GAP for bulb vegetables is 0.3 kg ai/ha, PHI 14 days.

No trials matching these GAPs were available and the Meeting agreed the data was not sufficient to estimate a maximum residue limit for green onions.

Cabbage, head

The Meeting received results of residue trials in USA on cabbage.

In trials in USA matching the GAP of Cuba (0.2–0.23 kg ai/ha, PHI 7 days for vegetables) residues of dimethomorph in cabbages (including wrapper leaves) were < 0.05, 0.14, 0.25, 0.4, 0.69, 1.1 and 1.4 mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg for dimethomorph in cabbage and estimated an STMR of 0.4 mg/kg and an HR of 1.4 mg/kg.

Broccoli

The Meeting received results of residue trials in the USA on broccoli.

In trials in USA matching the GAP of Cuba (0.2–0.23 kg ai/ha, PHI 7 days for vegetables), residues of dimethomorph in broccoli were: < 0.05, 0.12, 0.17, 0.2, 0.25 and 0.52 mg/kg.

The Meeting estimated a maximum residue level of 1 mg/kg for dimethomorph in broccoli and estimated an STMR of 0.19 mg/kg and an HR of 0.52 mg/kg.

Kohlrabi

GAP in Germany for kohlrabi is 0.3 kg ai/ha (maximum 2 applications per season), PHI 14 days and in two outdoor trials and three indoor trials in Germany matching this GAP, residues in kohlrabi were: < 0.02, < 0.02, < 0.02, < 0.02 and < 0.02 mg/kg.

The Meeting estimated a maximum residue level of 0.02 mg/kg for dimethomorph in kohlrabi and estimated an STMR of 0.02 mg/kg and an HR of 0.02 mg/kg.

Fruiting vegetables, cucurbits

Cucumber

The Meeting received results of residue trials in outdoor cucumbers in Hungary and Germany. No GAP matched these trials.

The Meeting received results of residue trials on protected cucumbers from France, Greece, Italy and Spain.

GAP for cucurbits in the USA is 0.22 kg ai/ha (maximum 5 applications/season), PHI 0 days. In protected cucumber trials, matching the GAP of USA, residues were: 0.02, 0.05 and 0.08 mg/kg in trials in Spain, 0.03 mg/kg in one trial in France, 0.05 mg/kg in one trial in Italy and 0.07 and 0.07 mg/kg in trials in Greece.

The Meeting noted that these trials involved 3–4 applications per season but agreed to use these results because 1–2 additional treatments applied more than 3–4 weeks before harvest would not contribute significantly to the final residue in rapidly growing protected cucumbers. Residues were: 0.02, 0.03, 0.05, 0.05, 0.07, 0.07 and 0.08 mg/kg.

Squash, summer:

The Meeting received results of residue trials on protected summer squash (courgettes) in Greece, Italy and Spain and on outdoor summer squash (zucchini) in Australia.

Residues from five protected summer squash trials in Greece, Italy and Spain, matching the GAP for cucurbits in the USA (0.22 kg ai/ha, maximum of 5 applications per season, PHI 0 days) were: 0.2 and 0.24 mg/kg (Greece), 0.07, 0.13 and 0.17 mg/kg (Italy) and 0.02 mg/kg (Spain).

The Meeting noted that these trials involved 3 applications per season and agreed that the contribution of 2 additional treatments applied more than 3–4 weeks before harvest would not contribute significantly to the final residue.

In one outdoor summer squash trial in Australia matching the Australian GAP (0.18 kg ai/ha, maximum 4 applications per season, PHI 7 days), residues were < 0.02 mg/kg.

The Meeting noted that the residues in protected summer squash trials matching the USA GAP were higher than those from the outdoor summer squash trial in Australia and agreed to use the data on protected summer squash. Residues found were: 0.02, 0.07, 0.13, 0.17, 0.2 and 0.24 mg/kg.

Melons, except watermelons

The Meeting received results of residue trials from Australia, Brazil, France, Italy and Spain.

Residues in trials in France matching the GAP of Israel (0.18 kg ai/ha, PHI 3 days) were: 0.03 and 0.04 mg/kg (whole fruit).

In two trials in Italy matching the GAP of Israel, whole fruit residues were 0.04 and 0.11 mg/kg.

In trials in Spain matching the GAP of Israel, whole fruit residues were: 0.02, 0.02, 0.2 and 0.24 mg/kg and in a further four trials, residues in melon flesh were: < 0.02, < 0.02, < 0.02 and 0.05 mg/kg.

The Meeting agreed to combine the results of the trials in France, Italy and Spain matching the GAP in Israel. Whole fruit residues were: 0.02, 0.02, 0.03, 0.04, 0.04, 0.11, 0.2 and 0.24 mg/kg and residues in melon flesh were: < 0.02, < 0.02, < 0.02 and 0.05 mg/kg.

The Meeting agreed that the data on cucumbers, summer squash and melons were sufficient to support a group MRL and estimated a maximum residue level of 0.5 mg/kg for dimethomorph in fruiting vegetables (cucurbits).

The Meeting estimated an STMR of 0.15 mg/kg and an HR of 0.24 mg/kg for cucurbits with an edible peel (based on the summer squash data) and an STMR of 0.02 mg/kg and an HR of 0.05 mg/kg for cucurbits with an inedible peel (based on the melon data).

Fruiting vegetables, other than cucurbits

Tomato

In protected tomato trials from France, Greece, Italy and Spain, matching the GAP of Japan (0.025 kg ai/hL, maximum 3 applications per season, PHI 1 day), residues were: 0.03, 0.05, 0.06, 0.07, 0.1, 0.1, 0.1, 0.11, 0.11, 0.13, 0.16, 0.16, 0.19 and 0.26 mg/kg.

Residues in outdoor tomato trials in USA matching the USA GAP (0.22 kg ai/ha, maximum 5 applications per season, PHI 4 days) were: 0.06, 0.08, 0.21, 0.26 and 0.41 mg/kg (n=5).

Residues in a further seven trials from the USA matching this GAP but with 6–7 applications per season were: < 0.05, < 0.05, < 0.05, 0.05, 0.14, 0.14, and 0.51 mg/kg (n=7).

The Meeting agreed that the contribution of 1–2 additional treatments applied more than 4 weeks before harvest would not contribute significantly to the final residue and agreed to use these results to give a combined data set of: < 0.05, < 0.05, < 0.05, 0.05, 0.06, 0.08, 0.14, 0.14, 0.21, 0.26, 0.41 and 0.51 mg/kg (n=12) for outdoor tomatoes.

The Meeting noted that the residues from the protected tomato trials matching the GAP of Japan and the outdoor tomato trials matching the GAP of the USA were from similar populations and agreed to combine the results. Residues in ranked order (median underlined) were: 0.03, < 0.05, < 0.05, < 0.05, 0.05, 0.05, 0.06, 0.06, 0.07, 0.08, 0.1, 0.1, 0.1, 0.11, 0.11, 0.13, 0.14, 0.14, 0.16, 0.16, 0.19, 0.21, 0.26, 0.26, 0.41 and 0.51 mg/kg (n=26).

Peppers sweet

In trials on protected sweet peppers in Greece, Italy and Spain matching the GAP of the USA for fruiting vegetables, except tomatoes (0.22 kg ai/ha, maximum 5 applications per season, PHI 0 days), residues in ranked order (median underlined) were: 0.13, 0.13, 0.16, 0.17, 0.18, 0.21, 0.21, 0.26, 0.31, 0.38, 0.48 and 0.56 mg/kg (n=12).

The Meeting noted that these trials involved 3 applications per season but agreed to use this data because the contribution of 2 additional treatments applied more than 3 weeks before harvest would not contribute significantly to the final residue in rapidly growing protected peppers.

Peppers, chilli

The GAP for peppers in the Republic of Korea is 0.3 kg ai/hL with a maximum of 4 applications per season with a PHI of 3 days. In three outdoor chilli pepper trials in Korea, matching this GAP, residues were 0.22, 0.31 and 0.53 mg/kg.

The Meeting noted that the results of the trials on peppers, sweet and peppers, chilli were from similar populations and agreed to combine the results. Residues in ranked order (median underlined) were: 0.13, 0.13, 0.16, 0.17, 0.18, 0.21, 0.21, 0.22, 0.26, 0.31, 0.31, 0.38, 0.48, 0.53 and 0.56 mg/kg.

The Meeting noted that GAP existed in the USA for the fruiting vegetable group and based on the data for peppers and tomatoes, agreed to establish a group MRL for 'fruiting vegetables, other than cucurbits' except mushrooms and sweet corn of 1 mg/kg and estimated an STMR of 0.22 mg/kg and an HR of 0.56 mg/kg.

Lettuce, head

In protected head lettuce trials in Germany, Greece, Italy and Spain matching the GAP in the USA (0.22 kg ai/ha, maximum 5 applications per season, PHI 0 days), residues were: 1.5, 2.2, 2.2, 2.3, 2.7, 2.9, 3.1, 3.6, 3.9, 3.9, 4.2, 4.3, 4.6, 7.1 and 7.2 mg/kg (n=15).

The Meeting noted that these trials involved 2–3 applications per season and agreed to use these results because the contribution of 2–3 additional treatments applied more than 3 weeks before harvest would not contribute significantly to the final residue in rapidly growing protected lettuce.

In outdoor lettuce trials in Spain, matching the GAP of Spain (0.23 kg ai/ha, PHI 7 days), residues found were: 0.05, 0.06, 0.07, 0.1, 0.16, 0.38, 0.39 and 0.43 mg/kg.

The Meeting noted that the residues from the protected lettuce trials and the outdoor lettuce trials were from different populations and agreed to use the data from the protected lettuce trials.

The Meeting estimated a maximum residue level of 10 mg/kg for dimethomorph in lettuce, head and estimated an STMR of 3.6 mg/kg and an HR of 7.2 mg/kg.

Corn salad

The Meeting received results of residue trials in protected corn salad (Lambs lettuce) from Italy and Spain. Residues in trials matching the GAP for lettuce (including Lambs lettuce) in Spain (0.23 kg ai/ha, PHI 7 days) were: 0.79, 0.79, 1.9, 4.8, 5.3 and 7.1 mg/kg.

The Meeting estimated a maximum residue limit of 10 mg/kg for dimethomorph in corn salad and estimated an STMR of 3.4 mg/kg and an HR of 7.1 mg/kg.

Spinach

The Meeting received results of residue trials in spinach in USA.

No GAP matching these USA trials was available and the Meeting agreed the data was not sufficient to estimate a maximum residue limit for spinach.

Potatoes

The Meeting received results of residue trials from Argentina, Australia, Belgium, Brazil, Canada, Denmark, France, Greece, Germany, Italy, New Zealand, Spain, UK and USA on potatoes.

In trials in Brazil matching the GAP of Brazil (0.4 kg ai/ha, maximum 4 applications per season, PHI 14 days), residues were: < 0.03 (9) and 0.03 mg/kg (n=10).

In trials in USA matching USA GAP (0.22 kg ai/ha, maximum 8 applications per season, PHI 4 days), residues were: < 0.01 (6) and 0.02 mg/kg (n=7).

Residues in trials in UK matching the GAP of the UK (0.15 kg ai/ha, maximum 8 applications per season, PHI 7 days), were: < 0.01 (12), < 0.02 (18), 0.02 and 0.04 mg/kg (n=32).

Residues in trials in France matching the GAP of France (0.18 kg ai/ha, maximum 4 applications per season, PHI 7 days) were: < 0.01 (4) and < 0.05 mg/kg (n=5).

The Meeting agreed to combine the results to give a total data set of: < 0.01(22), < 0.02(18), 0.02(2), < 0.03(9), 0.03, 0.04, < 0.05 mg/kg (n=54).

The Meeting estimated a maximum residue level of 0.05 mg/kg for dimethomorph in potatoes and estimated an STMR of 0.02 mg/kg and an HR of 0.05 mg/kg.

Rape seed

GAP in Germany for rape seed is for a pre-plant seed treatment using 5 g ai/kg of seed and in two trials from Germany matching this GAP, residues in rape seed from plants grown from treated seed were both < 0.02 mg/kg. In two related trials, residues of < 0.02 mg/kg were reported in rape seed from treated plots. However the presence of residues of 0.02 mg/kg in control samples suggested that the samples had been mislabelled.

The Meeting agreed that while residues would not be expected in rape seed following a pre-plant seed treatment, there was insufficient data to estimate a maximum residue level for dimethomorph in rape seed.

Hops

In Austria and Germany, GAP on hops is 0.015 kg ai/hL (maximum 6 applications per season in two sets of three applications), PHI 10 days.

One trial in Germany matched the GAP in Germany, with residues of 28 mg/kg in dried hops. A further eight trials in Germany matching GAP but with 4 applications per season reported residues of 8.3, 8.7, 9.3, 24, 26, 26, 29 and 42 mg/kg.

The Meeting agreed that the final 3 applications in these trials would contribute most to the final residue and agreed to use these results to give a combined data set: 8.3, 8.7, 9.3, 24, 26, 28, 26, 29 and 42 mg/kg for dried hops.

The Meeting estimated a maximum residue level of 80 mg/kg for dimethomorph in hops, dry and estimated an STMR of 26 mg/kg.

Fate of residues during processing

Dimethomorph is stable under the standard hydrolysis conditions used to simulate food processing.

The Meeting received information on the fate of incurred residues of dimethomorph during the processing of grapes, tomatoes, potatoes and hops. The processing factors (PF) shown below were calculated from the residues for the commodities for which MRLs, STMRs and HRs were estimated.

Raw commodity (RAC)	Processed commodity	Calculated processing factors.	Median or best estimate	
Grapes	Red wine	0.06, 0.12, 0.16, 0.17, 0.17, 0.17, 0.17, 0.22, 0.24, 0.24, 0.25, 0.25, 0.27, 0.28, 0.29, 0.29, 0.30, 0.31, 0.34, 0.34, 0.35, 0.36, 0.38, 0.38, 0.47, 0.53, 0.58, 0.67, 0.69, 0.70, 0.8	0.29	0.29
	White wine	0.10, 0.12, 0.13, 0.14, 0.17, 0.18, 0.31, 0.43, 0.50, 0.51, 0.61, 1.24	0.24	
	Pomace, wet (red wine)	1.6, 2.4, 2.7, 2.8, 3.1, 3.3, 4.1, 7.3	3.0	2.75
	Pomace, wet (white wine)	1.7, 2.3	2.0	

Raw commodity (RAC)	Processed commodity	Calculated processing factors.	Median or best estimate
	Raisins	1.5, 2.1	1.8
Tomatoes	Juice	0.5	0.5
	Paste	2.4	2.4
Potatoes	Wet peel	6.4	6.4
Hops	Beer	0.0011, < 0.0012, 0.0025, 0.0035	0.002

Grapes were processed into wine and dried grapes (raisins). Processing factors were 0.29 (wine), 1.8 (raisins) and 2.75 (grape pomace). Based on the STMR value of 0.39 mg/kg for grapes and the median processing factors of 0.29 (red and white wine combined) 1.8 for raisins and 2.75 for wet pomace, the STMR-Ps for dimethomorph residues were 0.11 mg/kg in wine, 0.7 mg/kg in dried grapes and 1.07 mg/kg in grape pomace, wet.

Based on the HR of 1.7 mg/kg estimated for grapes and the processing factor of 1.8 for raisins, the Meeting estimated a maximum residue level of 5 mg/kg for dimethomorph in dried grapes.

Tomatoes were processed into juice, puree and paste with processing factors of 0.5, 1.2 and 2.4 respectively. Based on the STMR value of 0.11 mg/kg for tomato, the STMR-Ps for dimethomorph residues were 0.055 mg/kg (tomato juice) and 0.264 mg/kg (tomato paste).

Potatoes, based on a processing factor of 6.4 for wet peel and an STMR of 0.02 mg/kg, the Meeting estimated an STMR-P for dimethomorph residues in potato process waste of 0.128 mg/kg.

Hops were processed into beer with a processing factor of 0.002. Based on the STMR value of 26 mg/kg for hops, dry, the STMR-P for dimethomorph residues in beer was 0.052 mg/kg.

Peppers, chilli dried. Based on the HR value of 0.56 mg/kg and the STMR value of 0.22 mg/kg for fresh peppers (including chilli peppers) and using the new generic processing factor of 7 for dried chilli peppers, the Meeting estimated a maximum residue level of 5 mg/kg and an STMR-P of 1.54 mg/kg for dimethomorph in peppers, chilli dried.

Estimated maximum and mean dietary burdens of farm animals

The Meeting estimated the dietary burden of dimethomorph in farm animals on the basis of the diets listed in Annex 6 of the 2006 JMPR Report (OECD Feedstuffs Derived from Field Crops). Calculation from highest residue, STMR (some bulk commodities) and STMR-P values provides the levels in feed suitable for estimating MRLs, while calculation from STMR and STMR-P values for feed is suitable for estimating STMR values for animal commodities. The percentage dry matter is taken as 100% when the highest residue levels and STMRs are already expressed as dry weight.

Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are provided in Annex VI. The calculations were made according to the animal diets from US-Canada, EU and Australia in the OECD Table (Annex 6 of the 2006 JMPR Report).

	Animal dietary burden, dimethomorph, ppm of dry matter diet					
	US-Canada		EU		Australia	
	max	mean	max	mean	max	mean
Beef cattle	0.32	0.32	2.3 [1]	0.96	1.48	1.48 [2]
Dairy cattle	0.11	0.11	2.19	0.85	1.43	1.43 [3]
Poultry - broiler	0	0	0.03	0.01	0	0
Poultry - layer	0	0	0.5 [4]	0.14 [5]	0	0

[1] Highest maximum beef or dairy cattle dietary burden suitable for MRL estimates for mammalian meat and milk.

[2] Highest mean beef or dairy cattle dietary burden suitable for STMR estimates for mammalian meat.

[3] Highest mean dairy cattle dietary burden suitable for STMR estimates for milk.

[4] Highest maximum poultry dietary burden suitable for MRL estimates for poultry meat and eggs.
[5] Highest mean poultry dietary burden suitable for STMR estimates for poultry meat and eggs.

Farm animal feeding studies

The Meeting received information on feeding studies with lactating cows.

A residue transfer study in livestock was conducted with 4 groups of 3 Friesian cows that were fed for 28 to 35 days with diets containing dimethomorph, administered (in corn oil) in the diet, corresponding to feeding levels of 0–12.5–37.5–125 ppm. Milk was collected daily at morning and afternoon milking and pooled for analysis. Sub-samples of milk were separated into cream and skim milk on days 14 and 28, with the day 28 milk also being pasteurised, separated into cream (35% butterfat) and skimmed milk (fat content about 0.1%) or treated and centrifuged to obtain acid whey. Liver, kidney muscle, and fat (subcutaneous and peritoneal) were taken within 24 h of the final administration for analysis. Residues in whole milk, pasteurised milk, skimmed milk, acid whey and cream were all below the limits of quantitation (0.01 mg/kg for dimethomorph and metabolite Z89) and 0.02 mg/kg for metabolites Z67/Z69) except in the 125 ppm dose group, where trace residues of dimethomorph (0.01 mg/kg) were found in cream samples.

In animals from the 12.5ppm dose group, residues of dimethomorph and metabolites Z69 and Z67 were not detectable or below the limit of quantification (0.01 mg/kg) in all tissues analysed. Residues were also all below the limit of quantification for all tissues from the 37.5 ppm dose group except for liver, where residues of up to 0.02 mg/kg of the Z69 metabolite were found. Only in the highest dose group (125 ppm) were significant residues found, mostly in liver and kidney, where residues of the Z69 metabolite were measured at levels up to 0.15 mg/kg and 0.14 mg/kg respectively and residues of the parent compound were found in liver (up to 0.05 mg/kg), and in fat (up to 0.03–0.04 mg/kg).

Residues in animal commodities

The maximum calculated animal burden estimated for dairy and beef cattle is 2.3 ppm. In the cattle feeding study, where lactating cows were dosed at 12.5 ppm (more than 5 times higher than the calculated animal burden), no dimethomorph residues were detected in tissues and milk. Therefore, the Meeting concluded that no residues are to be expected at the maximum calculated dietary burden.

The maximum animal burden estimated for poultry (layers) is 0.5 ppm. In the metabolism study where laying hens were fed the equivalent of 40 ppm in feed for seven days, dimethomorph residues in fat and skin were < 0.02 mg/kg and were not detected in eggs or other edible tissues. Metabolites Z67 and Z69 were the major residue components identified in liver (0.13 mg/kg), egg yolks (0.07 mg/kg), kidney (0.032 mg/kg) and muscle (0.003 mg/kg). Low levels (0.02–0.05 mg/kg) of the Z43 and Z95 metabolites were reported in kidney and/or egg yolks.

On the basis that the maximum calculated dietary burden is about 80 times lower than the dose rate in the metabolism study, the Meeting concluded that no residues of dimethomorph, or its primary metabolites, are to be expected at the maximum calculated dietary burden of 0.5 ppm.

The Meeting estimated a maximum residue level of 0.01* mg/kg in meat (from mammals except marine mammals) and estimated HRs and STMRs of 0 mg/kg.

The Meeting also estimated a maximum residue level of 0.01* mg/kg in edible offal (mammalian) and estimated HRs and STMRs of 0 mg/kg.

For milks, the Meeting estimated a maximum residue level of 0.01* mg/kg and estimated an STMR of 0 mg/kg.

The Meeting estimated a maximum residue level of 0.01* mg/kg in poultry meat, poultry offal and eggs and estimated HRs and STMRs of 0 mg/kg.

DIETARY RISK ASSESSMENT

Long term intake

The evaluation of dimethomorph has resulted in recommendations for MRLs and STMRs for raw and processed commodities. Consumption data was available for 31 food commodities and was used in the dietary intake calculation. The results are shown in Annex 3.

The International Estimated Daily Intakes in the 13 GEMS/Food cluster diets, based on the estimated STMRs were in the range 0–1% of the maximum ADI of 0.2 mg/kg bw (Annex 3). The Meeting concluded that the long-term intake of residues of dimethomorph from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The international estimated short-term intake (IESTI) for dimethomorph was calculated for the food commodities (and their processing fractions) for which maximum residue levels and HRs were estimated and for which consumption data was available. The results are shown in Annex 4.

The IESTI varied from 0–10% of the ARfD (0.6 mg/kg bw) for the general population. The IESTI varied from 0–20% of the ARfD for children 6 years and below. The Meeting concluded that the short-term intake of residues of dimethomorph from uses considered by the Meeting was unlikely to present a public health concern.

5.12 FENITROTHION (037)

TOXICOLOGY

Fenitrothion is the ISO approved name for O,O-dimethyl O-4-nitro-m-tolyl phosphorothioate (IUPAC) (CAS No. 122-14-5), a broad-spectrum organophosphorus pesticide. Its toxicity was first evaluated by the JMPR in 1969, and re-evaluated in 1974, 1977, 1982, 1984, 1986, and 1988. The 2000 JMPR confirmed the ADI of 0–0.005 mg/kg bw based on a NOAEL of 0.5 mg/kg bw per day in a 2-year study of toxicity in rats, that had been established by the 1988 JMPR. Also at the 2000 JMPR, an ARfD of 0.04 mg/kg bw was established based on a NOAEL of 0.36 mg/kg bw per day for inhibition of erythrocyte acetylcholinesterase activity in a study in human volunteers.

The 2004 JMPR noted that some estimations of long-term and short-term intake exceeded the ADI or ARfD that had been established by the 2000 JMPR. The 2004 JMPR concluded that a review of the toxicological database of fenitrothion might enable a refinement of the ADI or ARfD, particularly when concepts such as setting of an overall NOAEL or deriving compound-specific adjustment factors, were taken into account. Owing to the intake concerns identified, the CCPR at its 38th Session in 2006[28] asked JMPR to consider possible refinement of the ADI and ARfD for fenitrothion. Since no relevant new toxicological data had been submitted for evaluation, the data from previous evaluations conducted by the JMPR were reconsidered by the present Meeting.

For technical fenitrothion, specifications have been published as *WHO specification and evaluation for public health pesticides: technical fenitrothion* (1999).[29] Specifications have also been established for other formulations of fenitrothion.

Toxicological evaluation

[28] Codex Alimentarius Commission. *Report of the 38th Session of the Codex Committee on Pesticide Residues, 3–8 April 2006, Fortaleza, Brazil* (ALINORM06/29/24).

[29] Available from: http://www.who.int/whopes/quality/en/Fenitrothion.pdf

The Meeting reviewed the toxicological database for fenitrothion with regard to establishing an overall NOAEL as a basis for the ADI. Inhibition of brain cholinesterase activity was identified as the critical effect after administration of repeated doses to rats. Based on a NOAEL of 0.5 mg/kg bw per day in a 2-year study of toxicity in rats, a NOAEL of 0.6 mg/kg bw per day in a 6-month study of toxicity in rats and a NOAEL of 0.57 mg/kg bw per day in a 3-month study of ocular toxicity in rats, an overall NOAEL of 0.6 mg/kg bw per day was established. The LOAELs for these studies were 1.5, 2.0 and 1.7 mg/kg bw per day, respectively. The NOAEL of 1.3 mg/kg bw per day in a 3-month study of neurotoxicity in rats was considered to be unsuitable as an overall NOAEL, since it was only slightly lower than the lowest LOAEL of 1.5 mg/kg bw per day and was associated with statistically significant inhibition of brain cholinesterase activity by 15%.

The Meeting also reviewed the toxicological database for fenitrothion with regard to deriving a chemical-specific assessment factor (CSAF). The available information was considered to be insufficient for the assessment of toxicokinetic and toxicodynamic differences between rodents and humans. Neither reliable data on concentrations in the general circulation (such as clearance or AUC) nor data on the concentration–effect relationship in target tissues were available for rats. Also, the Meeting considered that the use of a CSAF for human variability was inappropriate. The available data on plasma toxicokinetics were derived from 12 individuals only, which is an adequate sample to define the central tendency, but inadequate to define the potential variability in the human population. With regard to the acute toxicity of fenitrothion, the Meeting concluded that critical effects (inhibition of brain and/or erythrocyte cholinesterase activity) may not be related to the C_{max} but to AUC, on the basis of the slow recovery of the inhibition of cholinesterase activity and the evidence of slow clearance. Consequently, no modification of the standard safety factor for establishing the ARfD was considered to be justified.

The Meeting refined the ADI to 0–0.006 mg/kg bw based on the overall NOAEL of 0.6 mg/kg bw per day for inhibition of brain cholinesterase activity in repeat-dose studies of toxicity in rats and a safety factor of 100. The 4-day study in human volunteers was not considered suitable for establishing an ADI because of its short duration and the associated absence of steady-state kinetics.

The Meeting identified the 4-day study in human volunteers to be the most suitable basis for setting the ARfD. The Meeting confirmed the ARfD of 0.04 mg/kg bw that was established by the 2000 JMPR, based on a NOAEL of 0.36 mg/kg bw for inhibition of erythrocyte cholinesterase activity in humans and a safety factor of 10.

A toxicological monograph was not prepared.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Rat	Six-month study of toxicity[a]	Toxicity (inhibition of brain acetylcholinesterase activity)	10 ppm, equal to 0.6 mg/kg bw per day	30 ppm, equal to 2.0 mg/kg bw per day
	Two-year study of toxicity and carcinogenicity[a]	Toxicity (inhibition of brain acetylcholinesterase activity)	10 ppm, equal to 0.5 mg/kg bw per day	30 ppm, equal to 1.5 mg/kg bw per day
	Thirteen-week study of neurotoxicity[a]	Toxicity (inhibition of brain acetylcholinesterase activity)	20 ppm, equal to 1.3 mg/kg bw per day	60 ppm, equal to 4.0 mg/kg bw per day
	Thirteen-week study of ocular toxicity[a]	Toxicity (inhibition of brain acetylcholinesterase activity)	10 ppm, equal to 0.57 mg/kg bw per day	30 ppm, equal to 1.7 mg/kg bw per day

Human	Four-day study of toxicity[c]	Toxicity (inhibition of erythrocyte acetylcholinesterase activity)	0.36 mg/kg bw per day[b]	—

[a] Dietary administration.

[b] Highest dose tested.

[c] Capsule administration.

Estimate of acceptable daily intake for humans

0–0.006 mg/kg bw

Estimate of acute reference dose

0.04 mg/kg bw

Information that would be useful for the continued evaluation of the compound

Additional toxicokinetic data in rats

Results from epidemiological, occupational health and other such observational studies of human exposures.

RESIDUE AND ANALYTICAL ASPECTS

Fenitrothion was evaluated for residues by the 2003 JMPR in the Periodic Re-evaluation Programme of the CCPR. The 2003 Meeting recommended an MRL of 10 mg/kg for cereals (post-harvest use only) and identified some data gaps. Additional data were provided to the 2004 JMPR, together with results of supervised trials on apples, pears, beans, peas, and soya beans. The 2004 JMPR confirmed the cereal MRL also for pre-harvest uses and recommended MRLs for apple and for animal commodities. Due to an insufficient number of trials corresponding to GAP, MRLs could not be recommended for pears, beans, peas, and soya beans.

The present Meeting received new labels covering uses on soya bean and cereals, a method of analysis, and additional residue trials on soya beans. Dietary intakes calculated by the 2004 JMPR exceeded the ADI and ARfD. As a consequence CCPR has returned the MRL for cereals to Step 6 several times. To resolve the issue the submission of alternative GAP data for cereals was requested.

Methods of analysis

The Meeting received descriptions and validation data for an analytical method for the determination of residues of fenitrothion in soya bean. The analytical method used in the Brazilian trials involves extraction of fenitrothion with ethyl acetate in the presence of sodium sulphate, partitioning by a mixture of cyclohexane and ethyl acetate, and cleaning by gel permeation chromatography. The analyte is determined quantitatively by pulsing flame photometric detection (FPD).

Although the method performed satisfactorily, it was only validated in the range of 0.1–1.0 mg/kg.

Results of supervised trials on crops

Pulses

The Meeting received information on supervised trials on soya beans from Brazil, and considered this information together with Japanese trials previously found to be matching GAP in 2004. In 2004, four trials were found to comply with Japanese GAP (foliar application, 4 times 0.025–0.050 kg ai/hL, PHI 21 days). Residues found were 0.004 (2), < 0.01 (2) mg/kg. The 2004 Meeting decided that four trials (of which two showed finite residues) were not sufficient to estimate a MRL for soya bean, dry.

The present Meeting received six additional soya bean trials from Brazil. The analytical method used in these trials was not validated below 0.1 mg/kg, but the chromatograms showed well-defined peaks below that level. Two of the six trials were decline trials, in which fenitrothion peaks could be observed at day 0 indicating that the use of fenitrothion on soya beans does not result in a nil-residue situation. However, in both of the decline trials (one at GAP rate, one at double rate) no peaks were observed later than 3 days after treatment. One of the trials was according to Brazilian GAP (foliar spray treatment together with esfenvalerate, 2 treatments at 0.1–0.2 kg/hL, interval 7–10 days, PHI 7 days). Residues were < 0.1 mg/kg. At the double rate, residues found were < 0.1 mg/kg. In the remaining four trials residues were only measured 14 days after the final treatment, residues < 0.1 mg/kg.

Based on the Japanese trials (residues in rank order: 0.004 (2), < 0.01 (2)) and using the Brazilian trials to support on the basis that current uses would not lead to detectable residues at harvest, the Meeting estimated a maximum residue level of 0.01 mg/kg, and an STMR of 0.01 mg/kg to replace the previous recommendations for soya bean.

Cereal grains

Five trials on stored wheat were performed in Australia and Argentina and reported by the 2003 JMPR. The Argentinean trials complied with the GAP of Argentina for post-harvest use on cereals: 6 g ai/t with a waiting period of 1 day. The residues found were: 3.1, 3.5, 5.0, 5.6 mg/kg. The Australian trial complied with the GAP of Australia for post-harvest use on wheat: 12 g ai/t with a waiting period of 3 months. The residue found was 7.6 mg/kg. The previous recommendation of the JMPR of 10 mg/kg (Po) was based upon the Australian trial result. In response to a request examine alternative GAP, the Meeting evaluated the available trials against Argentinean GAP.

The Meeting decided to estimate a maximum residue level for cereals based on the post-harvest use at 6 g ai/t. Residues were 3.1, 3.5, 5.0, 5.6 mg/kg. The Meeting decided to withdraw the previous recommendation for cereal grain of 10 mg/kg (Po). Taking into account the results of the dietary risk assessment (see below) the Meeting recommended a new maximum residue level of 6 mg/kg (Po) for cereal grain, excluding maize and estimated an HR of 5.6 mg/kg and a STMR of 4.25 mg/kg.

Fate of residues during processing

In the table below (taken from the 2004 JMPR evaluation), processing factors for wheat, barley and rice commodities are summarized. STMR-P and HR-P values were updated as the cereal grain MRL recommendation had changed.

commodity	Processing factor, range (no. of trials)	Processing factor (mean or best estimate)	STMR-P	HR-P/highest residue
Wheat bran	3.9-4.0 (2)	3.95	16.79	22.12
Wheat flour	0.21-0.26 (2)	0.235	1.00	
White bread	0.089-0.11 (2)	0.10	0.425	
Wholemeal bread	0.33-0.43 (2)	0.38	1.615	
Barley malt	0.16-0.24 (2)	0.20	0.85	
Husked rice	0.031-0.64 (22)	0.64	2.72	
Polished rice	< 0.002-0.15 (26)	0.15	0.638	
Rice hulls	0.12-10 (21)	10	42.5	56
Rice bran	0.018-7.2 (23)	7.2	30.6	40.3
Cooked husked rice	0.11 (1)	0.11	0.468	
Cooked polished rice	0.04 (1)	0.04	0.17	
Washed polished rice	0.041-0.049 (4)	0.046	0.196	
Cooked washed polished rice	0.0060-0.033 (13)	0.020	0.085	

Using the HR for cereal grains (5.6 mg/kg) and the processing factors as indicated above, the Meeting estimated a maximum residue level of 25 mg/kg in wheat bran, and 40 mg/kg in rice bran. The Meeting maintained its decision to withdraw the current recommendations for polished rice,

wheat flour, white bread and wholemeal bread of 1, 2, 1 and 3 mg/kg (PoP) respectively, as the MRLs would be lower than that of the raw agricultural commodity.

Using the HR for cereal grains (5.6 mg/kg) the Meeting estimated HR-P/highest residues for wheat bran, rice hulls, rice bran, as shown in the table above.

Furthermore, using the STMR for cereal grains (4.25 mg/kg) the Meeting estimated STMR-Ps for wheat bran, wheat flour, white bread, wholemeal bread, barley malt, husked rice, polished rice, rice hulls, rice bran, cooked husked rice, cooked polished rice, washed polished rice and cooked washed polished rice, as shown in the table above.

For the purpose of undertaking a dietary risk assessment, the Meeting decided to extrapolate the processing factor for wheat flour to all other cereal flours (except maize flour as processing was considered to be different) and estimated STMR-Ps of 1 for all cereal flours except maize flour. The Meeting extrapolated the processing factor for wheat bran to buckwheat bran estimating an STMR-P of 16.79 for buckwheat bran. Since fenitrothion is used post-harvest, and the residue is a surface residue, the Meeting considered that removal of the hull and further polishing would reduce the residue in a similar way for all cereals. The Meeting therefore decided to extrapolate the processing factor for husked rice to pot barley[30], estimating an STMR-P of 2.72 for pot barley, and the processing factor for polished rice to pearled barley, estimating an STMR-P of 0.638 for pearled barley. Furthermore the processing factor from wholemeal bread was extrapolated to wheat bulgur[31] wholemeal, yielding an STMR-P of 1.615 and the processing factor from white bread was extrapolated to wheat macaroni and wheat pastry, yielding STMR-Ps of 0.425.

The Meeting decided to use the STMR-Ps for cooked husked rice and cooked polished rice in the dietary intake calculations for rice.

Data were only available for the transfer of fenitrothion residues into malt rather than beer (see JMPR 2004 Evaluation). The Meeting received, at a very late stage, two new studies on the processing of barley to malt. However, upon consideration of these studies the Meeting decided to maintain the existing processing factor as the results of the new studies would not have resulted in an amended estimate. As a consequence the Meeting decided not to include the new data and to extrapolate the existing processing factor for malt to barley beer, millet beer, and sorghum beer yielding a STMR-P of 0.85 for barley beer, millet beer, and sorghum beer.

Farm animal dietary burden

The Meeting estimated the dietary burden of fenitrothion in farm animals on the basis of the diets listed in Annex 6 of the 2006 JMPR Report (OECD Feedstuffs Derived from Field Crops). Calculation from highest residue, STMR (some bulk commodities) and STMR-P values provides the levels in feed suitable for estimating MRLs, while calculation from STMR and STMR-P values for feed is suitable for estimating STMR values for animal commodities. The percentage dry matter is taken as 100% when the highest residue levels and STMRs are already expressed as dry weight.

Estimated maximum and mean dietary burdens of farm animals

Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are provided in Annex 6. The calculations were made according to the animal diets from US-Canada, EU and Australia in the OECD Table (Annex 6 of the 2006 JMPR Report).

		Animal dietary burden, fenitrothion, ppm of dry matter diet		
		US-Canada	EU	Australia
Beef cattle	max	14.9	7.0	24.5 [1]
	mean	14.3	6.7	22.2 [2]

[30] Pot barley = hulled or husked barley; pearled barley = hulled barley with the ends of the kernel removed forming a round shape.

[31] Bulgur (wheat) = wheat that has been cooked, dried, and coarsely ground.

Dairy cattle	max	14.0	15.0	22.5
	mean	13.7	14.5	22.2 [3]
Poultry - broiler	max	19.6	11.6	14.4
	mean	19.2	10.6	13.5
Poultry - layer	max	19.6 [4]	9.9	14.1
	mean	19.2 [5]	8.9	13.2

[1] Highest maximum beef or dairy cattle dietary burden suitable for MRL estimates for mammalian meat and milk.

[2] Highest mean beef or dairy cattle dietary burden suitable for STMR estimates for mammalian meat.

[3] Highest mean dairy cattle dietary burden suitable for STMR estimates for milk.

[4] Highest maximum poultry dietary burden suitable for MRL estimates for poultry meat and eggs.

[5] Highest mean poultry dietary burden suitable for STMR estimates for poultry meat and eggs.

Animal commodity maximum residue levels

The calculated maximum dietary burden for dairy and beef cattle is 24 ppm. In the cattle feeding study described in 2004, no residues were found above the LOQ (0.05 mg/kg) in muscle, fat, liver or kidney at feeding levels of 10, 30 and 100 ppm. Therefore, no residues above the LOQ are to be expected at the calculated dietary burden. Residues of fenitrothion in milk were below the LOQ of 0.01 mg/kg for all dose groups.

The calculated dietary burden for poultry is 20 ppm. In the poultry feeding study no residues were detected in muscle, liver, fat and eggs (< 0.05 mg/kg) at feeding levels of 10, 30 and 100 ppm.

The Meeting confirmed its previous recommendation of maximum residue levels of 0.05* mg/kg in meat (from mammals other than marine mammals), in edible offal (mammalian), in poultry meat, and eggs. Further the Meeting recommended a maximum residue level of 0.01 mg/kg in milks. The HRs for muscle, fat, liver, kidney, poultry meat and fat are estimated to be 0 mg/kg, and the STMRs are all estimated to be 0 mg/kg.

DIETARY RISK ASSESSMENT

In previous evaluations (JMPR 2003, 2004) the Meeting identified both long-term and short-term intake exceedances of the ADI and ARfD. The Meeting noted at the time that the intake calculations were conservative, as they did not take into account any reduction in residue obtained by processing of cereal grains, except the processing of wheat, barley and rice. Processing information on maize was identified as necessary allow a refinement of intake calculations. The present Meeting did not receive processing information on maize, as a result intake problems arising for clusters B, C and M (long-term intake) as well as for the short-term intake remain. The Meeting considered that the group MRL for cereal grains would not go forward as processing data on one of the members of that group, with significant consumption, was lacking. The Meeting therefore decided to recommend a maximum residue level for cereal grains, *excluding maize.*

Long term intake

The evaluation of fenitrothion has resulted in recommendations for MRLs and STMRs for raw and processed commodities. Consumption data were available for 37 food commodities and was used in the dietary intake calculation. The results are shown in Annex 3.

The International Estimated Daily Intakes in the 13 GEMS/Food cluster diets, based on the estimated STMRs were in the range 30–80% of the maximum ADI of 0.006 mg/kg bw (Annex 3). The Meeting concluded that the long-term intake of residues of fenitrothion from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The international estimated short-term intake (IESTI) for fenitrothion was calculated for the food commodities (and their processing fractions) for which maximum residue levels, STMRs and HRs were estimated and for which consumption data was available. The results are shown in Annex 4. The IESTI varied from 0–80 % of the ARfD (0.04 mg/kg bw) for the general population. The IESTI varied from 0–110% of the ARfD for children 6 years and below. The intake of 110% was for unprocessed wheat bran. Since this is not the edible commodity and further processing is likely to reduce the level of residues, the Meeting assumed that the intake of fenitrothion from processed wheat bran would be below the ARfD. The Meeting concluded that the short-term intake of residues of fenitrothion from uses considered by the Meeting was unlikely to present a public health concern.

5.13 FENPYROXIMATE (193)

TOXICOLOGY

Evaluation for an acute reference dose

Fenpyroximate is the ISO approved name for the phenoxypyrazole acaricide, *tert*-butyl (*E*)-α-(1,3-dimethyl-5-phenoxypyrazol-4-ylmethylene aminooxy)-*p*-toluate (International Union of Pure and Applied Chemistry, IUPAC), also known as 1,1-dimethylethyl 4-[[[(*E*)-[(1,3-dimethyl-5-phenoxy-1*H*-pyrazol-4-yl)methylene]amino]oxy]methyl] benzoate (CAS; CAS No. 134098-61-6). Fenpyroximate is a contact acaricide with a mode of action involving the inhibition of mitochondrial proton-translocating NADH-quinone oxidoreductase (complex I).[32]

Fenpyroximate was evaluated by the JMPR in 1995, when an ADI of 0–0.01 mg/kg bw was established based on the NOAEL for reduced body-weight gain in a 2-year study in rats. In 2004, the JMPR established an ARfD of 0.01 mg/kg bw based on the LOAEL of 2 mg/kg bw per day for the induction of diarrhoea at the beginning of a 13-week study of toxicity in dogs. It was unclear whether the diarrhoea was the result of a direct irritant or pharmacological effect of fenpyroximate. Since a NOAEL for diarrhoea was not identified, an additional safety factor of 2 was applied to the usual 100 to establish the ARfD. The Meeting concluded that the ARfD was conservative and could be refined if a suitable study became available.

The present Meeting reconsidered the ARfD following submission of a new study of acute toxicity in dogs. The Meeting also reconsidered the existing database on fenpyroximate, as previously evaluated. The submitted study in dogs complied with GLP requirements.

Toxicological data

Previously evaluated study in dogs

In a 13-week study, groups of four male and four female dogs received capsules containing fenpyroximate (purity, 98.4–98.6%) at a dose of 2, 10 or 50 mg/kg bw per day. Controls (four dogs of each sex per group) received the empty gelatin capsules. Dogs were inspected throughout the working day and daily observation of each animal was carried out. A more detailed weekly examination was also carried out. A detailed veterinary examination was carried out before the start of the study and after 4, 8 and 12 weeks of treatment. Ophthalmoscopic examination of the eyes was undertaken after 4, 8 and 12 weeks of treatment. Debilitated animals were carefully observed and those in extremis were killed, blood samples having been taken ante-mortem. Body weight was measured at the start of the study, and then weekly and before death. Food consumption was measured daily. Water consumption was measured during 3 days in week 6. Electrocardiography was performed before the start of treatment and at weeks 6 and 12; at weeks 6 and 12, electrocardiography was performed 2 h

[32]Nakamaru-Ogiso, E., Sakamoto, K., Matsuno-Yagi, A., Miyoshi, H. & Yagi, T. (2003) The ND5 subunit was labelled by a photoaffinity analogue of fenpyroximate in bovine mitochondrial complex I. *Biochemistry*, **42**, 7.

and 24 h after dosing. Before the start of treatment and after 6 and 12 weeks of dosing, blood was taken for haematological investigations and clinical chemistry studies; during the treatment period, samples were taken before dosing. Urine analysis was carried out before the start of the study and after 11 weeks of treatment. Surviving dogs were killed at 12 weeks and a detailed necropsy undertaken. Selected organs were removed and weighed. Samples of selected organs and any macroscopical abnormalities were processed for histopathological examination.

Two females at the highest dose were killed in extremis during the study, because of severe weight loss and loss of appetite. Dogs in all treated groups had diarrhoea, and in the males this appeared to be dose-related and was apparent from week 1 (see Tables 9 and 10).

Table 9. The mean percentage[a] of dogs having diarrhoea after treatment with capsules containing fenpyroximate for 13 weeks

Sex	Dogs with diarrhoea (%)			
	Dose (mg/kg bw per day)			
	0	2	10	50
Males	8.5	22.7	21.2	70.0
Females	5.0	30.8	50.0	48.0

From Broadmeadow (1989)

[a] The percentage of dogs having diarrhoea was recorded each day. The mean percentage of dogs having diarrhoea was calculated by adding the daily percentage for each group and dividing by the number of days on which observations had been carried out.

Table 10. Incidence of diarrhoea in individual dogs before dosing and during week 1 of dosing with fenpyroximate[a]

Dog	Incidence of diarrhoea (days)															
	Dose (mg/kg bw per day)															
	Males								Females							
	0		2		10		50		0		2		10		50	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
1	0	3	0	4	0	4	0	7	0	0	0	5	0	5	0	3
2	0	0	0	2	0	6	0	7	0	0	1	6	0	6	1	7
3	0	0	0	0	1	0	0	2	3	3	0	2	0	0	0	2
4	0	0	0	1	0	1	0	6	0	0	0	0	0	1	0	0

From Broadmeadow (1989)

[a] 'Pre' refers to the number of days during the week before dosing that each beagle had diarrhoea; 'Post' refers to the number of days during the first week of dosing that each beagle had diarrhoea.

Emesis was seen in both sexes at 10 and 50 mg/kg bw per day. Emaciation was seen at 50 mg/kg bw per day (and in one female at 2 mg/kg bw per day). Lethargy (torpor) was seen in some females at 2 and 10 mg/kg bw per day, and in males and females at 50 mg/kg bw per day. Weight loss was seen in week 1, in females receiving fenpyroximate at 10 mg/kg bw per day and in males and females at 50 mg/kg bw per day. Body-weight gain was clearly depressed at 50 mg/kg bw per day in males, and at 50 and 10 mg/kg bw per day in females, compared with that of the controls. Body-weight gain in females was marginally depressed, compared with that of the controls, in the group receiving fenpyroximate at 2 mg/kg bw per day. Food consumption was unaffected by treatment in males, but was reduced by treatment in a dose-related fashion in females.

No treatment-related ocular lesions were noted. Slight bradycardia was seen in all treatment groups in both sexes, but especially in the groups receiving fenpyroximate at 10 and 50 mg/kg bw per day. There was no consistent difference between the measurements made 2 h after dosing and 24 h after dosing, and the bradycardia was not consistently present at 2 mg/kg bw per day. In males at all doses and in females at 2 and 10 mg/kg bw per day, no differences in haematological parameters were seen, compared with those of the concurrent controls. In females at 50 mg/kg bw per day, low total leukocyte counts at 6 weeks and 12 weeks, prolonged activated partial thromboplastin times at 6 weeks and high platelet counts at 12 weeks were recorded relative to these values for the concurrent controls. The two decedents (both females at 50 mg/kg bw per day) had low leukocyte counts. Raised concentrations of blood urea nitrogen were seen in females at 50 mg/kg bw per day at week 6, and at 2 and 50 mg/kg bw per day at week 12; it is unclear whether these effects were treatment-related as there was no clear dose–response relationship. Low concentrations of glucose were seen in males at 10 mg/kg bw per day and in both sexes at 50 mg/kg bw per day at weeks 6 and 12. The two decedents (both females at 50 mg/kg bw per day) had high blood urea concentrations and low plasma butyrylcholinesterase activities, and one of them had a low concentration of blood glucose. No inter-group differences were seen in the results of urine analysis.

Slightly higher absolute and relative weights of the adrenals were observed in males at 50 mg/kg bw per day and slightly higher relative weights of the adrenals in females at that dose. Relative weights of the liver were increased in both sexes at 50 mg/kg bw per day. Macroscopic examination post mortem showed emaciation in one surviving female at 50 mg/kg bw per day. The decedents showed emaciation. There was depleted hepatic glycogen and fine renal medullary cytoplasmic vacuolation in the two decedent females at the highest dose, as well as in one surviving female at 50 mg/kg bw per day. The lowest-observed-adverse-effect level (LOAEL) for the study was 2 mg/kg bw per day on the basis of clinical signs at that dose (diarrhoea in both sexes, and lethargy in females) and reduced body-weight gain in females. This LOAEL was probably close to the NOAEL.[33, 34]

Study evaluated for the first time by the present Meeting

In a study designed to establish the maximum tolerated dose and a NOAEL for acute toxicity, two male and two female beagle dogs (age 34–37 weeks) were given fenpyroximate (purity, 99.8%) at a concentration of 5 ml/kg (suspended in 0.5% w/v methylcellulose) by gavage. In the first phase of the study, the four dogs were given a single dose at 2 mg/kg bw on day 1, followed by 5 mg/kg bw on day 8, and finally 20 mg/kg bw on day 15. In the second phase, the same four dogs were dosed on day 23 at 5 mg/kg bw per day for five consecutive days.

Food consumption was measured daily and the body weight was measured before the day of dosing during the incremental dosing phase and then twice per week for the repeat-dosing phase until necropsy. Clinical monitoring, with an emphasis on neurobehavioural effects, was performed daily. Haematology parameters (erythrocyte volume fraction, haemoglobin, mean cell haemoglobin concentration (MCHC), mean corpuscular volume, erythrocyte count, leukocyte differential count, reticulocyte count, platelet count and prothrombin time) were determined before treatment (day–5) and again on the morning following each incremental change in dose before feeding, and at the end of the fixed-dose phase.

Clinical chemistry was carried out to measure blood glucose, blood urea nitrogen, total serum protein, bilirubin, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, sodium, potassium, chloride, calcium, phosphorus, cholesterol, creatinine, albumin, gamma globulins and the

[33] Broadmeadow, A. (1989) NNI-850: toxicity study by oral (capsule) administration to CD beagle dogs for 13 weeks. Unpublished report No. 89/NNH036/1111 (amended from 89/NNH036/614) from Life Sciences Research, Eye, Suffolk, England. Submitted to WHO by Nihon Nohyaki Co. Ltd, Tokyo, Japan. GLP: USA, USEPA (40 CFR 160); UK DHSS; OECD (1981); MAFF, Japan. Guidelines: USEPA/FIFRA, 1982; MAFF Japan, 1985.

[34] Annex 5, reference *101*.

albumin : globulin ratio. Surviving dogs were killed on day 28 and a detailed necropsy was undertaken. Selected organs were removed and weighed. Samples of selected organs and any macroscopic abnormalities were processed for histopathological examination.

There were no treatment-related deaths or changes in body weight at any dose. The only clinical sign observed was soft or liquid faeces in all dogs at 20 mg/kg bw. The diarrhoea started 2–3.5 h after dosing and lasted for up to 6 h. Surprisingly, two out of four dogs (one male, one female) who received fenpyroximate at a dose of 5 mg/kg bw in the second phase of the test on day 23 had diarrhoea 3 h after dosing, but no dogs exposed to the same dose on day 8 had any clinical signs. All four dogs had clinical signs at about 3–6 h after the second consecutive dose at 5 mg/kg bw on day 24. The investigators suggested that this may have been due to pre-exposure to fenpyroximate at a high dose (20 mg/kg bw) 8 days earlier. Although blood had been collected 1, 3, 6 and 24 h after dosing at 5 mg/kg bw (fixed-dose phase) for toxicokinetic purposes, it was not possible to test this assertion owing to the absence of any blood collection before dosing.

The haematological and clinical chemistry analyses revealed values that were well within the range for historical controls. Necropsy revealed no apparent effects on organ weights, but macroscopically there were lesions observed in the gastrointestinal tract of three dogs (two males, one female). In two of the dogs, the mucosa of the ileo-caecal junction was red and dark. In the third dog, the mucosa of the stomach fundus was reported to be pale. The NOAEL was 2 mg/kg bw on the basis of clinical signs (diarrhoea in both sexes) at the next higher dose of 5 mg/kg bw.[35]

Toxicological evaluation

An examination of the existing toxicological database indicated that the toxic effects of fenpyroximate are diarrhoea, reduced body-weight gain and haematological and clinical chemistry changes. The most sensitive end-point, namely diarrhoea, was observed in all studies in dogs, but not in other species. In a 13-week study in dogs given capsules containing fenpyroximate, diarrhoea with reduced body-weight gain and food consumption was observed. A NOAEL was not identified in the 13-week study and the LOAEL was 2 mg/kg bw per day on the basis of diarrhoea occurring at all doses. In that study it was unclear whether the diarrhoea occurred after a single dose, since only the incidence per week was reported. In a follow-up study of acute toxicity, diarrhoea was again observed in some dogs at 5 mg/kg bw, but not at 2 mg/kg bw.

After considering previous evaluations of fenpyroximate and the new submitted study, the Meeting established an ARfD of 0.02 mg/kg bw based on the NOAEL of 2 mg/kg bw identified on the basis of induction of diarrhoea after a single dose in dogs and using a safety factor of 100. Since it remained unclear whether the diarrhoea observed in dogs was the result of a direct irritant or pharmacological effect of fenpyroximate, it was not possible to consider a modification in the safety factor.

A toxicological monograph was not prepared.

[35] Harvey, P.W. (2006) Fenpyroximate: tolerated dose and 5-day repeat dose study by bolus oral gavage dosing in the dog to assist in setting the acute reference dose. Unpublished report No. 0608-073 from Covance Laboratories Ltd, North Yorkshire, England. Submitted to WHO by Nihon Nohyaki Co. Ltd, Osaka, Japan. GLP: UK DHSS; OECD (1981).

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Dog	Acute toxicity[a]	Diarrhoea	2 mg/kg bw	5 mg/kg bw
	Three-month studies of toxicity[b]	Clinical signs and reduced body-weight gain in females	—	2 mg/kg bw per day

[a] Gavage administration [b] Capsule administration.

Estimate of acute reference dose

0.02 mg/kg bw

Information that would be useful for the continued evaluation of the compound

Results from epidemiological, occupational health and other such observational studies of human exposure.

5.14 FLUSILAZOLE (165)

TOXICOLOGY

Flusilazole is the ISO approved name for 1-[[bis(4-fluorophenyl)methyl]silyl]methyl]-1*H*-1,2,4-triazole (CAS No. 85509-19-9). It is a broad-spectrum fungicide that belongs to the triazole subclass of ergosterol biosynthesis inhibitors. Flusilazole was previously evaluated by the Joint Meeting in 1989 (Annex 5, references *56*, *58*) and in 1995. An ADI of 0–0.001 mg/kg bw was allocated in 1989, based on a NOAEL of 0.14 mg/kg bw per day (5 ppm) for liver toxicity in a 1-year feeding study in dogs. This was confirmed in 1995. The compound was re-examined by the present Meeting as part of the Periodic Re-evaluation Programme of CCPR. Three new studies were provided, two studies of developmental toxicity in rats (one of oral and one of dermal administration) and a 28-day mechanistic study in dogs.

Owing to the age of the database, some studies predate GLP; however, all critical studies complied with GLP.

Biochemical aspects

In rats, orally administered [^{14}C] labelled flusilazole was readily absorbed from the gastrointestinal tract and rapidly excreted in urine (72% of triazole label) and faeces (up to 87% of phenyl label), with little or no radioactivity recovered in the expired air. The excretion half-life was approximately 34 h and > 90% of the administered dose was eliminated within 96 h. Tissue retention of radiolabelled material was low. Total tissue residues excluding the carcass (which accounted for approximately 2% of the administered dose) was < 1%, therefore demonstrating no evidence of bioaccumulation.

[^{14}C]Flusilazole was extensively metabolized in rats. Recovered parent compound accounted for only 2–11% of the given dose, found predominantly in the faeces (urinary concentration, < 1%). After absorption, flusilazole was cleaved at the triazole ring. With phenyl-labelled test material, the major faecal metabolites identified were [bis(4-fluorophenyl)methyl] silanol, [bis(4-fluoro - phenyl)methylsilyl] methanol and its fatty acid conjugates, and disiloxane. Except for the fatty acid conjugates, the same metabolites were found in the urine. With triazole-labelled material, the main metabolite identified was 1*H*-1,2,4-triazole, which was found predominantly in the urine (63.8% of the administered dose in males, 51.6% in females); faeces contained only a small amount of the metabolite.

Toxicological data

Flusilazole is moderately to slightly toxic in rats when given as a single oral dose; and minimally toxic to rats and rabbits when administered as a single dose dermally or by inhalation. The oral LD_{50} in rats was 672–1216 mg/kg bw, the dermal LD_{50} in rabbits was > 2000 mg/kg bw and the inhalation LC_{50} in rats was 6.8–7.7 mg/L. Flusilazole was found to be minimally irritating to the eyes and the skin of New Zealand White rabbits. It was practically non-irritating to the skin and was not a dermal sensitizer in guinea-pigs in a Buehler test.

Short- and long-term studies of repeated oral doses of flusilazole in mice (90-day dietary study), rats (90-day studies of gavage and dietary administration) and dogs (90-day and 1-year dietary studies) resulted primarily in lesions of the liver (hepatocellular hypertrophy, fatty change, focal inflammation/necrosis (mouse only) and vacuolation) and urinary bladder (urothelial hyperplasia and vacuolation). In addition, the gastrointestinal tract was a target in dogs. Clinical chemistry was not assessed in the studies in mice, the only finding in the studies in rats was a decrease in cholesterol in both sexes in the 90-day study and increase in cholesterol in females only in the long-term studies. On the basis of the hepatic and/or urinary bladder histopathology, the NOAEL was 75 ppm (equal to 12 mg/kg bw per day) in mice, 125 ppm (equal to 9 mg/kg bw per day) in rats and 20 ppm (equal to 0.7 mg/kg bw per day) in dogs (1-year study). Lymphoid hyperplasia of the gastric mucosa was observed in all treated dogs in the 90-day study, but not in the controls. In the 1-year study, this finding was observed in all dogs, including controls, with severity increasing in a dose-related manner. Effects at the LOAEL in the 1-year study in dogs included hepatocellular hypertrophy, inflammatory infiltration and vacuolation (males only), decreased cholesterol, total protein and albumin, and increased alkaline phosphatase activity and leukocyte counts. A mechanistic study in male dogs at the doses used in the 1-year study indicated that after 28 days of exposure, the effects observed on the liver were adaptive and reversible (weight, increased aspartate aminotransferase activity and cytochrome P450). The dog appeared to be the most sensitive species in these studies, with a NOAEL of 0.7 mg/kg bw per day in the 1-year study, on the basis of histopathology changes in the liver and stomach and changes in clinical chemistry.

After repeated short-term (21-day) dermal application of flusilazole, there was no evidence of any treatment-related systemic toxicity in rabbits given doses of up to 200 mg/kg bw per day.

Flusilazole was tested for genotoxicity in an adequate range of assays in vitro and in vivo. It was not genotoxic in mammalian or microbial systems. The Meeting concluded that flusilazole was unlikely to be genotoxic.

Two 18-month dietary studies with flusilazole were conducted in mice. In the first study in which flusilazole was administered at concentrations of up to 200 ppm in the diet, the target organs identified were the liver (hepatocellular fatty changes), kidney (decreased weight), and urinary bladder (histopathological change). There was no evidence of carcinogenicity in this study. Concentrations from 100 to 2000 ppm were used in the second 18-month study. Systemic toxicity was observed at all doses. At doses of 500 and 1000 ppm in males (73.1 and 144 mg/kg bw per day, respectively) or 1000 and 2000 ppm in females (200 and 384 mg/kg bw per day, respectively), overt hepatic lesions (increased foci of hepatocellular alteration and hepatocellular hypertrophy with cytoplasmic vesiculation and/or vacuolation) and cellular hyperplasia in the urinary bladder were observed. Increased incidences of liver tumours (hepatocellular adenomas and carcinomas) were observed at concentrations of more than 1000 ppm. Liver tumours occurred at doses in excess of the maximum tolerated dose (MTD) and were preceded at lower concentrations by clear histopathological changes in the liver. The overall NOAEL for systemic toxicity was 25 ppm, equal to 3.4 mg/kg bw per day, on the basis of hepatotoxicity and urinary bladder hyperplasia at 100 ppm (14.3 mg/kg bw per day) in males and hepatocellular fatty changes at 200 ppm (27 mg/kg bw per day) in both sexes. The overall NOAEL for carcinogenicity was 200 ppm (equal to 36 mg/kg bw per day) in females and 1000 ppm (equal to 144 mg/kg bw per day) for males. The incidence of tumours at the NOAEL was within the range for historical controls.

The toxicity and carcinogenicity of flusilazole were investigated in two 2-year studies in rats. The target organs identified were the liver and bladder. The overall NOAEL for systemic toxicity was 50 ppm, equal to 2.0 mg/kg bw per day, on the basis of mild nephrotoxicity (pyelonephritis in females) and hepatotoxicity (hepatocellular hypertrophy in both sexes), acidophilic foci, and diffuse fatty change (females only). There was no treatment-related increase in the incidence of any tumour type AT up to 250 ppm (the highest dose tested in the first study). Concentrations of between 125 and 750 ppm, the latter exceeding the MTD, were used in the second study. Flusilazole was found to be tumorigenic at the highest dose of 750 ppm (30.8 mg/kg bw per day) causing bladder transitional cell neoplasia in both sexes and testicular Leydig cell tumours in males. There was no evidence of any treatment-related increase in tumour incidence at a dietary concentration of 375 ppm. The overall NOAEL for carcinogenicity was 375 ppm (14.8 mg/kg bw per day)

A special 2-week study to investigate the possible mechanism for the induction of testicular Leydig cell tumours was conducted in rats. The results demonstrated that flusilazole caused a dose-dependent lowering of estradiol concentrations at 20 mg/kg bw per day and above, and of serum and interstitial testosterone concentrations at 150 mg/kg bw per day in vivo after subcutaneous exposure (n=10) and a dose-related decrease in testosterone and androstenedione production in testicular Leydig cell cultures by inhibition of enzymes involved in steroid biosynthesis in vitro at less than 5 μmol/l. In the 90-day mechanistic study in rats given flusilazole at doses similar to those used in the second long-term study in rats (0, 10, 125, 375 or 750 ppm), there were no changes in serum concentrations of testosterone, estradiol or LH, which would be expected for this mode of action. However, there was appreciable inter-animal variability in the hormone measurements. Overall, the data suggested that flusilazole may induce Leydig cell tumours via an endocrine-related mechanism—inhibition of testosterone and estradiol biosynthesis could contribute to disruption of the hypothalamus–pituitary–testis axis, resulting in over stimulation of the testicular endocrine tissues. Exposure to flusilazole at doses not causing disruption of the hypothalamus–pituitary–testis axis would, therefore, be unlikely to induce an increase in Leydig cell tumours. Although this mode of action is relevant to humans, there was good evidence to suggest that humans are less sensitive to chemically-induced Leydig cell tumours than are rats, owing to differences in sensitivity to LH on the basis of number of Leydig-cell receptors and control of LH-receptor expression (e.g., by prolactin in rodents but not in humans).

The Meeting concluded that the weight of evidence indicated that the mode of action for bladder tumours was via cell injury and regenerative hyperplasia.

In view of the lack of genotoxicity and the finding of hepatocellular tumours in mice and testicular and bladder transitional cell tumours in rats only at doses at which marked toxicity was observed, the Meeting concluded that flusilazole is not likely to pose a carcinogenic risk to humans at dietary levels of exposure.

The effect of flusilazole on reproduction in rats was investigated in two two-generation studies. The first was a part of a 2-year feeding study. No parental toxicity was observed at doses of up to 250 ppm. The same doses were used in the second definitive two-generation study. The NOAEL for parental systemic toxicity was 50 ppm, equal to 4.04 mg/kg bw per day, on the basis of slightly lower body-weight gain in F_1 females. The main reproductive effects at 250 ppm included increased duration of gestation and increased maternal mortality during parturition. The NOAEL for reproductive toxicity was 50 ppm, equal to 3.46 mg/kg bw per day. Toxicity observed in offspring at 250 ppm included a reduced number of live pups per litter and decreased pup growth. The NOAEL for offspring toxicity was 50 ppm, equal to 4.04 mg/kg bw per day.

Nine studies of developmental toxicity were carried out with flusilazole administered orally, of which five were in rats (one dietary study and four with gavage administration) and four (one dietary study and three with gavage administration) in rabbits to characterize potential teratogenicity observed in some studies.

In most of the studies in rats, the NOAEL for maternal toxicity was 10 mg/kg bw per day on the basis of reduced body-weight gain and decreased food consumption. In one study, the NOAEL for maternal toxicity was 2 mg/kg bw per day on the basis of increased incidence of red vaginal discharge

during the latter part of gestation and an increase in placental weights at 10 mg/kg bw per day, which was not assessed in the other studies. At maternally toxic doses, specific malformations noted were cleft palate, nares atresia and absent renal papillae. An increased incidence of anomalies (extra cervical ribs, patent ductus arteriosis) was also observed. The incidence of rudimentary cervical ribs was slightly, but not statistically significantly increased at 2 mg/kg bw per day (3 out of 3, 4 out of 4, 9 out of 6, 27 out of 15, and 141 out of 22 foetuses per litter in the groups at 0, 0.5, 2, 10, 50 mg/kg bw per day, respectively). The overall NOAEL for embryo/fetotoxicity was 2 mg/kg on the basis of a higher incidence of skeletal variations (extra cervical ribs) at 10 mg/kg bw per day. No malformations were found at doses of less than 50 mg/kg bw per day.

In four studies of developmental toxicity in rabbits, the NOAEL for maternal and embryo/foetal toxicity was 7 mg/kg bw per day on the basis of clinical signs of toxicity, increased incidence of abortion and total resorption at 15 mg/kg bw per day. There was no evidence for any teratogenic potential in rabbits given flusilazole at doses of up to 15 mg/kg bw per day, the maximum tolerated dose in this study.

A major metabolite identified was 1*H*-1,2,4-triazole, which was found predominantly in the urine (63.8% of the administered dose in males, 51.6% in females). Studies with this metabolite are summarized in the evaluation of difenoconazole in the present report.

No neurotoxic effects were seen during conventional repeat-dose studies with flusilazole.

There were no reports of adverse health effects in manufacturing plant personnel or in operators and workers exposed to flusilazole formulations during their use. Also, there was no evidence or data to support any findings in relation to poisoning with flusilazole.

The Meeting concluded that the existing database on flusilazole was adequate to characterize the potential hazards to foetuses, infants and children.

Toxicological evaluation

The Meeting established an ADI of 0–0.007 mg/kg bw based on the NOAEL of 0.7 mg/kg bw per day for lymphoid hyperplasia in the gastric mucosa, liver histopathology (hypertrophy, inflammatory infiltration in males and females, and vacuolation in males only), and clinical chemistry (decreased concentrations of cholesterol, total protein and albumin and increased alkaline phosphatase activity and leukocyte counts) in the 1-year dietary study in dogs and a safety factor of 100.

The Meeting established an ARfD of 0.02 mg/kg bw based on the NOAEL of 2 mg/kg bw per day for skeletal anomalies in the study of developmental toxicity in rats treated orally and a safety factor of 100.

A toxicological monograph was prepared.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Mouse	Two-year studies of toxicity and carcinogenicity [a]	Toxicity	25 ppm, equal to 3.4 mg/kg bw per day	200 ppm, equal to 27 mg/kg bw per day
		Carcinogenicity[d]	200 ppm equal to 36 mg/kg bw per day (females)	1000 ppm equal to 384 mg/kg bw per day
Rat	Two-year studies of toxicity and carcinogenicity [a,c]	Toxicity	50 ppm, equal to 2 mg/kg bw per day	250 ppm, equal to 10 mg/kg bw per day
		Carcinogenicity	375 ppm, equal to 14.8 mg/kg bw per day	750 ppm, equal to 30.8 mg/kg bw per day

Species	Study	Effect	NOAEL	LOAEL
	Multigeneration reproductive toxicity[a,c]	Parental toxicity	50 ppm, equal to 4.04 mg/kg bw per day	250 ppm, equal to 19.6 mg/kg bw per day
		Offspring toxicity	50 ppm, equal to 4.04 mg/kg bw per day	250 ppm, equal to 19.6 mg/kg bw per day
		Reproduction	50 ppm, equal to 4.04 mg/kg bw per day	250 ppm, equal to 19.6 mg/kg bw per day
	Developmental toxicity [a,b,c]	Maternal toxicity	2 mg/kg bw per day	10 mg/kg bw per day
		Embryo/fetotoxicity	2 mg/kg bw per day	10 mg/kg bw per day
Rabbit	Developmental toxicity[a,b,c]	Maternal toxicity	7 mg/kg bw per day	15 mg/kg bw per day
		Embryo/fetotoxicity	7 mg/kg bw per day	15 mg/kg bw per day
Dog	One-year study of toxicity [a]	Toxicity	20 ppm, equal to 0.7 mg/kg bw per day	75 ppm, equal to 2.4 mg/kg bw per day

[a] Dietary administration.
[b] Gavage administration.
[c] Two or more studies combined.
[d] Greater than the maximum tolerated dose (MTD).

Estimate of acceptable daily intake for humans

0–0.007 mg/kg bw

Estimate of acute reference dose

0.02 mg/kg bw

Information that would be useful for the continued evaluation of the compound

Results from epidemiological, occupational health and other such observational studies of human exposures.

Critical end-points for setting guidance values for exposure to flusilazole

Absorption, distribution, excretion and metabolism in mammals	
Rate and extent of oral absorption	Rapid and extensive (up to 80%)
Dermal absorption	Data not available
Distribution	Widely
Potential for accumulation	Low
Rate and extent of excretion	Rapidly excreted
Metabolism in animals	Extensively metabolized
Toxicologically significant compounds in animals, plants and the environment	Parent compound,1,2,4-triazole
Acute toxicity	
Rat, LD_{50}, oral	674 mg/kg bw
Rat, LD_{50}, dermal	> 2000 mg/kg bw
Rat, LC_{50}, inhalation	2.7–3.7 mg/L, 4 h

Guinea-pig, skin sensitization (test method used)	Non-sensitizing (Buehler)
Short-term studies of toxicity	
Target/critical effect	Liver and urinary bladder
Lowest relevant oral NOAEL	0.7 mg/kg bw per day (1-year study in dogs)
Lowest relevant dermal NOAEL	5 mg/kg bw per day (21-day study in rabbits)
Lowest relevant inhalation NOAEC	No data presented
Genotoxicity	
	Not genotoxic
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	Liver and bladder
Lowest relevant NOAEL	2.0 mg/kg bw per day (2-year study in rats)
Carcinogenicity	No carcinogenic concern at levels of dietary exposure
Reproductive toxicity	
Reproduction target/critical effect	Increased gestation length, reduced live born pups/litter and decreased pup growth
Lowest relevant reproductive NOAEL	50 ppm (4.04 mg/kg bw per day)
Developmental target/critical effect	Skeletal anomalies, malformations at higher doses
Lowest relevant developmental NOAEL	2 mg/kg bw per day (rats)
Neurotoxicity/delayed neurotoxicity	
	No indications of neurotoxicity in studies of acute toxicity or repeated doses
Other toxicological studies	Disruption of the hypothalamus–pituitary–testis axis
Mechanistic studies	Necrosis and hyperplasia in the rat bladder
Medical data	
	No occupational or accidental poisoning reported

Summary

	Value	Study	Safety factor
ADI	0–0.007 mg/kg bw	Dog, 1-year study	100
ARfD	0.02 mg/kg bw	Rat, study of developmental toxicity	100

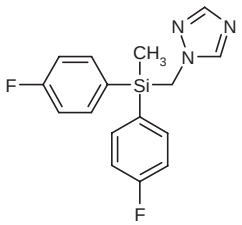
RESIDUE AND ANALYTICAL ASPECTS

Flusilazole is a fungicide belonging to the ergosterol biosynthesis inhibitor class. It was evaluated by the JMPR for residues in 1989, 1990, 1991 and 1993. Toxicology was reviewed in 1989 and 1995, establishing an ADI of 0–0.001 mg/kg bw in 1989 (confirmed in 1995). Flusilazole was listed for the Periodic Re-Evaluation Programme at the 38th Session of the CCPR for periodic review by the 2007 JMPR for toxicology and residues.

Chemical name:

Flusilazole
Bis(4-fluorophenyl)(methyl)(1H-1,2,4-triazol-l-ylmethyl)silane (IUPAC)

1-[[Bis(4-fluorophenyl)methyl)silyl]methyl]-1*H*-1,2,4-triazole (CA)



Animal metabolism

The Meeting received results of animal metabolism studies in rats, lactating goats, and laying hens.

Flusilazole is extensively metabolized in rats. Eight metabolites were identified. In addition to unchanged flusilazole, the major metabolites identified in urine and faecal samples were [bis(4-fluorophenyl)methyl]silanol (IN-F7321); [bis(4-fluorophenyl)methylsilyl]methanol (IN-H7169) and its glucuronide; 1H-1,2,4-triazole (IN-H9933); and 1,3-dimethyl-1,1,3,3-tetrakis(4-fluorophenyl)disiloxane (IN-G7072). Cleavage and rapid excretion of IN-H9933 (1H-1,2,4 triazole) was the primary step in the metabolism of flusilazole in rats. The silane molecule may then be excreted or further metabolized to fatty acid metabolites, β-D-gluco-pyranuronic acid conjugate and further degrade to more polar molecules.

Two lactating goats received daily doses of [^{14}C] labelled flusilazole orally by gelatine capsule at a level equivalent to 50 ppm in their diet. One lactating goat was dosed daily for 6 consecutive days (phenyl label) and one goat was dosed for 5 consecutive days (triazole label) with 50 mg of [^{14}C]-labelled flusilazole. For the goat dosed with phenyl-labelled flusilazole, muscle contained 0.05–0.07% of the total dose (0.41–0.70 mg/kg flusilazole equivalents); liver accounted for 5.3% (13.5 mg/kg); kidney had 1.2% of the dose (8.7 mg/kg); and fat contained 0.15–0.50% of the total administered dose (4.07–5.15 mg/kg). For the goat dosed with triazole-labelled flusilazole, muscle contained 0.10–0.15% of the total dose (0.52–0.53 mg/kg parent equivalents); liver accounted for 1.5% (3.5 mg/kg); kidney had 0.05% of the dose (0.75 mg/kg); and fat contained 0.01–0.07% of the total administered dose (0.15–0.94 mg/kg).

The transfer of radioactive residues to milk and tissues was low. Only 0.34 and 1.3% of the dose was present in milk for the phenyl and triazole labels, respectively. After 6 and 5 consecutive days of dosing, concentrations of total residues in milk were only 0.74 and 0.63 mg/kg (flusilazole equivalents) for the phenyl- and triazole-dosed goats, respectively. Residue levels in milk reached a plateau 2–5 days after the initial dose.

Percentages of extractable radioactivity varied from 89 to > 99% of the total radioactivity in the tissues for the goat dosed with phenyl-labelled flusilazole, and 90 to 94% for the goat dosed with triazole-labelled flusilazole. Flusilazole was extensively metabolized. Cleavage between the triazole and the silicon moieties was the predominant early metabolic transformation, followed by glucuronidation of one of the products. Except in the liver, unchanged flusilazole accounted for less than 10% of the tissue radioactivity. IN-F7321 (silanol) and IN-H9933 (1H-1,2,4-triazole) were the major metabolites found in tissues of goats dosed with phenyl- and triazole-labelled flusilazole, respectively.

In milk, unchanged flusilazole varied between 13–30% of TRR for the goat dosed with phenyl-labelled flusilazole, and < 1–13% for the goat dosed with triazole-labelled flusilazole. In the latter, metabolite IN-H9933 (1H-1,2,4-triazole) accounted for 87 to > 99% of the TRR in milk, which represented 0.16–0.30% of the administered dose. Metabolites IN-F7321 (silanol) and IN-G7072 (disiloxane) together accounted for 34 to 63% of the TRR in milk from the goat dosed with phenyl-labelled flusilazole. Polar material accounted for 7 to 28% of the radiolabel present in the milk of the goat dosed with phenyl-labelled flusilazole.

Laying hens were administered flusilazole ([^{14}C]-labelled at either the phenyl group or at the triazole group) at 0.36 or 18 mg/day, equivalent to 3 and 150 ppm in the diet. Hens from the low dose group were dosed for 14 days while those from the exaggerated dose group were dosed for 5 days (the higher dose served for metabolite isolation and identification only). Eggs and excreta were collected over the experimental period; edible tissues and blood were taken for analysis at sacrifice (approximately 6 h after the last dose).

Approximately 80% of the total radioactivity (both labels) was eliminated in the excreta. Elimination of radioactivity in the excreta became steady after 48 h. Residues in edible tissues were low, less than 1% of administered dose; thus bioaccumulation potential for flusilazole residues is low.

In hens receiving phenyl-labelled flusilazole at 0.36 mg/day dose level, highest residues were found in the liver (0.60 mg/kg flusilazole equivalents), followed by fat (0.52 mg/kg) and kidney (0.32 mg/kg). Residue levels in the muscle were the lowest. Residue levels in the hens dosed with triazole-labelled flusilazole were highest and essentially equal in whole blood (0.39 mg/kg), liver (0.38 mg/kg), kidney (0.38 mg/kg), and breast muscle (0.35 mg/kg) and much lower in fat (0.07 mg/kg). In eggs from hens dosed at 3 ppm for 14 days, radioactivity reached a steady state after about 8 days with a plateau residue level of approximately 0.2 mg flusilazole equivalents/kg (both labels).

[(4-Fluorophenyl)methyl]silanediol (IN-V5771) was the main metabolite in liver, kidney and muscle of hens dosed with phenyl-labelled flusilazole (33, 29 and 73–88% of the TRR, respectively). IN-F7321 (silanol) was the main residue in the fat (82% of the TRR) and a major one in the liver (17% of the TRR). Residues identified in the hens dosed with triazole-labelled flusilazole were IN-H9933 (1H-1,2,4-triazole), thymine and flusilazole, with IN-H9933 being the major metabolite in all tissues (76, 79 and 75–83% of the TRR in liver, kidney and muscle, respectively). 1H-1,2,4-triazole residues ranged from 0.057 mg triazole/kg in liver to non-detectable levels in fat. Flusilazole levels ranged from 0.018 mg/kg in kidney to 0.049 mg/kg in fat. No flusilazole was detected in muscle.

In eggs, the two major metabolites from the phenyl label dosed hens were IN-F7321 (silanol) and IN-V5771 (silanediol), at 32 and 38% of the TRR, respectively at 12 days. The major metabolite in eggs from the triazole label dosed hens was 1H-1,2,4-triazole (IN-H9933), with much smaller amounts of thymine and unchanged flusilazole. At 12 days, triazole, thymine and flusilazole residues were 0.197, 0.023 and 0.006 mg flusilazole equivalents/kg, respectively (77, 9 and 2% of the TRR, respectively). When calculated on a molar equivalent basis, the triazole and thymine residues were 0.043 and 0.009 mg/kg in the 12 day egg samples.

The residues found in goats and hens indicated a similar metabolic pathway to the rat. Generally, unchanged flusilazole was present at levels lower than the metabolites. In goat liver and chicken fat of animals dosed with triazole-labelled flusilazole, flusilazole levels were higher than levels of the metabolite 1,2,4-triazole, (IN-H9933) perhaps due to the polar nature of the triazole. Except in goat liver and chicken fat, 1,2,4-triazole was the major metabolite arising from triazole-labelled flusilazole. The silanol metabolite (IN-F7321) was also common to both goats and hens. The main difference between the goat study and the hen studies was the occurrence of the silanediol (IN-V5771) as a major metabolite in hens. Other phenyl-labelled metabolites, resulting from hydroxylation and conjugation reactions, were present at relatively low levels in chicken tissues and eggs.

Based on the results of the submitted studies, the Meeting concluded that, in rats, goats, and hens, flusilazole was rapidly and extensively converted to polar metabolites.

Plant metabolism

The Meeting received plant metabolism studies for flusilazole in wheat, sugar beet, apples, grapes, bananas and peanuts. The wheat, bananas and sugar beet were greenhouse grown. The grapes, apples and peanuts were grown in the field.

Wheat was treated with [phenyl(U)-^{14}C]flusilazole and [triazole-3-^{14}C]flusilazole at 200 g ai/ha. In forage, labelled residues (expressed as flusilazole) fell from initial values of 32 and

8.6 mg/kg for phenyl and triazole labels, respectively, to approximately 6 mg/kg by days 5 to 12. Flusilazole accounted for 56–59% of the residue in forage for days 5–12. Residues in straw were 8.6 and 7.9 mg/kg for phenyl and triazole labels, respectively. Unchanged flusilazole accounted for only about 14% of the residue in mature straw, and there was extensive metabolism to at least seven phenyl-labelled and six triazole-labelled metabolites. No single straw or forage metabolite accounted for more than 13.5% of the total radioactivity present. Unidentified minor metabolites were present in triazole and phenyl [^{14}C]flusilazole treated wheat straw; however, no unidentified metabolites exceeded 4% of the total radioactive residue.

There were negligible radioactive residues (0.01 mg/kg) in the grain from phenyl-labelled wheat. In the triazole-labelled wheat, grain residues of 4.4 mg/kg flusilazole equivalents (at 52 days after the treatment) were comprised of triazolyl alanine (IN-V9462) and triazole acetic acid (IN-D8722). No flusilazole was found in triazole-labelled grain samples harvested 69 days after the treatment. This data indicates that although metabolites containing the triazole ring can be translocated, intact flusilazole is not translocated to grain.

The metabolic pathway of flusilazole in wheat included hydroxylations, conjugations, and cleavage of the silicon-methylene bond. The major phenyl-labelled metabolites in straw and forage were glucose-6-phosphate of IN-37722 (2-fluoro-5-[(4-fluorophenyl) (methyl) (1H-1,2,4-triazol-1-ylmethyl)silyl]phenol); mono[6-deoxy-2-0-[2-fluoro-5-[(4-fluorophenyl) (methyl) (1H-1,2,4-triazol-1-ylmethyl) silyl] phenyl]-β-D-glucopyranos-6-yl] propanedioate (IN-37735); a conjugate of IN-37738 (2-fluoro-5-[(4-fluorophenyl) (hydroxy) (methyl) silyl] phenol) ; and [bis(4-fluorophenyl)methyl] silanol (IN-F7321). The major triazole-labelled metabolites were triazolyl alanine (IN-V9462); triazole acetic acid (IN-D8722); the glucose-6-phosphate of IN-37722; IN-37735; and IN-37722. Triazolyl alanine and triazole acetic acid accounted for 69 and 24% of the radioactivity in the grain, respectively.

The leaves and detached unpeeled green fruits of immature banana plants growing under greenhouse conditions were treated directly with phenyl- or triazole- labelled flusilazole, each formulated as an emulsifiable concentrate and diluted to a final concentration six times the label rate. The bananas were analysed at intervals of 0, 2, 4, 7, and 11 days and the leaves were analysed at intervals of 0, 7, 14, and 18 days. Autoradiographs showed that flusilazole applied to banana leaves did not translocate from the treated areas. In the case of banana fruit, flusilazole distribution from the peel to the pulp was negligible since 98–99% of the radioactivity applied to the peel remained in the washings and peel. Intact flusilazole accounted for more than 87% of the radioactivity in the peel rinses and peels.

Sugar beets were treated post-emergence with either phenyl- or triazole-labelled flusilazole as an over the top spray at application rates of 124–131 g ai/ha (three times at 14-day intervals). The sugar beets were harvested at 0, 14, 28, and 59 or 77 days (maturity). At each sampling interval, radioactive residues were consistently higher in the foliage than in the roots. Immediately after the third treatment, total radioactive residues in the foliage ranged between 1.5 and 7.2 mg/kg for triazole- and phenyl-labelled flusilazole, respectively. At each sampling interval, total radioactive residues in the roots were lower for the phenyl-treated plants (0.008 mg/kg maximum) than for the triazole-treated plants (0.15 mg/kg maximum). With time, the total radioactive residues in both the foliage and roots decreased.

Flusilazole was the major residue in the foliage, accounting for a maximum of 89% of the total radioactivity present in the foliage. Minor metabolites found included 1,3-dimethyl-1,1,3,3-tetrakis(4-fluorophenyl) disiloxane (IN-G7072) and 2-fluoro-5-[(4-fluorophenyl) (methyl) (1H-1,2,4-triazol-1-ylmethyl)silyl]phenol (IN-37722). No flusilazole was detected in root extracts. Other residues in the foliage and roots consisted of polar materials that were not resolved by HPLC.

Grape vines (separate branches of foliage and grapes) were treated with phenyl- or triazole-labelled flusilazole under field conditions. The berries were harvested 41 days after the application. Flusilazole was the predominant residue, extracted from grape berries, treated with either the phenyl-labelled or triazole-labelled compounds, comprising between 57 and 31% of the recovered radioactivity, respectively. The principal degradation product from phenyl-labelled flusilazole was

[bis(4-fluorophenyl)methylsilyl] methanol (IN-H7169), accounting for 11% of the residue. Four identified minor metabolites containing the phenyl label together accounted for < 10% of the recovered radioactivity. Those four minor metabolites included [bis(4-fluorophenyl)methyl] silanol (IN-F7321); [(4-fluorophenyl)methyl]silanediol (IN-V5571); bis(4-fluorophenyl) (1H-1,2,4-triazol-1-yl)silanol (IN-A7634); and bis(4-fluorophenyl)silanediol (IN-T7866). In addition to flusilazole, triazolyl alanine (IN-V9462) was a major degradation product in triazole-labelled grape berries, accounting 30% of the total radioactivity. Unextractable residues from fruit accounted for between 5 and 14% of the recovered radioactivity.

Apple trees were treated four times at 14-day interval with either phenyl- or triazole-labelled flusilazole at rates of approximately 8 mg/100 mL. Mature fruit were harvested 14 days after the final application. Flusilazole was the predominant residue extracted from apple fruit treated with either phenyl-labelled or triazole-labelled compounds, comprising between 71 and 48% of the recovered radioactivity, respectively. Three identified minor metabolites containing the phenyl label (IN-F7321, IN-V5571, and IN-H7169) together accounted for approximately 11% of the recovered radioactivity. Triazolyl alanine (IN-V9462) was a significant triazole-containing metabolite, accounting for 22% of TRR. Unextractable residues from the apple fruit accounted for between 8 and 14% of the recovered radioactivity.

Peanuts were treated with [phenyl (U)-^{14}C]flusilazole applied to the foliage at 140 g ai/ha, 52 days prior to harvest. Peanuts (nut and shells) were harvested at 52 days (maturity). Total radioactive residues in the foliage of peanut plants declined from 3.4 mg/kg at day 0 to 0.38 mg/kg at day 52. There was no significant translocation of phenyl-labelled metabolites to the peanut seed (total residue in the seed was 0.018 mg/kg) or peanut shell (0.03 mg/kg). Flusilazole was the major residue in the foliage at all sampling intervals, declining from 3.2 mg/kg at day 0 to 0.19 mg/kg at day 52. Flusilazole at 0.006 mg/kg and "water soluble metabolites," also at 0.006 mg/kg, were present in the seed with the remaining residue unextractable.

Based on the results of the submitted studies on wheat, apples, grapes and sugar beets, the Meeting concluded that qualitatively similar metabolism occurred among these crops. The metabolic pathway of flusilazole in plants involves hydroxylations, conjugations, and cleavage between the silicon and the triazole ring. As the interval between treatment and sampling increases, the residues of unchanged flusilazole decreased and the metabolism and conjugation increased.

Due to the extensive degradation of flusilazole by multiple mechanisms to many minor metabolites, there are no major flusilazole metabolites in plants, other than triazolyl alanine. With the exception of triazolyl alanine and triazole acetic acid, individual metabolites generally account for less than 14% of the total radioactivity in the plants.

Environmental fate

Soil

The Meeting received information on aerobic and anaerobic degradation of flusilazole in soil; photolysis on soil surface; mobility in soil; field dissipation studies; and flusilazole residues in rotational crops.

The aerobic degradation of [phenyl(U)-^{14}C] and [triazole-3-^{14}C] flusilazole was studied in two soils (sandy and silt loam soils) incubated in the dark at 25 °C for 1 year.

The primary route of degradation in non-sterile soils was cleavage of the methylene-silicon bond to form IN-F7321 (silanol) which was found < 5% of applied radioactivity after one year and IN-H9933 (triazole) which was not detected.

The anaerobic degradation of [phenyl(U)-^{14}C] and [triazole-3-^{14}C]-flusilazole was studied in two pond water/sediment systems (silt loam and a sand) under anaerobic conditions at 25 °C at a nominal concentration of 1.0 mg/kg sediment.

The major radiolabelled metabolite (found at 2% of the applied radioactivity) was identified as bis(4 fluoro-phenyl)methyl silanol (IN-F7321).

The photodegradation of flusilazole was studied using silt loam soils under artificial and natural sunlight. No significant degradation was observed in the studies. Under the artificial sunlight conditions, the observed half-life was greater than 30 days. Under the natural sunlight conditions, flusilazole degraded slowly with a DT_{50} of about 97 days. Based on these results, the Meeting concluded that photolysis on soil is not an important mode of degradation for flusilazole.

Field dissipation studies on bare soil and cropped soils were performed in the United States, Canada and Europe.

The studies showed substantial metabolism of flusilazole with the majority of the applied radioactivity found near the top of the soil (5–15 cm). The major metabolite was the silanol (IN-F7321) which was present at no more than 14% of the applied radioactivity while the triazole metabolites reached a maximum of < 3%. In all studies, very limited mobility was observed. The DT_{50} values ranged from 71–755 days. However, the residue in soil remained low after multiple applications, and the soil residues continued to decline after application of flusilazole was discontinued.

A field study designed to measure the potential for off-target movement of flusilazole into water-bodies adjacent to orchards showed low to undetectable levels of flusilazole detected in water and sediments adjacent to orchards. The study concluded that environmental exposure to non-target areas would be extremely low under normal use conditions.

A similar pattern was seen in the presence of a wide range of crops (e.g., cereals, oilseed rape and sugar beets). Soil samples of flusilazole remained low (< 0.09 mg/kg) even after a six year accumulation study (up to 3 kg flusilazole applied) and continued to decline after discontinuation of application. No accumulation was seen in soil or crops when used according to recommended use rates. Based on these results, the Meeting concluded that there is a little potential for flusilazole accumulation in soil or crops after multiple years of continuous use.

Residues in rotational crops

The Meeting received results of two confined [^{14}C]flusilazole rotational crop studies. The first study examined the potential for uptake of phenyl-containing residues into four crops (barley, beets, cabbage, and soya beans) from soil (sandy loam) treated with phenyl-labelled flusilazole at rates of 289 or 543 g ai/ha and aged for 30 or 120 days under greenhouse conditions. The second study examined the potential for uptake of phenyl- or triazole-containing residues into three crops (cabbage, wheat and beets) from soils (silt loam) treated with phenyl- or triazole-labelled flusilazole at 1129 g ai/ha and then aged for 120 or 360 days in the field.

During both confined rotational crop studies, radioactive residue levels in the soil remained relatively constant during the aging and plant growth periods. Soil residues ranged from 0.04 to 0.12 mg/kg (289 g ai/ha application rate), 0.12 to 0.20 mg/kg (543 g ai/ha application rate) and 0.21 to 0.44 mg/kg (1129 g ai/ha). Flusilazole levels and the percentage of extractable radioactivity decreased with time. Major soil residues included flusilazole and the silanol (IN-F7321).

There was no significant accumulation of residues from either label in cabbage, soya beans or beets in the confined rotation studies. Accumulation did occur in mature small grain fractions of wheat grown in soil treated with [triazole-3-^{14}C]flusilazole. Parts of matured wheat grown in 360-day aged soilcontained pheny and triazole labelled residues, respectively: chaff 0.60–9.5 mg/kg, straw 1.4–7.9 mg/kg and grain 0.081–17.5 mg/kg.The extent of accumulation was similar in comparable samples from all aging periods. A major wheat metabolite was triazolyl alanine with flusilazole comprising < 20% of the radioactivity in the wheat grain or straw. This suggests that a triazole-containing fragment, rather than intact flusilazole, translocates from soil into wheat.

The Meeting concluded that there is no significant uptake of flusilazole into rotational (succeeding) crops, except ceral grains.

Methods of Analysis

The Meeting received description and validation data for analytical methods for flusilazole and its important metabolites, mainly [bis(4-fluorophenyl)methyl] silanol (IN-F7321), in samples of plant and animal origin.

The described methods are mostly based on extraction with an organic solvent (usually ethyl acetate or acetone); followed by a partition step, gel permeation chromatography (GPC) clean-up, and often also a silica solid-phase extraction (SPE) clean-up. The determination step employs mainly capillary GC with nitrogen-phosphorus detection (NPD), followed by a mass spectrometric (MS) confirmation, or a single-step GC-MS determination.

The typical LOQ is 0.01 mg/kg for most plant and animal matrices, with mean recoveries typically ranging between 70–120%.

Multiresidue methods, such as the DFG S19, are available for flusilazole.

The Meeting concluded that adequate multi- and single-residue methods exist for both gathering data in supervised trials and other studies and for monitoring and enforcing flusilazole MRLs in samples of plant and animal origin.

Stability of pesticide residues in stored analytical samples

The Meeting received information on the stability of flusilazole and its silanol IN-F7321 metabolite in freezer-stored samples (at approximately -20 °C) of plant and animal origin, including apples, grapes, wheat grain, wheat straw, oilseed rape (seed and shoots) and bovine matrices (milk, muscle, kidney, liver and fat). Fortified samples were stored up to the following intervals: wheat grain: 40 months; wheat straw: 40 months; apples: 48 months (flusilazole) and 26 months (IN-F7321); grapes: 17 months (flusilazole) and 25 months (IN-F7321); oilseed rape: 14 months (flusilazole only); whole milk: 6 months (flusilazole) and 11 months (IN-F7321); bovine muscle: 6 months (flusilazole) and 15 months (IN-F7321); bovine kidney: 3.5 months (IN-F7321); bovine liver: 6 months (flusilazole) and 14.25 months (IN-F7321); and bovine fat: 6 months (flusilazole) and 16 months (IN-F7321).

No significant degradation of flusilazole and its silanol metabolite IN-F7321 was observed in the tested plant and bovine matrices and storage intervals, with the exception of IN-F7321 in liver (residues remained and corrected for recoveries were 35, 84, and 38% for 1, 3, and 14.25 months of storage, respectively). In the case of 3 month-storage of IN-F7321 in liver, samples were only partially thawed and rapidly refrozen after fortification, whereas the other samples (1 and 14.25 months of storage) were completely thawed and remained in contact with the fortification solution at ambient temperature for at least 30 minutes. The partially thawed and rapidly refrozen samples showed limited degradation, probably due to a much lower rate of enzyme activity at lower temperatures. While this does not directly reflect the stability of incurred residues of IN-F7321 in liver, it emphasises the need, when analysing residues in liver, to ensure that samples are processed expeditiously and are not allowed to remain at elevated temperatures prior to extraction and analysis.

Residue definition

Flusilazole is extensively metabolized in animals and plants. The major metabolic reaction is cleavage of the Si-CH_2 bond to form silanol and triazole related metabolites.

In plants, there are no predominant metabolites with the exception of triazole alanine and triazole acetic acid. These plant metabolites are produced by all fungicides in the triazole class and are therefore excluded from the definition of the residue for flusilazole.

In ruminants (goats), the most abundant metabolites in tissues and milk were flusilazole, [bis(4-fluorophenyl)methyl] silanol(IN-F7321), and 1H-1,2,4-triazole(IN-H9933). In poultry, metabolites in tissues and eggs were flusilazole, [bis(4-fluorophenyl)methyl]silanol, 1H-1,2,4-triazole, and [(4-fluorophenyl)methyl]silanediol(IN-V771). As 1H-1,2,4-triazole is a common metabolite to all triazole fungicides, it is not deemed suitable as an indicator of flusilazole exposure to ruminants or

hens. The silanediol metabolite is only found in poultry tissues, and is not expected to be detectable at anticipated dietary exposure levels to laying hens.

Based on the above, the Meeting agreed in the following residue definitions:

Definition of the residue in plant commodities for estimation of dietary intake and for compliance with MRLs: flusilazole

Definition of the residue in animal commodities for estimation of dietary intake and for compliance with MRLs: flusilazole plus [bis(4-fluorophenyl)methyl]silanol (IN-F7321)

The log K_{ow} is 3.87 (at 20 °C, pH 7), suggesting that flusilazole is fat-soluble. Both in the goat and hen metabolism studies the residues of flusilazole and its silanol, IN-F7321, in muscle was generally less than one-tenth that in the various fat depots. The Meeting concluded that the flusilazole residue is fat soluble.

Results of supervised trials on crops

The Meeting received supervised trials data for flusilazole on apple, pear, apricot, nectarine, peach, grapes, banana, cucumber, sweet corn, soya bean, sugar beet (root and leaves), barley (grain, forage, and straw), rye (grain, forage, and straw), wheat (grain, forage, and straw), maize, rice, rape seed, sunflower seed and oat (forage and fodder).

Pome fruit

Apple

The Meeting received results from supervised trials with flusilazole used on apples in southern Europe (Italy, Spain and southern France), Argentina, Canada, India, New Zealand and South Africa.

None of the trials in Argentina, India, or New Zealand were conducted according to the respective GAPs of Argentina (4 applications at 4 g ai/hL with a PHI of 21 days), India (4 g ai/hL with a PHI of 10 days), and New Zealand (3 g ai/hL, up to 6 applications, with a PHI of 35 days).

The critical GAP for the southern European trials conducted in Spain, Italy and southern France is the GAP of Spain that specifies a spray concentration of 4.8 g ai/hL in high-volume applications (more than 1500 L water/ha, i.e., a maximum of $\geq$ 72 g ai/ha), maximum of 4 applications per year, and a PHI of 14 days. Flusilazole residues from ten trials according to the GAP of Spain, in ranked order, were: 0.01, 0.01, 0.02, 0.04(2), 0.05(2), 0.06, 0.12 and 0.13 mg/kg.

Two trials in Canada were conducted according to the GAP of Canada: 40 g ai/ha, maximum of 4 applications, and a PHI of 77 days. Flusilazole residues (at 88 and 130% GAP) were < 0.01 mg/kg (below LOQ of the analytical method used).

The GAP of South Africa specifies a spray concentration of 2.4 g ai/hL in high-volume applications (1500–3500 L water/ha, i.e., 36–84 g ai/ha), 5 applications, and a PHI of 14 days. One trial was conducted according to this GAP. The residue of flusilazole from this trial was 0.06 mg/kg.

Pear

The Meeting received results from supervised trials with flusilazole used on pears in Italy, South Africa and China.

Trials in Italy were not conducted according to the critical GAP of the southern European region, i.e., that of Spain (the same treatment regime as for apples).

The GAP of South Africa specifies a spray concentration of 1.6 g ai/hL in high-volume applications (1500–3500 L water/ha, i.e., 24–56 g ai/ha), 5 applications, and a PHI of 14 days. Two trials were conducted at a higher application rate of 2 g ai/hL (125% GAP), 6 applications and 2-day longer PHI of 16 days. Flusilazole residues from these trials were 0.02 and 0.03 mg/kg.

Four trials in China were conducted according to the GAP of China (5 g ai/hL, 3 applications, with a PHI of 21 days), with the exception four applications were made instead of three. Flusilazole residues from these trials were: 0.01, 0.02, 0.03, and 0.13 mg/kg.

The Meeting agreed that the data on apples from southern Europe and South Africa and on pears from China appear to be from similar populations and could be used to support a "pome fruit" commodity group maximum residue level. Pome fruit is registered for use in New Zealand. Flusilazole residues in pome fruit, in ranked order, were: 0.01(3), 0.02(2), 0.03, 0.03, 0.04(2), 0.05(2), 0.06(2), 0.12 and 0.13(2) mg/kg. The Meeting estimated a maximum residue level for pome fruit of 0.3 mg/kg to replace the previous recommendation of 0.2 mg/kg, an STMR value of 0.04 mg/kg, and an HR value of 0.13 mg/kg.

Apricot, nectarine and peach

The Meeting received results from supervised trials with flusilazole used on apricots in France, on peaches in southern Europe (Greece, Italy, Spain, and southern France) and on peaches and nectarines in New Zealand.

The GAP of New Zealand for stone fruit (4 g ai/hL) does not specify a PHI. The label states that the product should not be applied after the start of shuck fall, which should be 86–113 days before harvest for most peach and nectarine cultivars. Nine trials were reported (three on peach and six on nectarine). The spray concentrations in these trials were 5, 10 and 20 g ai/hL, with very long PHIs of 91–113 days. All flusilazole residues from these trials were < 0.01 mg/kg (below LOQ of the analytical method used).

The critical GAP for the southern European trials conducted on peach in Spain, Greece, Italy and southern France is the GAP of Spain that specifies a spray concentration of 5 g ai/hL, maximum of 3 applications per year, and a PHI of 7 days. Flusilazole residues from twelve trials according to the GAP of Spain, in ranked order, were: 0.03, 0.04, 0.05(4), 0.06, 0.07, 0.08, 0.09 and 0.10 mg/kg.

The GAP of France for apricot (4 g ai/hL) does not specify a PHI. The critical GAP in the region is the GAP of Spain (5 g ai/hL, maximum of 2 applications per year, and a PHI of 7 days). Three apricot trials were conducted with a PHI of 7, one with 4 g ai/hL (8 applications) and two with 14 g ai/hL (4 and 6 applications). Flusilazole residues from these trials were 0.08, 0.05 and 0.06, respectively.

The critical GAP for the southern European trials (the GAP of Spain) is the same for peach and nectarine. The critical GAP for apricot (the GAP of Spain) specifies the same spray concentration and PHI as for peach and nectarine, with maximum of two applications instead of three. Flusilazole residues for apricot (a smaller fruit than peach) fell within the range of residues obtained for peach, even though exaggerated spray concentration (280% GAP) and/or significantly higher number of applications were used.

The Meeting decided to use the residue data from the eleven trials on peach in southern Europe to estimate a maximum residue level of 0.2 mg/kg for apricot, nectarine and peach to replace the previous recommendation of 0.5 mg/kg. The Meeting also estimated an STMR value of 0.05 mg/kg, and an HR value of 0.10 mg/kg for apricot, nectarine and peach.

Grapes

The Meeting received results from supervised trials with flusilazole on grapes in southern Europe (Greece, Italy, Portugal, Spain and southern France), Germany, Australia, China, India and South Africa.

None of the trials in India and South Africa were conducted according to the respective GAPs of India (4 g ai/hL with a PHI of 15 days) or South Africa (5 g ai/hL with a PHI of 21 days).

Flusilazole is not registered for use on grapes in Germany but it is registered in France, Switzerland and the Czech Republic. The GAPs of France and Switzerland do not specify a PHI. The

GAP of the Czech Republic for grapes specifies 30 g ai/ha (spray volume 1000 L water/ha, i.e., 3 g ai/hL), spraying interval 7–14 days (number of applications not specified), and a PHI of 42 days.

Five trials in Germany were conducted with a 42-day PHI and 32–36 g ai/ha (106–120% of GAP). Flusilazole residues in these trials were: 0.02, 0.03, 0.04, 0.10 and 0.11 mg/kg.

The GAP of Australia specifies maximum of 3 applications at 2 g ai/hL or 20 g ai/ha with a PHI of 14 days. In one trial in Australia, flusilazole was applied as a single application with 2 g ai/hL and a PHI of 14 days. Flusilazole residue from that trial was 0.11 mg/kg.

The critical GAP for the southern European trials conducted on grapes in Spain, Portugal, Greece, Italy and southern France is the GAP of Spain, specifying a spray concentration of 5 g ai/hL, a maximum of 5 applications and a PHI of 14 days. Flusilazole residues from eight trials according to the GAP of Spain (with 5–6 applications), in ranked order (median underlined), were: 0.01(2), 0.02(2), 0.03, 0.04, 0.10, and 0.11 mg/kg. One trial with a PHI of 15 days was also included as a higher residue of 0.11 mg/kg was recorded than from trials with a 14-day PHI.

The GAP of China specifies a spray concentration of 5 g ai/hL and 3 applications but does not specify a PHI or growth stage and could not be evaluated.

The Meeting decided to use the residue data from southern Europe and Germany to estimate a maximum residue level for grapes. Residues from these trials in ranked order were: 0.01(2), 0.02(3), 0.03(2), 0.04(2), 0.10(2) and 0.11(2) mg/kg. The Meeting estimated a maximum residue level of 0.2 mg/kg to replace the previous recommendation of 0.5 mg/kg, an STMR value of 0.03 mg/kg, and an HR value of 0.11 mg/kg.

Banana

The Meeting received results from supervised trials with flusilazole used on bananas in the Caribbean Basin (Belize, Costa Rica, Guatemala, Honduras, Jamaica and West Indies, including Guadeloupe, Martinique and St. Lucia). The Meeting considered the GAP of Columbia (100 g ai/ha, 4–6 applications, and a PHI of 1 day) as the critical GAP for the evaluation of the submitted trials.

In the eleven submitted trials, bananas were treated with flusilazole at 100 g ai/ha (4–7 applications) using aerial application to bagged bunches with washing (normal practice) or without washing at the harvest. With a PHI of 1 day, flusilazole residues in the pulp were < 0.01 mg/kg for all the trials. With the same PHI, flusilazole residues in the peel of washed bananas (three trials) were: < 0.01 (2) and 0.01 mg/kg. Residues in the peel of unwashed bananas (eight trials) were: < 0.01 (3), 0.011, 0.012, 0.013, 0.017 and 0.02 mg/kg. Flusilazole was not analysed in the whole fruit.

Based on data in the published literature[36] an average pulp to peel ratio for bananas at harvest is 1.82. Assuming this ratio and combining the results from washed and unwashed bananas, flusilazole residues in whole fruit, in ranked order, were: < 0.01 (5) and 0.01 (6) mg/kg.

The Meeting estimated a maximum residue level for flusilazole in banana (whole fruit) of 0.03 mg/kg to replace the previous recommendation of 0.1 mg/kg. Based on the pulp data, the Meeting estimated an STMR value of 0.01 mg/kg and an HR value (for pulp) of 0.01 mg/kg for banana pulp.

Cucumber

Flusilazole is registered for foliar application on cucumber in China (5 g ai/hL, 3 applications, a PHI of 7 days) and Korea (2.5 g ai/hL, 3 applications, and a PHI of 3 days). The Meeting received results from supervised trials with flusilazole on cucumber in China. None of the trials were conducted according to the GAPs of China or Korea. Therefore, the Meeting could not estimate a maximum residue level for flusilazole in cucumber.

[36] Stover, R.H. and Simmonds, N.W., 1987, Bananas. Tropical Agriculture Series, Longman Scientific & Technical, 468 pp

Sweet corn

The Meeting received results from supervised trials with flusilazole on sweet corn in France and South Africa.

The GAP of France (200 g ai/ha, 2 applications) does not specify a PHI. The six reported trials on sweet corn in France were conducted as a single application at 200–420 g ai/ha (100–210% GAP) with PHIs of 10–31 days. Flusilazole residues in sweet corn kernels were < 0.01 mg/kg in all these trials.

The GAP of South Africa specifies a maximum of 2 applications at 125 g ai/ha with a PHI of 14 days. One trial conducted in South Africa at 250 g ai/ha (200% GAP) with 2 applications, resulted in flusilazole residues in cobs < 0.01 mg/kg for both tested PHIs of 0 and 14 days.

The Meeting estimated a maximum residue level for flusilazole in sweet corn (corn-on-the-cob) of 0.01* mg/kg an STMR value of 0.01 mg/kg and an HR value of 0.01 mg/kg.

Soya beans (dry)

The Meeting received results from supervised trials with flusilazole used on soya beans in Argentina, Canada, France, South Africa and the United States. The trials in France could not be evaluated because there is no GAP for soya beans in Europe.

None of the six trials reported from Argentina were conducted according to the GAP of Argentina (100 g ai/ha, 2 applications, and a PHI of 35 days). In three of these trials, a single application rate of 200 g ai/ha (200% GAP) resulted in flusilazole residues < 0.005 mg/kg (below LOQ of the used analytical method) 38–60 days after the application.

The critical GAP of South Africa specifies 125 g ai/ha for aerial application or 100 g ai/ha for ground application, maximum of 2 applications, and a PHI of 30 days. Four trials in South Africa were conducted with a PHI of 34 days and using either 75 or 150 g ai/ha in two applications (75 or 150% GAP assuming ground application). Flusilazole residues were < 0.005 mg/kg (below LOD of the used analytical method) in all these trials at 34 days.

The GAP of the United States specifies 116 g ai/ha, 2 applications, and a PHI of 30 days. Twenty-one trials in the United States and two trial in Canada were conducted at 103–109% of the GAP rate, resulting in flusilazole residues of < 0.01(3), 0.01(8), 0.02(9) and 0.03(3) mg/kg.

Based on the residues obtained in the trials in the United States and Canada, the Meeting estimated a maximum residue level for flusilazole in soya beans (dry) of 0.05 mg/kg, an STMR value of 0.02 mg/kg and an HR value of 0.03 mg/kg.

Sugar beet (root)

The Meeting received results from supervised trials with flusilazole used on sugar beet in southern Europe (Greece, Italy, and Spain) and in northern Europe (Belgium, Denmark, northern France, Germany, the Netherlands and the United Kingdom).

Five trials in southern Europe (two in Greece, two in Italy, and one in Spain) were conducted according to the GAP of Greece (80 g ai/ha, 3 applications, and a PHI of 15 days). The Meeting noted that there were four other trials conducted in southern Europe with a shorter PHI of 14 days (3 or 6 applications) or a higher application rate (132.5% GAP) that resulted in flusilazole residues of < 0.01 mg/kg. Thus, results of these trials were also included. Flusilazole residues in sugar beet root, in ranked order, were: < 0.01 (6), and 0.01 (3) mg/kg.

Sixteen trials in northern Europe (ten in Germany, two in the UK, and one in Belgium, Denmark, the Netherlands and northern France) were conducted according to the GAP of Germany (150 g ai/ha, 2 applications, a PHI of 42 days). Among these trials, one trial in northern France had only a 35-day PHI but the flusilazole residue was < 0.01 mg/kg. Flusilazole residues in sugar beet root, in ranked order, were: < 0.01 (11), 0.01(2), 0.02, < 0.03, and 0.03 mg/kg.

The Meeting noted that the residues obtained in southern and northern Europe were from similar populations and agreed to combine the results. Flusilazole residues in sugar beet root, in ranked order, were: ≤ 0.01 (17), 0.01 (5), 0.02, < 0.03, and 0.03 mg/kg.

The Meeting estimated a maximum residue level for flusilazole in sugar beet root of 0.05 mg/kg to replace the previous recommendation of 0.01* mg/kg, an STMR value of 0.01 mg/kg, and a highest residue value of 0.03 mg/kg.

Cereal grains

Barley

The Meeting received information on flusilazole residues in barley grains from supervised trials in Germany, the United Kingdom and South Africa.

The GAP of Germany specifies 200 g ai/ha, 2 applications, the second application up to the growth stage of BBCH 51 and a PHI of 42 days. Twelve trials in Germany on winter barley were conducted at 160-221 g ai/ha (80–111% GAP), 2 applications, with the growth stage at the last application of BBCH 51 (PHI of 57–86 days). Flusilazole residues, in ranked order, were: < 0.01 (3), 0.02, 0.03, 0.04 (2), 0.05, 0.06, 0.07 (2), and 0.08 mg/kg.

The critical GAPs of the United Kingdom specify 156–160 g ai/ha, 1 application, and the BBCH 71 or 73 (watery ripe stage or early milk stage, respectively) growth stage at the last application. Four trials in the United Kingdom on spring barley were conducted at 160 g ai/ha, 2 applications, and the BBCH 71 growth stage at the last application. Flusilazole residues, in ranked order, were: < 0.01 (2), 0.06, and 0.07 mg/kg.

The critical GAP of South Africa specifies 112.5 g ai/ha (aerial application) or 100 g ai/ha (ground application), 1–2 applications and a PHI of 56 days. One trial in South Africa was conducted as a single application at 125 g ai/ha with a PHI of 56 days (application method and spray volume were not specified). Flusilazole residue from this trial was < 0.02 mg/kg.

The Meeting noted that the residues obtained in Germany, the United Kingdom and South Africa were from similar populations and agreed to combine the results. Flusilazole residues in barley grain, in ranked order, were: < 0.01 (5), < 0.02, 0.02, 0.03, 0.04 (2), 0.05, 0.06 (2), 0.07 (3), and 0.08 mg/kg.

Rye

The Meeting received information on flusilazole residues in rye grains from supervised trials in winter rye Germany. The GAP of Germany specifies 200 g ai/ha, 2 applications, the second application up to the growth stage of BBCH 55. The Meeting noted that the growth stages (BBCH of 49, 65, 69, or 72) at the last application in the trials did not match the GAP specification. Two trials were conducted at 100–130% of the GAP rate, with 3 applications and a PHI of 42 days (BBCH 65). One additional trial resulted in a higher flusilazole residue at a PHI of 48 days *vs.* 35 days (BBCH 69). Flusilazole residues obtained in these trials were: 0.04 (2), and 0.05 mg/kg.

Wheat

The Meeting received information on flusilazole residues in wheat grains from supervised trials in Germany, Spain, the United Kingdom and South Africa.

None of the trials in South Africa were conducted according to the critical GAP of South Africa: 112.5 g ai/ha (aerial application) or 100 g ai/ha (ground application), 1–2 applications and a PHI of 56 days.

The GAP of Germany specifies 200 g ai/ha, 2 applications, the second application up to the growth stage of BBCH 55, and a PHI of 42 days. The Meeting agreed that the growth stage at the last application is a better indication of the GAP than the PHI. Three trials in Germany were conducted at 160–250 g ai/ha (80–125% GAP), with 2-3 applications, and the last application at the growth stage of BBCH 55 (PHI of 58–63 days). Flusilazole residues were < 0.01 mg/kg. The Meeting noted that

several other trials at approx. the GAP rate (2–3 applications) but with later growth stages at the last application also resulted in flusilazole residues < 0.01 mg/kg.

The GAP of Spain specifies 200 g ai/ha, 1 application, and the BBCH 61 (beginning of flowering) growth stage at the last application. The trials in Spain were conducted at approximately 200 g ai/ha, with 2 applications, but the growth stage at the last application was in the range of 73–85 (a PHI of 28 days). Flusilazole residues from two of these trials (at BBCH 75 and 83) were < 0.01 mg/kg.

The critical GAPs of the United Kingdom specify 156–160 g ai/ha, 1–2 applications, and the BBCH 71 or 73 (watery ripe stage or early milk stage, respectively) growth stage at the last application. Four trials in the United Kingdom on winter wheat were conducted at 160 g ai/ha, 3 applications, and the BBCH 71 growth stage at the last application. Flusilazole residues were: < 0.01(4) mg/kg. Three other trials that were conducted as a single at 200 or 400 g ai/ha and later growth stages at the last application (75, 84, or 90) resulted in flusilazole residues < 0.01 (3) mg/kg.

The Meeting noted that flusilazole residues in wheat grain obtained in the sixteen trials in Germany, Spain and the United Kingdom were all < 0.01(16) mg/kg.

Maize

The Meeting received information on flusilazole residues in maize grains from supervised trials in France.

The GAP of France (200 g ai/ha, 2 applications) does not specify a PHI (the other available GAP in Europe, the GAP of Romania for cereal grains, specifies 100 g ai/ha and a PHI of 42 days). Five trials on maize were conducted at approx. 200 g ai/ha (2 applications) with a PHI of 28 days. Flusilazole residues in maize grain were < 0.01 mg/kg in all these trials.

The Meeting agreed that the data on barley, rye, wheat and maize could be used to support a "cereal grains" commodity group maximum residue level. The Meeting decided to recommend a maximum residue level of 0.2 mg/kg for cereals except rice, an STMR value of 0.04 mg/kg based on the barley data and a highest residue of 0.08 mg/kg based on the barley data.

The Meeting also agreed to withdraw its previous recommendations of maximum residue levels of 0.1 mg/kg for barley, rye and wheat grains.

Rice

The Meeting received information on flusilazole residues in rice grains from supervised trials in Spain. The GAP of Spain specifies 125 g ai/ha, 2 applications and a PHI of 30 days. Four trials were conducted at 129 g ai/ha (2 applications) with PHIs of 30 or 33 days. Flusilazole residues in rice grain, in ranked order, were: 0.06, 0.09, 0.11, and 0.18 mg/kg.

The meeting considered four trials insufficient to estimate a maximum residue level for flusilazole in rice.

Rape seed

The Meeting received results from supervised trials with flusilazole used on oilseed rape in Belgium, Denmark, France, Germany, the Netherlands and the United Kingdom. The critical GAPs in France, Germany, and the United Kingdom specify 200 g ai/ha, 1–2 applications and a PHI of 56 days (Germany) or a PHI that is not specified. The submitted trials were conducted at about the GAP rate with a PHI longer than 56 days. Flusilazole residues in these trials were generally below the LOQ of the used analytical methods: < 0.01 (9) or < 0.02 (5) mg/kg (PHIs in the range of 58–92 days). Results above LOQ: 0.01, 0.01, 0.03, and 0.04 mg/kg; were obtained with a PHI of 72, 109, 61, and 77, respectively.

Flusilazole residues in ranked order were: < 0.01(9), 0.01(2), < 0.02(5), 0.03 and 0.04 mg/kg.

The Meeting estimated a maximum residue level of 0.1 mg/kg for flusilazole in rape seed, an STMR value of 0.01 mg/kg and a highest residue of 0.04 mg/kg.

The meeting recommended withdrawal of the previous recommendation for rape seed of 0.05 mg/kg.

Sunflower seed

Flusilazole is registered for foliar application on sunflower in Czech Republic, Bulgaria, France, Hungary, Romania and Slovakia. The GAPs for sunflower in these countries specify 75–200 g ai/ha, 1–2 applications, and a PHI of 56 or 60 days (or a PHI is not specified, which is the case of the highest rate of 200 g ai/ha).

The Meeting received results from supervised trials with flusilazole used on sunflower in France. The critical GAP of France specifies 200 g ai/ha and 2 applications (1 application for late infections) but does not specify a PHI. Eight trials in France were conducted at approx. 200 g ai/ha, one application, and a PHI of 50 days (BBCH 63–71). Flusilazole residues, in ranked order, were: < 0.01 (4), 0.01, 0.03, and 0.04 (2) mg/kg.

The Meeting estimated a maximum residue level of 0.1 mg/kg for flusilazole in sunflower seed, an STMR value of 0.01 mg/kg and a highest residue value of 0.04 mg/kg.

Barley, rye and wheat forage

The Meeting received information on flusilazole residues in barley, rye and wheat forage from supervised trials in Germany. The GAP of Germany for barley, rye and wheat specifies 200 g ai/ha, 2 applications, the second application up to the growth stage of BBCH 51 (barley) or BBCH 55 (rye and wheat). In the case of livestock grazing, it is assumed that animals are unlikely to be foraging within 7 days of the application of the fungicide. Data was available for residues in forage at 0, 21, 34 and 42 days according to the above gap. For the purposes of animal exposure through grazing, a value at 7 days, interpolated from the 0 and 21 day values is a satisfactory measure of the average residue that livestock would be exposed to for a 14 day period.

The results were considered from all trials conducted at the GAP rate (± 30%) with 2 applications (independent of the growth stage at the last application). Five trials on barley matching the criteria resulted in flusilazole residues of 0.9 (2), 1.35, 2.2, and 3.0 mg/kg. One trial on rye matched the criteria with flusilazole residues being 2.0 mg/kg. Five trials on wheat matching the criteria resulted in flusilazole residues of 0.9, 1.2, 3.3, 4.2 and 4.5 mg/kg. Combined flusilazole residues, in ranked order, were: 0.9 (3), 1.2, 1.35, 2.0, 2.2, 3.0, 3.3, 4.2 and 4.5 mg/kg; resulting in an STMR value of 2.0 mg/kg and a highest residue value of 4.5 mg/kg for flusilazole in barley, rye and wheat forage.

Barley, rye, and wheat straw and fodder, dry

The Meeting received information on flusilazole residues in barley straw from supervised trials in Germany. The GAP of Germany specifies 200 g ai/ha, 2 applications, the second application up to the growth stage of BBCH 51 and a PHI of 42 days. Thirteen trials in Germany on winter barley were conducted at 160–221 g ai/ha (80–111% GAP), 2 applications, with the growth stage at the last application of BBCH 51 (PHI of 57–86 days). Flusilazole residues, in ranked order, were: 0.11, 0.48, 0.62, 1.2, 1.4, 1.5, 2.0 (2), 2.1 (2), 2.2, 2.3, and 2.5 mg/kg.

The Meeting received information on flusilazole residues in rye straw from supervised trials on winter rye in Germany. The GAP of Germany specifies 200 g ai/ha, 2 applications, the second application up to the growth stage of BBCH 55 and a PHI of 42 days. The Meeting noted that the growth stages (BBCH of 49, 65, 69, or 72) at the last application in the trials did not match the GAP specification.

The Meeting received information on flusilazole residues in wheat straw from supervised trials in Germany, Spain and the United Kingdom.

The GAP of Germany specifies 200 g ai/ha, 2 applications, the second application up to the growth stage of BBCH 55, and a PHI of 42 days. Three trials in Germany were conducted at 160–

250 g ai/ha (80–125% GAP), with 2–3 applications and the last application at the growth stage of BBCH 55 (PHI of 58–63 days). Flusilazole residues, in ranked order, were: 0.12, 0.23 and 1.6 mg/kg.

The GAP of Spain specifies 200 g ai/ha, 1 application and the BBCH 61 (beginning of flowering) growth stage at the last application. The trials in Spain were conducted at approx. 200 g ai/ha, with 2 applications, but the growth stage at the last application was in the range of 73–85.

The critical GAPs of the United Kingdom specify 156–160 g ai/ha, 1–2 applications, and the BBCH 71 or 73 (watery ripe stage or early milk stage, respectively) growth stage at the last application. None of the submitted trials on wheat (straw) in the United Kingdom matched were conducted according to the GAP (growth stage at the last application was in the range of 39–65).

The Meeting noted that flusilazole residues obtained in barley and wheat straw in Germany appeared to be from similar populations and agreed to combine the results. Flusilazole residues, in ranked order, were: 0.11, 0.12, 0.23, 0.48, 0.62, 1.2, 1.4, 1.5, 1.6, 2.0 (2), 2.1 (2), 2.2, 2.3 and 2.5 mg/kg. The Meeting also agreed to extrapolate the results for barley and wheat straw to rye straw and estimated a maximum residue level of 5 mg/kg for flusilazole in barley, rye and wheat straw and fodder, dry (to replace the previous recommendation of 2 mg/kg), an STMR value of 1.6 mg/kg and a highest residue value of 2.5 mg/kg.

Oat forage and fodder

The Meeting received information on flusilazole residues in oat forage and dry foliage (dry fodder) from two supervised trials in South Africa. The GAP of South Africa for oat fodder specifies 75 g ai/ha, one application, and a PHI of 30 days. One trial was conducted at the GAP rate with a PHI of 29 days. Flusilazole residue in dry foliage (fodder) was < 0.1 mg/kg.

The Meeting considered one trial insufficient to estimate a maximum residue level for oat fodder.

Sugar beet leaves or tops

The Meeting received information on flusilazole residues in sugar beet leaves from supervised trials on sugar beet in southern Europe (Greece, Italy, and Spain) and in northern Europe (Belgium, Denmark, northern France, Germany, the Netherlands and the United Kingdom).

Six trials in southern Europe (two in Greece, three in Italy and one in Spain) were conducted according to the GAP of Greece (80 g ai/ha, 3 applications, and a PHI of 15 days). Flusilazole residues in sugar beet leaves, in ranked order, were: 0.10, 0.31, 0.45, 0.66, 0.89 and 1.0 mg/kg.

Sixteen trials in northern Europe (ten in Germany, two in the UK, and one in Belgium, Denmark, the Netherlands, and northern France) were conducted according to the GAP of Germany (150 g ai/ha, 2 applications, a PHI of 42 days). Flusilazole residues in sugar beet leaves, in ranked order, were: 0.11(2), 0.17, 0.19, 0.21, 0.22, 0.25(2), 0.26, 0.27, 0.33, 0.34, 0.37, 0.58, 0.84 and 0.88 mg/kg.

The Meeting noted that the residues obtained in southern and northern Europe were from similar populations and agreed to combine the results. Flusilazole residues in sugar beet leaves, in ranked order (median underlined), were: 0.10, 0.11 (2), 0.17, 0.19, 0.21, 0.22, 0.25 (2), 0.26, 0.27, 0.31, 0.33, 0.34, 0.37, 0.45, 0.58, 0.66, 0.84, 0.88, 0.89 and 1.0 mg/kg.

The Meeting estimated an STMR value of 0.29 mg/kg and a highest residue value of 1.0 mg/kg for flusilazole in sugar beet leaves.

Rice hulls

The Meeting received information on flusilazole residues in rice hulls (husks) from supervised trials in Spain. The GAP of Spain specifies 125 g ai/ha, 2 applications and a PHI of 30 days. Four trials were conducted at 129 g ai/ha (2 applications) with PHIs of 30 or 33 days. Flusilazole residues in rice hulls, in ranked order, were: 0.34, 0.39, 0.44, and 0.68 mg/kg.

The Meeting made no recommendation for rice hulls as none could be made for the primary commodity rice.

Fate of residues during processing

The Meeting received information on the fate of flusilazole residues during processing of apples, grapes, soya beans, wheat and barley grain and on flusilazole fate under hydrolysis conditions simulating commercial food processing.

In a high-temperature hydrolysis study greater than 99% of flusilazole remained unchanged under conditions simulating industrial processing (temperatures ranging from 90–120°C; pH 5 and 7). Therefore, flusilazole can be considered stable to simulated pasteurization, baking, brewing, boiling and sterilization.

The STMR-P values calculated from the processing factors are summarized in the table below.

Raw agricultural commodity		Processed commodity		
Commodity	STMR (mg/kg)	Commodity	Processing factor*	STMR-P (mg/kg)
Apple	0.04	Apple juice	0.19(2)	0.008
		Apple pomace, wet	2.4(2)	0.094
		Apple pomace, dry	12(2)	0.48
Grapes	0.03	Grape juice	0.42(4)	0.012
		Wine	0.09(5)	0.003
		Dried Grapes (raisins)	1.8(3)	0.054
		Grape pomace, wet	3.6(2)	0.108
		Grape pomace, dry	11(2)	0.33
Soya beans	0.02	Soya bean meal	0.38	0.008
		Soya bean hulls	1.1	0.022
		Soya bean oil, refined	2.2	0.044
Wheat	0.04	Wheat bran	0.29	0.012
		Wheat flour, low-grade	< 0.91	< 0.036
		Wheat milled by products	0.59	0.024

*mean value of (no. trials) except for soya beans where only one trial was performed

The Meeting estimated a maximum residue level of 2 mg/kg for *apple pomace, dry*, based on the highest residue of 0.13 mg/kg in pome fruits and the processing factor of 12.

Based on the HR value of 0.11 mg/kg in grapes and the processing factor of 1.8, the Meeting estimated a maximum residue level of 0.3 mg/kg for *dried grapes (including currants, raisins, and sultanas)* to replace its previous recommendation of 1 mg/kg.

Based on the highest residue of 0.03 mg/kg in soya beans and the processing factors of 1.1 and 2.2, the Meeting estimated a maximum residue level of 0.05 mg/kg for *soya bean hulls* and 0.1 mg/kg for *soya bean oil, refined*.

Livestock dietary burden

The Meeting estimated the dietary burden of flusilazole in farm animals on the basis of the diets listed in Annex 6 of the 2006 JMPR Report (OECD Feedstuffs Derived from Field Crops). Calculation from the highest residue, STMR (some bulk commodities) and STMR-P values provides the levels in feed suitable for estimating maximum residue levels, while calculation from STMR and STMR-P values for feed is suitable for estimating STMR values for animal commodities.

The table below shows estimated maximum and mean dietary burdens for beef cattle, dairy cattle, broilers and laying poultry based on the animal diets from the United States/Canada, the European Union, and Australia. The calculations are provided in Annex 6.

	Flusilazole, Animal dietary burden (mg/kg)					
	US-Canada		EU		Australia	
	Maximum	Mean	Maximum	Mean	Maximum	Mean
Beef cattle	7.5	2.25	6.3	2.9	18[1]	8.0[2]
Dairy cattle	7.5	3.4	6.7	2.9	11.5[3]	5.3[4]
Poultry - broiler	0.04	0.04	0.04	0.04	0.04	0.03
Poultry - layer	0.04	0.04	2.3[5]	1.1[6]	0.02	0.02

[1] Highest maximum beef cattle dietary burden suitable for MRL estimates for mammalian meat.
[2] Highest mean beef cattle dietary burden suitable for STMR estimates for mammalian meat.
[3] Highest maximum dairy cattle dietary burden suitable for MRL estimates for milk
[4] Highest mean dairy cattle dietary burden suitable for STMR estimates for milk.
[5] Highest maximum poultry dietary burden suitable for MRL estimates for poultry meat and eggs
[6] Highest mean poultry dietary burden suitable for STMR estimates for poultry meat and eggs.

Farm animal feeding studies

The Meeting received information on lactating dairy cow and laying hen feeding studies.

Twelve lactating cows were randomly assigned among 4 dosing groups of 3 animals each: one control group and 3 groups dosed at one of 3 flusilazole feeding levels each (2, 10, and 50 mg/kg based on measured feed intake, corresponding. All groups were fed for 28 days. Residues in milk reached a plateau at about 7 days. During the withdrawal period, residues decreased significantly in all milk and tissue samples, indicating no bioaccumulation of flusilazole or its metabolites.

Total residues of flusilazole and [bis(4-fluorophenyl)methyl]silanol (IN-F7321) in whole milk (on days 7–28, i.e., at the plateau) and tissues obtained at the 2, 10, and 50 mg/kg dosing levels in the diet are summarized in the table below.

Matrix	Dose (mg/kg)	Highest residue	Mean residue
Whole milk	2	< 0.01	< 0.01
	10	0.05	0.02
	50	0.10	0.06
Muscle	2	< 0.01	< 0.01
	10	0.06	0.05
	50	0.19	0.19
Kidney	2	0.21	0.21
	10	0.85	0.77
	50	5.0	3.9
Liver	2	0.18	0.15
	10	0.65	0.55
	50	1.6	1.4
Fat [a]	2	0.06	0.06
	10	0.56	0.36
	50	1.4	1.35

[a]Residues for omental, renal, and subcutaneous fat for the 2, 10 and 50 mg/kg dose, respectively. These were the highest residues at the respective dose levels for the three kinds of analysed fat samples.

In a hen feeding study, eighty laying hens were divided into 4 groups and each group was divided into 4 subgroups of 5 hens each. Each subgroup of a group was dosed for 28 days at 0, 2, 10, or 50 mg/kg of flusilazole in the diet. Residues in eggs reached a plateau at about 7 days. During the withdrawal period, residues decreased significantly in all egg and tissue samples, indicating no bioaccumulation of flusilazole or its metabolites.

Total residues of flusilazole and [bis(4-fluorophenyl)methyl]silanol (IN-F7321) in eggs (on days 7–28, i.e., at the plateau) and tissues (on day 28) obtained at the 2, 10, and 50 mg/kg dosing levels in the diet are summarized in the table below.

Matrix	Dose (mg/kg)	Highest residue, mg/kg	Mean residue, mg/kg
Whole egg	2	0.05	0.03
	10	0.40	0.16
	50	1.8	0.85
Muscle	2	< 0.02	< 0.02
	10	0.10	0.05
	50	0.37	0.19
Liver [a]	2	0.08	0.04
	10	0.13	0.10
	50	0.58	0.41
Fat	2	0.10	0.09
	10	0.54	0.45
	50	3.7	3.2

[a] Flusilazole was not analysed in liver for the 2 and 10 mg/kg dosing levels, but the residues can be assumed to be < 0.01 mg/kg because < 0.01 mg/kg was obtained for the 50 mg/kg dosing level.

In both the cattle and poultry feeding studies, the flusilazole residues in muscle were significantly lower than in fat and confirms that the residue (sum of flusilazole and [bis(4-fluorophenyl)methyl]silanol) is fat-soluble and that fat is the target tissue.

Animal commodity maximum residue levels

The dietary burdens for the estimation of maximum residue levels for animal commodities are 18 mg/kg for beef cattle, 11.5 mg/kg for dairy cattle and 2.3 mg/kg for poultry. The dietary burdens for the estimation of STMR values for animal commodities are 8.0 mg/kg for beef cattle, 5.3 mg/kg for dairy cattle and 1.1 mg/kg for poultry. The sum of flusilazole and [bis(4-fluorophenyl)methyl]silanol (IN-F7321) residues was used for the estimation of "flusilazole residue" levels in animal commodities.

The maximum dietary burden of 18 mg/kg for beef cattle fell between the 10 and 50 mg/kg dosing levels in the cattle feeding study. The residues in muscle were significantly lower than in fat. The target tissue for flusilazole residues is fat. Using the highest residues of 0.56 and 1.4 mg/kg in fat for 10 and 50 mg/kg dosing levels, respectively, the interpolated highest residue in fat for the dietary burden of 18 mg/kg was 0.73 mg/kg. Similarly, for beef liver and kidney the highest residues were 0.84 and 1.68 mg/kg, respectively.

The mean dietary burden was 8.0 mg/kg for beef cattle. By interpolation, the mean residues obtained in fat, liver and kidney were 0.285, 0.45 and 0.65 mg/kg, respectively.

On the fat basis, the Meeting estimated a maximum residue level of 1.0 mg/kg for meat (fat) from mammals (other than marine mammals), an STMR value of 0.285 mg/kg and an HR value of 0.73 mg/kg. Based on the liver and kidney results, the Meeting estimated a maximum residue level of 2 mg/kg for mammalian edible offal and, based on the kidney data, an STMR value of 0.65 mg/kg and an HR value of 1.68 mg/kg.

The mean dietary burden of 5.3 mg/kg for dairy cattle fell between the 2 and 10 mg/kg dosing levels in the feeding study. The interpolated highest residue in whole milk, using the mean residues in the feeding study, was 0.03 mg/kg. Similarly, the mean residue based upon a dietary burden of 5.3 mg/kg, in whole milk was 0.01 mg/kg. The Meeting estimated a maximum residue level of 0.05 mg/kg for whole milk, an STMR value of 0.01 mg/kg and an HR value of 0.03 mg/kg.

Maximum and mean dietary burdens for poultry (2.3 and 1.1 mg/kg, respectively) were near the lowest dosing level of 2 mg/kg. By interpolation, the highest residues obtained in fat, liver and eggs between the 2 and 10 mg/kg feeding level were 0.13, 0.09 and 0.07 mg/kg, respectively. Extrapolating the mean residues gave 0.05 mg/kg for fat, 0.02 mg/kg for liver and 0.02 mg/kg for eggs.

On the fat basis, the Meeting estimated a maximum residue level of 0.2 mg/kg for poultry meat (fat), an STMR value of 0.05 mg/kg and an HR value of 0.13 mg/kg. Based on the liver results, the Meeting estimated a maximum residue level of 0.2 mg/kg for poultry edible offal, an STMR value of 0.02 mg/kg and an HR value of 0.09 mg/kg. The Meeting estimated a maximum residue level of 0.1 mg/kg for eggs, an STMR value of 0.02 and HR value of 0.07 mg/kg.

The Meeting agreed to withdraw its previous recommendations of maximum residue levels of 0.01* mg/kg for cattle fat, cattle meat, cattle milk, chicken meat, chicken eggs, and chicken edible offal; and 0.02* mg/kg for cattle edible offal.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes (IEDIs) of flusilazole based on STMR and STMR-P values estimated for 22 commodities for the thirteen GEMS/Food regional diets were 2–10% of the maximum ADI (0.007 mg/kg bw). The results are shown in Annex 3 of the Report. The Meeting concluded that the long-term dietary intake of flusilazole residues is unlikely to present a public health concern.

Short-term intake

The International Estimated Short Term Intake (IESTI) of flusilazole calculated on the basis of the recommendations made by the JMPR represented for the general population 0–40% and for children 0–100% of the ARfD (0.02 mg/kg bw). The results are shown in Annex 4 of the Report. The Meeting concluded that the short-term intake of residues of flusilazole resulting from uses that have been considered by the JMPR is unlikely to present a public health concern.

5.15 FOLPET (041)

TOXICOLOGY

Evaluation for an acute reference dose

Folpet, the ISO approved name for *N*-(trichloromethylthio)phthalimide, is registered for the control of fungal diseases in crops (CAS No. 133-07-3). The toxicology of folpet was evaluated by the JMPR in 1969 and 1995 and addenda to the monograph were prepared in 1973, 1984, 1986, 1990 and 2004. In 1995, an ADI of 0–0.1 mg/kg bw was established based on a NOAEL of 10 mg/kg bw per day in a 2-year study of toxicity and carcinogenicity in rats, a 1-year study of toxicity in dogs, and studies of reproductive toxicity in rats and rabbits, and using a safety factor of 100. In 2004, the Meeting established an ARfD for folpet of 0.2 mg/kg bw for women of childbearing age only, based on a NOAEL of 20 mg/kg bw per day for increased incidences of hydrocephalus at 60 mg/kg bw per day in rabbits and using a safety factor of 100.

The Meeting concluded that the database was insufficient (particularly with regard to information about the possible developmental effects of the metabolite phthalimide) to establish the mode of action by which the increased incidence of hydrocephalus was induced.

The sponsor conducted a study of developmental toxicity with phthalimide, and studies to evaluate the potential effects of folpet and phthalimide on the intestinal flora of the rabbit. It is known that the rabbit is dependent on the presence of caecotrophs for adequate nutrition. The sponsor suggested that disruption of the intestinal flora might result in maternal malnutrition, with possible consequent adverse effects on foetal development.

At the request of the CCPR at its 39th Session,[37] the present Meeting reconsidered the ARfD for folpet on the basis of new data.

All pivotal studies with folpet and phthalimide were certified as being compliant with GLP.

Toxicological data

Data evaluated by JMPR 2004

With respect to the kinetics and metabolism of folpet, the following description is quoted from JMPR 2004:

> In rodents treated orally, folpet is rapidly degraded to phthalimide and thiophosgene (via thiocarbonyl chloride). Studies of metabolism in vitro with human blood revealed that folpet is rapidly degraded to phthalimide, with a calculated half-life of 4.9 s. Thiophosgene is rapidly detoxified by reaction with cysteine or glutathione, for example, and is ultimately rapidly excreted.

With respect to the developmental toxicity of folpet the following description is quoted from JMPR 2004:

> In a study from the published literature, the teratogenic effects of a number of phthalimide derivatives, including folpet, were tested in pregnant golden hamsters. The Meeting noted that this study has major limitations (e.g., small number of animals per dose, limited reporting of the data) and is therefore of limited value. It does, however, suggest that developmental effects may occur after a single exposure to folpet, albeit at maternally toxic doses.
>
> Folpet has been tested in a number of studies of developmental toxicity in rats. In two out of three studies, no foetal developmental anomalies were found at doses of up to 800 mg/kg bw per day. In one study, however, a possible slight increase in developmental anomalies was reported at 150 mg/kg bw per day.
>
> Folpet has been tested in a number of studies of developmental toxicity in rabbits treated by gavage. In a study in which New Zealand white rabbits were given folpet at a dose of 0, 10, 20, or 60 mg/kg bw per day on days 6–28 of gestation, the NOAEL for maternal toxicity was 10 mg/kg bw per day on the basis of reduced body-weight gain and food consumption. The NOAEL for foetal toxicity was 10 mg/kg bw per day on the basis of reduced foetal body weights. The maternal toxicity and the associated reduction in foetal body weight are likely to be caused by high local concentrations of folpet and are not considered to be relevant to dietary exposure. At 60 mg/kg bw per day, there was a significant increase in the incidence of hydrocephaly in four foetuses out of three litters. In these same foetuses, skull, gastric, and pulmonary abnormalities were also observed. As the observation of hydrocephaly and cleft palate in one foetus at the intermediate dose was considered to be within the historical control range, the NOAEL for these effects was 20 mg/kg bw per day.
>
> In a second study, HY/CR New Zealand white rabbits were given folpet at a dose of 0, 10, 40, or 160 mg/kg bw per day on days 7–19 of gestation. The NOAEL for maternal toxicity was 10 mg/kg bw per day on the basis of reductions in body-weight gain and in gravid uterine weight. The NOAEL for foetal toxicity was 10 mg/kg bw per day on the basis of an increased incidence of bilateral lumbar ribs and delayed skeletal maturation.
>
> In a pulse-dose study, pregnant D1A *Hra:* (New Zealand white) rabbits were given folpet at a dose of 60 mg/kg bw per day by gavage on days 7–9, 10–12, 13–15, or 16–18 of gestation. There were occasional occurrences of abortion, but it was not clear whether these abortions were related to treatment with folpet. Maternal body weight and food consumption were significantly reduced in all treated animals. Two foetuses with hydrocephalus were observed, one in the group treated on days 10–12 of gestation and one in the group treated on days 16–18 of gestation. These incidences were considered to be within the historical control range. A significantly increased incidence (12.1%) of foetuses with an irregularly shaped fontanelle was observed in the group treated on days 13–15 of gestation; the incidence in controls was 4.5%. The significance of these effects was not clear.

The results of studies considered by the Meeting in 2004 suggested that folpet was rapidly degraded to phthalimide. The other component of the parent molecule, thiophosgene, is rapidly

[37] Codex Alimentarius Commission. *Report of the 39th Session of the Codex Committee on Pesticide Residues, 7–12 May 2007, Beijing, China* (ALINORM07/30/24).

detoxified by reaction with cysteine or glutathione, for example, and is ultimately rapidly excreted. During the present Meeting, the sponsor provided a toxicokinetic study in rats, not previously evaluated by JMPR.

Toxicokinetics

In a toxicokinetic study in rats, concentrations of folpet and its metabolites were measured in the faeces and urine. The study was evaluated by the present Meeting, focusing on concentrations of folpet in order to establish the amount of folpet that reaches the distal parts of the gastrointestinal tract.

Rats were given [^{14}C] labelled folpet at a dose of 10 or 500 mg/kg bw by gavage. Extracts of urine were qualitatively analysed by high-performance liquid chromatography (HPLC) and GC/MS. Phthalamic acid was found only in the urine. Extracts of faeces were qualitatively analysed by TLC by comparison with reference compounds. Quantification of faecal metabolites was performed by linear plate scanner and autoradiography. Several compounds were identified in faeces, including phthalimide, phthalamic acid, phthalic anhydride and parent folpet. Toxicokinetic data are presented in Table 11.

Table 11. Toxicokinetic data for rats given [^{14}C] labelled folpet by gavage

Dose	Radioactivity excreted, males/females (% of administered dose)		Folpet in urine (% of radioactivity)	Folpet in faeces	
	Urine	Faeces		% of radiolabel (males/females)	% of total dose
10 mg/kg bw, single dose	91.7/92.7	6.4/5.1	ND	15/27	0.5–1.5
10 mg/kg bw, repeated doses	88.3/84.0	7.6/7.8	ND	18/17	1.3–1.4
500 mg/kg bw	56.5/60.5	41.3/39.6	ND	93/92	36.8–38.4

ND, not detected.

After a single dose at 10 mg/kg bw, about 92% and 6% of the radiolabel administered was recovered from the urine and faeces, respectively. At this single dose, no folpet was detected in the urine. Of the radiolabel recovered from the faeces, 0.5–1.5% was associated with folpet. After 14 consecutive doses at 10 mg/kg bw per day, the proportions of folpet in faeces were similar to those found after a single dose at 10 mg/kg bw; folpet was not detected in the urine. At 500 mg/kg bw, 56–60% and 39–41% of the radiolabel administered was recovered from the urine and faeces, respectively. No folpet was detected in the urine. Of the radiolabel recovered from the faeces, 36.8–38.4% was identified as folpet.[38]

Developmental toxicity

In a study of developmental toxicity, groups of 25 time-mated female New Zealand White rabbits received daily administrations of phthalimide (purity, 100%) at a dose of 0, 5, 15 or 30 mg/kg bw per day by gavage from days 6 to 28 after mating. The vehicle was water containing 0.5% w/v Tween 80 and 0.7% w/v carboxymethylcellulose. In view of the relative molecular masses of folpet (296.6) and phthalimide (147.1), the dose of phthalimide of 30 mg/kg bw per day would be equimolar to a dose of folpet of about 60 mg/kg bw per day. All animals were examined twice per day for clinical signs. Body weight was recorded daily from the day of mating until day 29 of gestation, when they were

[38] Wood, S.G., Chasseaud, L.F., Cheng, K., Hall, M., Fitzpatrick, K., Iqbal, S., Barlett, A. (1991) Metabolic fate of ^{14}C-folpet in Sprague-Dawley rats. Unpublished report No HRC/MBS 41/91499 from Huntingdon Life Sciences Limited, Woolley Road, Alconbury, Huntingdon, Cambridgeshire. Submitted to WHO by Makhteshim Chemical Works, Beer-Sheva, Israel.

killed. Food intake was recorded daily from the first day after mating until day 29 of gestation. On day 29, the animals were killed and examined macroscopically. In females in the control group and in the group receiving the highest dose, the duodenum and sphincter of Oddi (hepatopancreatic sphincter) were examined microscopically. The ovaries and uterus were removed and the foetuses were weighed and examined for visceral and skeletal abnormalities.

There were no mortalities. At necropsy, in the control group, and the groups at 5 and 15 mg/kg bw per day, three, five and two females, respectively, did not appear to be pregnant. One female in the control group aborted on day 21 and one female in the group at 15 mg/kg bw per day appeared to have total litter resorption. In the dams, no treatment-related clinical signs or effects on body weight and food consumption, and no macroscopic or microscopic abnormalities were observed. Increases in implantation losses were observed in the treated groups (19.3%, 24.0%, 26.8% and 36.0% in the control group and the groups receiving the lowest, intermediate and highest dose, respectively), reaching statistical significance for pre-implantation loss in the group receiving the highest dose. Since implantation in rabbits occurs at around days 7–8 after mating, the effects on pre-implantation loss may have been treatment-related. Increases in pre-implantation losses were observed in the treated groups (13.4%, 16.9%, 19.5% and 25.7% in the control group and in the groups receiving the lowest, intermediate and highest dose, respectively), reaching statistical significance in the group receiving the highest dose. In the group at the highest dose, reductions in the mean number of implantations and number of live foetuses were considered to be the result of increased implantation loss. The slightly lower mean litter weights and slightly increased foetal weights in the group at the highest dose were considered to reflect the decreased number of implantations in this group.
In the foetuses, no treatment-related effects on visceral and skeletal parameters were observed.

The NOAEL for maternal toxicity was 30 mg/kg bw per day i.e., the highest dose tested. The NOAEL for embryo/fetotoxicity was 15 mg/kg bw per day on the basis of increased pre-implantation loss at the highest dose.[39]

Inhibition of microbial activity in vitro

A study was performed to determine minimum inhibitory concentrations (MIC) of folpet (purity, 95.8%) against two bacterial species (*Bacteroides* sp. and *Enterococcus faecalis*) and one species of yeast (*Candida albicans*). These bacteria were considered to be representative of anaerobic bacteria in the rabbit gut. *Candida albicans* was considered to be representative of yeast that may occur in the rabbit gut. The MIC values for *Bacteroides* sp., *Enterococcus faecalis* and *Candida albicans* were 20–50, 50–200 and 5 µg/mL, respectively. The Meeting concluded that folpet demonstrates antimicrobial activity against organisms considered representative of rabbit gut flora.[40]

In a study to determine MIC of phthalimide (purity, 100%), the MIC values for *Bacteroides* sp., *Enterococcus faecalis and Candida albicans* were all > 1000 µg/mL, except for one strain of *C. albicans* strain for which the MIC value was 1000 µg/mL. The Meeting concluded that phthalimide demonstrates no significant antimicrobial activity against organisms considered representative of rabbit gut flora.[41]

The Meeting concluded that the existing database, i.e., the new studies conducted after 2004 and the previously evaluated studies, was adequate to characterize the potential hazards of folpet to foetuses, infants and children.

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[39] Blee, M.A.B. (2006) Tetrahydrophthalimide. Prenatal toxicity study in the rabbit by oral gavage administration. Unpublished report No R-18202, MAK 864/053232 from Huntingdon Life Sciences Limited, Woolley Road, Alconbury, Huntingdon, Cambridgeshire. Submitted to WHO by Makhteshim Chemical Works, Beer-Sheva, Israel.

[40] Akhurst, L.C (2005a) Captan: determination of minimum inhibitory concentration against selected micro-organisms representative of rabbit gut microflora. Unpublished report No. R-18666, MAK 0888/052848 from Huntingdon Life Sciences Ltd, Huntingdon, Cambridgeshire, England. Submitted to WHO by Makhteshim Chemical Works, Beer-Sheva, Israel.

[41] Akhurst, L.C (2005b) THPI: determination of minimum inhibitory concentration against selected micro-organisms representative of rabbit gut microflora. Unpublished report No. R-18735, MAK 0890/053252 from Huntingdon Life Sciences Limited, Huntingdon, Cambridgeshire, England. Submitted to WHO by Makhteshim Chemical Works, Beer-Sheva, Israel.

Toxicological evaluation

In 2004 JMPR established an ARfD of 0.2 mg/kg bw for women of childbearing age only based on a NOAEL of 20 mg/kg bw per day identified on the basis of an increased incidence of hydrocephalus at 60 mg/kg bw per day in the study in rabbits and using a safety factor of 100.

On the basis of the study of developmental study with phthalimide in rabbits, the Meeting considered that it is unlikely that phthalimide (or its metabolites, including phthalamic acid) is a teratogenic agent.

In view of the results of studies of microflora inhibition, the hypothesis that the inhibition of caecal microflora in the rabbit by folpet causes malnutrition was plausible. However, although unchanged folpet was not detected in the urine of rats given single low or high doses, this does not necessarily imply a lack of systemic absorption of the parent compound, as folpet is rapidly metabolized. Certainly, toxicokinetic studies with structurally-related captan suggested that this compound is systemically available after oral administration. Thus it could not be excluded that the embryo/fetotoxic effects observed in a study of developmental toxicity with folpet in rabbits could be a result of a direct action of folpet or one of its metabolites. Furthermore, equivalent toxicokinetic and metabolism studies in rabbits, the species in which the critical developmental effects of concern were seen, did not appear to have been performed.

In view of these considerations, the Meeting concluded that there was no sound basis on which to change the ARfD established in 2004. The Meeting reconfirmed the ARfD of 0.2 mg/kg bw based on a NOAEL of 20 mg/kg bw per day identified on the basis of an increased incidence of hydrocephalus at 60 mg/kg bw per day in the study in rabbits and using a safety factor of 100. This ARfD applies to women of childbearing age. The Meeting concluded that it was unnecessary to establish an ARfD for the general population.

An addendum to the toxicological monograph was not prepared.

Estimate of acute reference dose

0.2 mg/kg bw, for women of childbearing age
Unnecessary for the rest of the general population

Information that would be useful for the continued evaluation of the compound

Results from epidemiological, occupational health and other such observational studies of human exposures.

5.16 INDOXACARB (216)

RESIDUE AND ANALYTICAL ASPECTS

Indoxacarb was evaluated for the first time by JMPR in 2005 and an ADI of 0-0.01 mg/kg bw was established. An ARfD of 0.1 mg/kg bw was also established. MRLs were recommended for a number of crop and animal commodities.

An MRL of 3 mg/kg was recommended for head cabbages.

CCPR at its 39th Session (2007) decided to return the MRL for head cabbages to Step 6 because of short-term intake concerns and noted that indoxacarb had been scheduled for evaluation by 2007 JMPR (alternative GAP) (ALINORM 07/30/24 – Rev 1, paragraph 127).

The 2005 JMPR evaluated the supervised residue trials for indoxacarb uses on cabbage. The recommended maximum residue level for cabbage was based on the combined residue data from USA (0.21, 0.34, 0.38 and 2.7 mg/kg) and South Africa (0.40, 0.47, 0.83 and 2.0 mg/kg). The IESTI was based on the estimated HR of 2.7 mg/kg.

Data on residues including and excluding wrapper leaves were provided in the US trials on head cabbage recorded in the JMPR Evaluations of 2005. The cabbages including wrapper leaves are intended to represent the commodity in trade, so data on cabbages including wrapper leaves are used to support the MRL. The Meeting was informed that, in the USA, cabbages excluding wrapper leaves are intended to represent the edible portion.

In the four US trials at the GAP PHI of 3 days, mean residues of indoxacarb + R enantiomer in cabbages including wrapper leaves were: 0.21, 0.34, 0.38 and 2.7 mg/kg; and without wrapper leaves were: 0.020, 0.034, 0.025 and 0.054 mg/kg respectively. The highest residue in edible portion from the US trials was 0.054 mg/kg.

In the four South African trials at PHI 3 days (GAP PHI of 3 days), mean residues of indoxacarb + R enantiomer in cabbages were: 0.40, 0.47, 0.83 and 2.0 mg/kg. The commodity analysed was described as "whole heads".

A letter from SABS Commercial[42], where the cabbage samples were analysed, explained that the laboratory policy is to remove obviously damaged, decomposed or withered leaves before shredding and mixing. The laboratory does not automatically remove the outer leaves of a fresh head of cabbage as the heads are picked in such a way that damaged and non-edible parts will remain on the fields.

This information suggests that the intention in the South African trials was to analyse edible portion. The highest residue in edible portion from the South African trials was 2.0 mg/kg.

The Meeting estimated an HR for head cabbage of 2.0 mg/kg.

DIETARY RISK ASSESSMENT

Short-term intake

The IESTI of indoxacarb calculated on the basis of the recommendations for cabbage made by the JMPR represented 90% of the ARfD (0.1 mg/kg bw) for children and 40% for the general population.

The Meeting concluded that the short-term intake of residues of indoxacarb resulting from uses that have been considered by the JMPR is unlikely to present a public health concern.

5.17 PHOSMET (103) – ALTERNATIVE GAP

Phosmet has been evaluated several times for residues by the JMPR from 1976 to 1997. Additional residue information on citrus fruits, pears, nectarines and blueberries was evaluated by the JMPR in 2002. The 2002 JMPR estimated short-term intakes that exceeded the ARfD of 0.02 mg/kg bw for apple, blueberry, citrus fruits, nectarine and pear. The Meeting noted that the ARfD of 0.02 mg/kg bw was conservative and might be refined.

A new ARfD of 0.2 mg/kg bw was established in 2003. The Meeting estimated short-term intakes that exceeded the ARfD for apple (230% children) and pear (150% children). No acute intake concern was estimated for the other commodities (JMPR Report 2003, p. 20 and p. 173).

At the 38th Session of the CCPR in 2006, the Committee noted the acute intake concerns expressed by Australia, the European Union and the USA. The Committee decided to return the draft MRLs for apricot, blueberries, citrus fruit, nectarine and pome fruits to Step 6 and decided to request JMPR to consider using alternative GAP to recommend lower MRLs for these commodities.

New data for GAP and new supervised residue trials were submitted to the 2007 JMPR for pome fruits. New supervised residue trials data were also submitted for oranges and peaches.

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[42] Garbers HV. 8-Jan-2007. Indoxacarb residues in cabbage. Letter. Reference 17/36/8. SABS Commercial (Pty) Ltd, Pretoria, South Africa.

Results of supervised residue trials on crops

Data from new supervised trials on oranges, apples, pears and peaches/nectarines were evaluated. Furthermore, data on citrus fruits, apricots/peaches/nectarines and blueberries which were reviewed in the 1997 and 2002 monographs were interpreted by the current Meeting in the light of the acute intake concerns expressed at the 38th Session of CCPR.

Citrus fruits

In Brazil, phosmet may be used on citrus fruits at 1.5 kg ai/ha and 0.075 kg ai/hL with a PHI of 14 days.

Two Brazilian trials on oranges carried out in 2002 were submitted to the current Meeting. In one Brazilian trial where phosmet was used five times at 2 kg ai/ha and 0.1 kg ai/hL with a PHI of 10 days, the residue found was 1.3 mg/kg. In the second trial (5 × 4 kg ai/ha, 0.2 kg ai/hL with a PHI of 10 days), the residue was 2.2 mg/kg. The Meeting noted that the field trial application rates did not match the GAP rates; as a consequence the residue data could not be used.

Phosmet is registered in Spain for use on citrus fruits at 0.075–0.15 kg ai/hL with a PHI of 30 days.

The 2002 JMPR estimated a maximum residue level and an STMR for phosmet in citrus fruits of 3 mg/kg and 0.64 mg/kg (whole fruit) on the basis of 16 residue supervised trials data for mandarins, tangerines and oranges matching the Spanish GAP. Furthermore, STMR and HR values for phosmet in citrus edible portion of 0.21 and 0.52 mg/kg were estimated.

The current Meeting noted that the acute dietary risk assessment for phosmet, as presented in the 2003 JMPR Report (ARfD: 0.2 mg/kg bw), is unlikely to present a public health concern for citrus (≤ 10% for children and the general population). Therefore, it is not necessary to retrospectively consider an alternative GAP for citrus fruits.

The Meeting estimated a maximum residue level of 3 mg/kg, confirming the previous recommendation, and an STMR and HR of 0.21 and 0.52 mg/kg for citrus edible portion.

Pome fruits

Phosmet is registered in the USA for use on apples at 1.7–4.1 kg ai/ha and on pears at 1.7–5.6 kg ai/ha with a PHI of 7 days.

Based on US residue trials and the US GAP, the 2002 JMPR estimated a maximum residue level, an STMR and an HR value for phosmet in pome fruits of 10, 3.3 and 7.3 mg/kg, respectively. The 2003 Meeting estimated short-term intakes that exceeded the ARfD of 0.2 mg/kg bw for apple (230% for children) and pear (150% for children).

New GAP data on pome fruit from Brazil and Spain were submitted to the 2007 JMPR. The Meeting also received new supervised residue trial data on apples and pears from Brazil, Spain, France and Italy.

Phosmet is registered in Brazil for use on apples at two applications of 1 kg ai/ha at 0.1 kg ai/hL with a PHI of 14 days.

Ten apple trials were carried out in Brazil from 2002–2006 (5 × 1–2 kg ai/ha, at 0.1–0.2 kg ai/hL, PHI 7 days) however, none matched the Brazilian GAP.

Phosmet is registered in Spain for use on pome fruits at 0.075–0.125 kg ai/hL with a PHI of 30 days.

In one French and one Italian trial on apples in 2004 (2 × 0.125 kg ai/hL, PHI 28 or 29 days) matching Spanish GAP, the residues were 0.34 and 0.41 mg/kg.

In Spain, residue trials were carried out from 2001 to 2002 on apples and pears with three applications of 0.125 kg ai/hL and a PHI of 21 days. The residues in apples were 0.06, 0.26, 0.31, 0.32, 0.47, 0.83, 0.92, 1.3 and 1.8 mg/kg. The residues in pears were 0.07, 0.16 and 0.79 mg/kg. The

Meeting noted that the PHI of 21 days was shorter than the registered 30 days but considered the trials for evaluation as they were within ± 30% of the GAP.

The Meeting decided to combine the European apple and pear data for pome fruit. The combined pome fruit data (14 values), in ranked order were: 0.06, 0.07, 0.16, 0.26, 0.31, 0.32, 0.34, 0.41, 0.47, 0.79, 0.83, 0.92, 1.3 and 1.8 mg/kg.

Based on the alternative GAP from Spain and new residue supervised trials data from Spain, Italy and France, the Meeting estimated a maximum residue level of 3 mg/kg for phosmet in pome fruit to replace the previous recommendation of 10 mg/kg.

The Meeting estimated an STMR and an HR for phosmet in pome fruits of 0.38 and 1.8 mg/kg.

Apricots and nectarines

The previous MRL recommendation was based on the GAP of the USA and USA residue data. New GAP data on peaches from Brazil and on stone fruit from Spain were submitted to the 2007 JMPR. The Meeting also received new supervised residue trial data on peaches and nectarines from Brazil and Spain.

Phosmet is registered in Brazil for use on peaches at three applications of 0.6–0.8 kg ai/ha and 0.075–0.1 kg ai/hL with a PHI of 7 days.

Ten trials on peaches and nectarines were carried out in 2000 in Brazil but only three of them matched GAP. Residues of phosmet were 0.5, 1.0 and 2.7 mg/kg.

Phosmet is registered in Spain for use on stone fruits at 0.075–0.125 kg ai/hL with a PHI of 30 days.

In Spain, residue trials were carried out in 2001 and 2002 on peaches and nectarines with two applications of 0.125 kg ai/hL and a PHI of 21 days. The residues were 0.31, 0.34, 0.37, 0.42, 0.71 and 1.5 mg/kg. The Meeting noted that the PHI of 21 days was shorter than the registered 30 days but considered the trials for evaluation as they were within ± 30% of the GAP.

Phosmet is registered in the USA for use on apricots, peaches and nectarines at 1.7–3.3 kg ai/ha with a PHI of 14 days.

The 1997 JMPR estimated a maximum residue level, an STMR and an HR value for phosmet in apricots of 10, 1.6 and 6.8 mg/kg, respectively, based on US residue data for peaches and apricots matching the US GAP. No maximum residue level was estimated for nectarines.

The 2002 JMPR noted that the GAP reported for peaches and apricots in the evaluation by the 1997 JMPR was the same as for nectarines. The 2002 Meeting agreed that the residues trials reported for peaches and apricots could be used to support a recommendation for nectarines. The Meeting estimated a maximum residue level, an STMR and an HR value for phosmet in nectarines of 10, 1.6 and 6.8 mg/kg, respectively, based on US residue data for peaches and apricots matching the US GAP.

Based on the estimations of the 1997 and 2002 Meetings, the 2007 JMPR noted that the acute dietary risk assessment for phosmet, as presented in the 2003 JMPR Report, shows an acceptable consumer risk for apricots (ARfD: 0.2 mg/kg bw per day - general population 20%, children 90%) and nectarines (general population 40%, children 100%). Therefore, it was deemed unnecessary to retrospectively consider an alternative GAP for both commodities. The current Meeting confirmed the recommendation by the 2002 JMPR.

The Meeting estimated a maximum residue level of 10 mg/kg which confirms the previous recommendation, and an STMR and HR of 1.6 and 6.8 mg/kg for apricots and nectarines.

Blueberries

US GAP permits application of phosmet to blueberries at 1 kg ai/ha and harvest 3 days after the final application.

Based on nine US residue trials, matching the GAP of the USA, the 2002 JMPR estimated a maximum residue level, an STMR value and an HR value for phosmet in blueberries of 15, 4.0 and 9.9 mg/kg, respectively.

The current Meeting noted that the acute dietary risk assessment for phosmet, which is presented in the 2003 JMPR Report (ARfD: 0.2 mg/kg bw per day), shows an acceptable consumer risk for blueberries (general population 10%, children 40%). Therefore, it was deemed unnecessary to retrospectively consider an alternative GAP for blueberries.

The Meeting estimated a maximum residue level of 15 mg/kg which confirms the previous recommendation, and an STMR and HR of 4.0 and 9.9 mg/kg for blueberries.

DIETARY RISK ASSESSMENT

Long-term intake

The estimates of long-term dietary intake for phosmet (ADI 0–0.01 mg/kg bw) calculated by the JMPR in 2002 for the five regional diets were 5–40% of the ADI. Because the STMR for pome fruit has changed, the dietary intakes were recalculated by the current Meeting for the 13 GEMS/Food Consumption Cluster Diets on the basis of the STMRs estimated by the JMPR in 2002 (cotton seed, grapes, peach, potato, tree nuts) and 2007 (apricot, blueberries, citrus fruits, nectarine, pome fruit). The results are shown in Annex 3.

The International Estimated Daily Intakes (IEDI) of phosmet, based on estimated STMRs were 2–90% of the maximum ADI (0.01 mg/kg bw). The Meeting concluded that the long-term intake of residues of phosmet from uses considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The International Estimated Short Term Intake (IESTI) of phosmet was calculated for the commodities for which residue levels were estimated. The results are shown in Annex 4.

The IESTI of phosmet calculated on the basis of the recommendations made by the 2007 JMPR represented 0–100% of the ARfD (0.2 mg/kg bw) for children and 1–50% for the general population. The Meeting concluded that the short-term intake of residues of phosmet resulting from uses considered by the JMPR is unlikely to present a public health concern.

5.18 PROCYMIDONE (136)

TOXICOLOGY

Procymidone is the ISO approved name for *N*-(3,5-dichlorophenyl)-1,2-dimethylcyclopropane-1,2-dicarboximide (IUPAC), CAS No. 32809-16-8. It is a dicarboximide fungicide that is used on a range of vegetables, fruits, soya bean, sunflowers, tobacco and oil seed rape, as well as on ornamental plants and flower bulbs. The mechanism of pesticidal action involves the inhibition of triglyceride synthesis in fungi.

Procymidone was previously evaluated by JMPR in 1981, 1982 and 1989 (Annex 5, references *37*, *39*, *58*). No ADIs were established when procymidone was evaluated by the JMPR in 1981 and 1982. In 1989, an ADI of 0–0.1 mg/kg bw was established based on the NOAEL of 12.5 mg/kg bw per day identified in studies of reproductive toxicity in rats. Procymidone was re-evaluated by the present Meeting as part of the Periodic Re-evaluation Programme of the CCPR. A range of new studies was submitted to the present Meeting; these studies addressed kinetics, developmental toxicity and hormonal effects across different species.

Many of the conventional studies of toxicity with procymidone were relatively old, were performed before the widespread use of GLP and some contained relatively limited information. Overall, the Meeting considered that the database was adequate for the risk assessment.

Biochemical aspects

Studies with [^{14}C] labelled procymidone showed that radiolabel was rapidly absorbed (C_{max}, 2–8 h) and rapidly eliminated (> 80% in 24 h) in mice and rats. Absorption was extensive, as shown by the high level of urinary excretion (> 80% of the administered dose), with similar results obtained in mice and rats receiving doses of up to 100 mg/kg bw. At higher doses, the proportion of the administered dose excreted in the faeces increased: at 250 mg/kg bw, 24–33% was eliminated by that route after 168 h; the increase in faecal radioactivity was mainly attributable to an increase in unabsorbed procymidone (18–27% of the administered dose). Only low levels (< 0.3%) of radioactivity were retained 168 h after oral administration; the highest levels were found in fat. The major metabolic pathway for procymidone in mice and rats involved the oxidation of the methyl groups to hydroxymethyl or carboxylic acid derivatives, cleavage of the imide, and glucuronide formation of the resultant metabolites. In cynomolgus monkeys, rabbits and chimeric mice with humanized livers (i.e., liver repopulated with human hepatocytes), there was more extensive urinary excretion of glucuronide conjugates than in rats or normal mice. In rats, the glucuronides were formed, but were present in the bile and appear to be deconjugated and the aglycone was reabsorbed giving a prolonged elimination phase and relatively high AUC. Studies in vitro with liver preparations from humans, rabbits, cynomolgus monkeys and rats showed that the rate of metabolism of procymidone and hydroxy-procymidone was significantly lower in rats than in the other species studied.

In female cynomolgus monkeys, there was an increase in C_{max} and AUC values after repeated doses. In other species, the routes and rates of tissue distribution, biotransformation and excretion of procymidone were similar in males and females and after single or repeated administration.

Procymidone has a high binding affinity in vitro (92–98% bound) for plasma proteins when incubated with plasma from female rats, cynomolgus monkeys, rabbits and humans. The alcohol metabolite PCM-CH_2OH had a slightly lower binding affinity (77–91% in all species) than procymidone, with the highest affinity being for human plasma proteins.

Kinetic studies in rats, rabbits and cynomolgus monkeys (dams and foetuses of each species) have been performed as part of investigations of the effects on male rat reproductive tissues. After a single dose, cynomolgus monkeys had much lower C_{max} values for total radioactivity than did rabbits and rats, but at doses of up to 125 mg/kg bw rabbits had relatively low AUC values owing to rapid elimination. In cynomolgus monkeys, the predominant compound in plasma was procymidone; in rabbits, acid metabolites and glucuronides of alcohol metabolites were the major components in plasma; in rats, free alcohol metabolites predominated. After 14 doses at 37.5–500 mg/kg bw per day, C_{max} and AUC values for total radioactivity were similar for rats and cynomolgus monkeys. These findings show that the doses used in the studies of developmental toxicity in cynomolgus monkeys would have produced similar plasma concentrations of total radioactivity, but with different metabolite profiles, to those in rats at doses resulting in hypospadias. Investigations of the transfer of procymidone and metabolites to foetuses again showed species differences. After dosing at 125 mg/kg bw per day, the concentrations of procymidone and metabolites in the foetus were significantly greater (10-fold or greater) in rats than in rabbits or cynomolgus monkeys. In rats, the relative concentrations of PCM-CH_2OH in the foetus versus the dam were much higher than in rabbits or cynomolgus monkeys.

Toxicological data

Procymidone was of low acute toxicity by the oral (LD_{50} > 5000 mg/kg bw) and dermal (LD_{50} > 2500 mg/kg bw) routes, and after a 4-h exposure by inhalation (LC_{50} > 1.5 mg/L). Procymidone is not an eye irritant, but is a slight, transient skin irritant. Procymidone did not produce delayed contact hypersensitivity in guinea-pigs in either the maximization or repeat-injection tests.

The primary target organs in rats and mice exposed to procymidone in repeat-dose studies were the liver and testes. The major effect of short-term dietary administration of procymidone in ICR mice was on the liver. Centrilobular hepatocyte hypertrophy was noted in male mice and hepatocyte granuloma in females that received procymidone at 500 ppm, equal to 71 mg/kg bw per day, for 13

weeks; the NOAEL was 150 ppm, equal to 22 mg/kg bw per day. In a subsequent study with B6C3F$_1$ mice, multifocal coagulative necrosis of hepatic parenchyma, centrilobular cytoplasmic swelling, nuclear enlargement, coarsely dispersed chromatin and multinucleate hepatocytes were noted in mice receiving procymidone at 10 000 ppm, equivalent to 1430 mg/kg bw per day. This was accompanied by increased liver weight and serum alanine aminotransferase activity in males and higher cholesterol concentrations in females. The histopathological effects were apparent to a lesser extent in animals treated with procymidone at 500 or 2500 ppm, equivalent to 71 and 355 mg/kg bw per day respectively. The NOAEL was 100 ppm, equal to 19.6 mg/kg bw per day. An increase in the incidence of testicular atrophy was noted in mice receiving procymidone at 500 ppm for 26 weeks, the NOAEL was 150 ppm, equal to 20 mg/kg bw per day. In an additional 6-month study, the NOAEL for effects on the testes was 300 ppm, equal to 37 mg/kg bw per day. The Meeting considered that the overall NOAEL in three short-term studies in mice was 300 ppm, equal to 37 mg/kg bw per day.

The only short-term study in rats included a 6-month exposure period with or without a 3-month recovery phase, and a 9-month exposure period. In Sprague-Dawley rats, there was a significant reduction in body-weight gain among females receiving procymidone at 1500 ppm, equivalent to 75 mg/kg bw per day, for 6 months (although this was not significant after an exposure of 9 months) and an increase in liver-to-body-weight ratio in both sexes. The liver-to-body-weight ratio was also increased in female rats at 500 ppm, equivalent to 25 mg/kg bw per day, and there was an increase in spleen-to-body-weight ratio at 500 and 1500 ppm. Absolute and relative weights of the testes were increased after 9 months at 1500 ppm. The only treatment-related histopathological effect was swelling of the liver cells in male rats at 1500 ppm. The findings showed clear evidence of reversal over the 3-month recovery phase. The NOAEL was 500 ppm, equivalent to 25 mg/kg bw per day.

In a 28-day study of dermal exposure, there were no treatment-related local or systemic changes when doses of up to 1000 mg/kg bw per day were applied to the shaved backs of rats.

Emesis and diarrhoea were the principal signs of toxicity in dogs given procymidone at 500 mg/kg bw per day for 26 weeks. At that dose, there was also an increase in serum alkaline phosphatase activity, blood urea nitrogen (BUN) and calcium concentrations. The NOAEL was 100 mg/kg bw per day. In a 52-week study in dogs, there was an increase in emesis and soft faeces and increases in serum globulin and alkaline phosphatase activity at 500 mg/kg bw per day. The NOAEL was 100 mg/kg bw per day.

Procymidone gave negative results in an adequate range of assays for genotoxicity in vitro and in vivo. The Meeting concluded that procymidone was unlikely to be genotoxic.

The toxicity and carcinogenicity of procymidone had been investigated in long-term studies in mice and rats. In the study in mice, treatment-related effects were limited to the liver. Higher liver weights and liver-to-body-weight ratios were apparent in males at 100 ppm, equal to 15 mg/kg bw per day, and in both sexes at 300 and 1000 ppm, equal to 46 and 153 mg/kg bw per day respectively, and there were histopathological changes in the liver, comprising increased incidences of centrilobular cytomegaly in males at 1000 and 300 ppm and in females at 1000 ppm. In addition, focal or multifocal hepatocellular hyperplasia, and eosinophilic foci were noted in females at 1000 ppm. There was an increased incidence of hepatocellular adenomas in females at the highest dose. There was also an increase in the incidence of hepatoblastomas in males receiving procymidone at 1000 ppm. The NOAEL for toxicity was 100 ppm, equal to 15 mg/kg bw per day, on the basis of a range of liver effects at 300 ppm. The NOAEL for carcinogenicity was 300 ppm, equal to 46 mg/kg bw per day, on the basis of increases in liver tumours in males and females at 1000 ppm.

In the long-term study in rats, the liver was a target organ and reproductive organs were also affected. There was a reduction in body-weight gain among rats given procymidone at 1000 and 2000 ppm , equal to 48 and 97 mg/kg bw per day respectively. Effects on organ weights were noted at both these doses and consisted of increased relative and absolute weight of the liver in both sexes and increased weights of the testes and ovaries at dietary concentrations of 1000 ppm and greater. Histopathology revealed an increased incidence of centrilobular cytomegaly in the liver of both sexes at dietary concentrations of 1000 ppm and greater. At 1000 and 2000 ppm, there were increases in the

incidence of interstitial cell tumours and interstitial cell hyperplasia in the testes; the incidence of ovarian stromal hyperplasia was statistically significantly increased at 2000 ppm. The NOAEL for general toxicity and for carcinogenicity was 300 ppm, equal to 14 mg/kg bw per day.

Procymidone induced liver tumours in mice and testicular tumours in rats. No specific mechanistic studies have been performed to investigate the liver tumours; however, hepatocellular hypertrophy was present in shorter-term studies, and mice are sensitive to the production of liver tumours in response to such effects produced by high levels of xenobiotics. Procymidone gave negative results in assays for genotoxicity in vitro and in vivo. A clear threshold for induction of liver tumours was identified in the study of carcinogenicity in mice. Investigative work on the endocrine effects of procymidone indicated that it binds to the androgen receptor with a similar potency to that of the prostate-cancer drug flutamide, and that in rats the mechanism of hormonal action appeared to be via binding to the androgen receptor, disrupting the feedback controls on LH and testosterone levels. Overall, the data suggest that procymidone may induce testicular interstitial cell tumours via an endocrine-mediated mechanism. Although this mode of action is relevant to humans, there is good evidence to suggest that humans are less sensitive to chemically-induced interstitial cell tumours of the testis than rats, owing to differences in sensitivity to LH based on Leydig-cell receptor number and control of LH receptor expression (e.g., via prolactin in rodents but not in humans).

The Meeting concluded that procymidone was unlikely to present a carcinogenic risk to humans at typical levels of dietary exposure.

The reproductive toxicity of procymidone had been investigated in two studies in rats. The developmental toxicity of procymidone had been studied in conventional studies in rats and rabbits and in special investigative studies in rats, rabbits and cynomolgus monkeys.

In the first generation of the two-generation study in rats, there was no effect on mating and reproduction, but at 750 ppm, equivalent to 50 mg/kg bw per day, there was an increase in the number of male pups with hypospadia and reduced anogenital distance. In the second generation, male fertility was reduced and the incidence of hypospadia was increased at 750 ppm. In parents and pups, there were increases in testes weights and decreases in body-weight gain, prostate and epididymis weights at 750 ppm, with the organ-weight changes also present in pups at 250 ppm. There were no adverse effects on female reproductive performance or on female offspring. The NOAELs for effects on parents and on reproduction were 250 ppm, equivalent to 17 mg/kg bw per day. The NOAEL for pup development was 50 ppm, equivalent to 3 mg/kg bw per day, on the basis of the alterations in weights of the testes, prostate and epididymis at 250 ppm. In a subsequent one-generation study, designed to investigate the effects on male pups in the previous study, there was a reduction in body-weight gain and reduced litter size at 37 mg/kg bw per day. Increases in the incidence of hypospadia and in testes weights, and decreases in weights of the prostate and seminal vesicles were seen in pups at 37 mg/kg bw per day. The NOAELs for parental toxicity, pup development and reproduction were 12.5 mg/kg bw per day.

Studies of developmental toxicity with procymidone have been performed in rats, rabbits and cynomolgus monkeys. In a conventional study of developmental toxicity in rats, there were significant (60%) reductions in maternal body-weight gain during the first 6 days of dosing at 300 mg/kg bw per day, but no adverse findings in pups. This study did not include specific investigations of anogenital distance or the external genitalia. The NOAEL for fetotoxicity and teratogenicity was 300 mg/kg bw per day, the highest dose tested. The NOAEL for maternal effects was 100 mg/kg bw per day. In a modified study of developmental toxicity, pregnant rats were dosed with procymidone on days 6–19 of gestation; on day 20, half the dams had caesarian sections and the other half were allowed to deliver normally. Examinations focused on the male reproductive tract. Maternal toxicity (body-weight loss and poor appearance) was evident at doses of 125 mg/kg bw per day and greater. A range of effects was seen on male foetuses and offspring from dams receiving doses of 125 mg/kg bw per day and greater: reduced anogenital distance, undescended testes, hypospadias, testicular atrophy, distended preputial grand, inflammatory changes in the accessory sex organs (seminal vesicles, prostate and coagulating glands), and lower organ weights of testes and prostate. At 500 mg/kg bw per day, there was a significant increase in the incidence of bifid thoracic vertebral centra in foetuses and prostate

lesions in male offspring. The NOAEL for maternal and developmental toxicity was 12.5 mg/kg bw per day. A further investigative study of developmental toxicity, in which dams were allowed to deliver normally, confirmed the production of hypospadia and undescended testes at 37 mg/kg bw per day, the lowest dose tested.

In rabbits, an initial study of developmental toxicity found no evidence of maternal toxicity or teratogenicity, but there was a reduction in sternebrae ossification at 1000 mg/kg bw per day, the highest dose tested. The NOAEL for developmental toxicity was 750 mg/kg bw per day. In a subsequent study that concentrated on the external genitalia of foetuses, maternal toxicity (anorexia and abortions) was seen at 125 mg/kg bw per day, the only dose used. There were equivocal effects on measurements of the external genitalia in female offspring. Only a single dose level, which produced overt maternal toxicity, was used in the study, and the findings are considered to be of uncertain toxicological relevance.

In an initial study focusing on effects on male foetuses, groups of four pregnant cynomolgus monkeys received doses of 62.5 or 125 mg/kg bw per day. There were no indications of maternal toxicity or fetotoxicity. In a more extensive investigation in groups of 16 pregnant cynomolgus monkeys, there was no maternal toxicity or effects on the external genitalia of offspring (six and eight male offspring in controls and in the test group, respectively) at 125 mg/kg bw per day, the only dose tested.

The characteristics of procymidone were similar in assays for binding to androgen receptors in rats and humans. The concentration required to inhibit activity by 50% (IC_{50}) values for procymidone (approximately 0.3 μmol/L) were similar to those of the anti-androgen prostate-cancer drug flutamide. The IC_{50} values for the procymidone metabolites PCM-CH_2OH, PA-CH_2OH and PCM-NH-COOH were approximately 5–10-fold that of procymidone; PCM-CH_2OH-glucuronide, PCM-COOH and PA-COOH showed no activity. However, these results might have been influenced by the non-enzymatic interconversion of procymidone metabolites. Under acid conditions ($pH < 6.4$), procymidone and PCM-CH_2OH are stable, but under alkaline conditions ($pH \geq 7.8$) the imide bond was shown to be cleaved to give PCM-NH-COOH and PA-CH_2OH.

The mechanism of the effect of procymidone on the reproductive organs has been investigated by measuring hormone levels in mice, rats and cynomolgus monkeys. Procymidone had no adverse effects on testes, sperm and serum or tissue levels of LH in cynomolgus monkeys receiving up procymidone at doses of up to 1000 mg/kg bw per day for 7 days or up to 100 mg/kg bw per day for 91 days. There was evidence of a reduction in ejaculate mass in cynomolgus monkeys at a dose of 100 mg/kg bw per day or greater, but there was no statistically significant effect on ejaculate sperm counts. The small group size and extent of variation between animals and in values recorded before dosing makes it difficult to reach firm conclusions about the toxicological significance of these results. The NOAEL in this study was considered to be 30 mg/kg bw per day. Two studies in rats provided qualitatively similar results, but although the protocols were similar and the same strain was used, there were differences in the doses that produced effects. There were increases in human chorionic gonadotrophin hormone (hCG) stimulated production of testosterone and circulating testosterone levels in rats receiving diets containing procymidone at 700 ppm, equal to 47 mg/kg bw per day, for 13 weeks. LH concentrations were increased at 6000 ppm after 2 weeks. Epididymis weights were reduced after exposure to procymidone at a dietary concentration of 2000 ppm or greater for 2 weeks, but not after 3 months. Testes weights were increased at dietary concentrations of 700 ppm and greater. All effects showed signs of reversal during a recovery phase. Findings in mice were similar to those in rats, but the stimulation of testosterone production by hCG had returned to control levels after 3 months owing to a decrease in the binding affinity of hCG to the LH/hCG receptor.

The Meeting concluded that the existing database on procymidone was adequate to characterize the potential hazards to foetuses, infants and children

Procymidone has not been studied specifically for neurotoxicity, but there were no indications from the results of conventional studies that it has significant neurotoxic potential.

A number of studies have been performed with procymidone metabolites. 3,5-Dichloroaniline (DCA) was of moderate acute toxicity in *dd* mice, having an oral LD_{50} of approximately 850 mg/kg

bw. Procymidone-NH-COOH was also of moderate acute toxicity in *dd* mice, with an oral LD_{50} of approximately 1450 mg/kg bw. 1,2-Dimethylcyclopropane-dicarboxylic acid (DMCPA) was of low acute toxicity in *dd* mice, having an oral LD_{50} of approximately 4400 mg/kg bw and a subcutaneous LD_{50} of approximately 2400 mg/kg bw. DMCPA gave negative results in an Ames test and an assay for micronucleus formation in vivo. DMCPA was rapidly absorbed and excreted with minimal metabolism. Retention of radioactivity in tissues was low.

Hydroxy-procymidone (PCM-CH_2OH) was investigated in a modified study of developmental toxicity in which rats were allowed to deliver normally. No abnormal findings were seen in dams or female offspring. In the male offspring, a dose-related shortening of the anogenital distance was seen and there were increases in the incidence of male offspring and litter with abnormities of the external genitalia. The incidence of hypospadia was increased in pups from dams receiving procymidone at 62.5 mg/kg bw per day, the lowest dose tested. In addition, small testis and epididymis and undescended testis and epididymis were observed occasionally in groups treated with hydroxy-procymidone. These results are similar to those seen with procymidone at similar doses. The benchmark dose (BMD) 95% lower limit for a 10% response ($BMDL_{10}$) for hypospadias was 43.8 mg/kg bw per day for hydroxy-procymidone and 23.7 mg/kg bw per day for procymidone. The Meeting considered the data on the relative androgen receptor and plasma-protein binding affinities of hydroxy-procymidone and procymidone, and the marked species differences in formation and elimination of procymidone and its metabolites. The Meeting concluded that while hydroxy-procymidone might be a significant contributor to the effects seen in rats, due to the much higher systemic and foetal exposure, the contribution of procymidone could not be discounted in other species, particularly due to limitations in the studies in cynomolgus monkeys.

Surveys of the medical records of production-plant workers had not identified any symptoms or diseases related to the manufacture of procymidone. There were no documented cases of procymidone intoxication nor any significant effects associated with its use.

Toxicological evaluation

The Meeting established an ADI of 0–0.1 mg/kg bw based on a NOAEL of 12.5 mg/kg bw per day in a two-generation study of reproductive toxicity and a study of developmental toxicity in rats, on the basis of hypospadias and alterations in testes, prostate and epididymis weights, and a safety factor of 100. The ADI was supported by NOAELs of 14 mg/kg bw per day in the 2-year study in rats and 15 mg/kg bw per day in the 2-year study in mice.

The Meeting established an ARfD of 0.1 mg/kg bw based on a NOAEL of 12.5 mg/kg bw on the basis of hypospadias, which might have been a consequence of a single exposure, in a study of developmental toxicity in rats, and using a safety factor of 100. The Meeting concluded that the effects on organ weights observed in the multigeneration study were largely a consequence of postnatal exposure over a period of time and therefore not appropriate for the establishment of the ARfD. The Meeting considered that, on the basis of the observed differences between species in terms of kinetics, metabolism and toxicological sensitivity to procymidone, this ARfD might be conservative. However, uncertainties regarding potential responses in species other than rats were such that it was not possible to modify the default safety factor.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Mouse	Two-year studies of toxicity and carcinogenicity[a]	Toxicity	100 ppm, equal to 15mg/kg bw per day	300 ppm, equal to 46mg/kg bw per day
		Carcinogenicity	300 ppm, equal to 46mg/kg bw per day	1000 ppm, equal to 153mg/kg bw per day

Rat	Two-year studies of toxicity and carcinogenicity [a]	Toxicity	300 ppm, equal to 14 mg/kg bw per day	1000 ppm, equal to 48mg/kg bw per day
		Carcinogenicity	300 ppm, equal to 14mg/kg bw per day	1000 ppm, equal to 48mg/kg bw per day
	Multigeneration study of reproductive toxicity[ae]	Parental toxicity	250 ppm, equivalent to 17mg/kg bw per day	750 ppm, equivalent to 50 mg/kg bw per day
		Offspring toxicity	12.5mg/kg bw per day	250 ppm, equivalent to 17mg/kg bw per day
	Developmental toxicity[b,e]	Maternal toxicity	100 mg/kg bw per day	125 mg/kg bw per day
		Embryo/fetotoxicity	12.5 mg/kg bw per day	37.5 mg/kg bw per day
Rabbit	Developmental toxicity[b,e]	Maternal toxicity	—	125 mg/kg bw per day [f]
		Embryo/fetotoxicity	750 mg/kg bw per day	1000 mg/kg bw per day
Monkey	Developmental toxicity[b,e]	Maternal toxicity	125 mg/kg bw per day[c]	—
		Embryo/fetotoxicity	125 mg/kg bw per day[c]	—
Dog	Six-month and 1-year studies of toxicity[d]	Emesis, soft faeces, increased alkaline phosphatase activity	100 mg/kg bw per day	500 mg/kg bw per day

[a] Dietary administration.
[b] Gavage administration.
[c] Highest dose tested.
[d] Capsule administration.
[e] More than one study combined.
[f] Lowest dose tested.

Estimate of acceptable daily intake for humans

0–0.1 mg/kg bw

Estimate of acute reference dose

0.1 mg/kg bw

Information that would be useful for the continued evaluation of the compound

Results from epidemiological, occupational health and other such observational studies of human exposure

Critical end-points for setting guidance values for exposure to procymidone

Absorption, distribution, excretion and metabolism in mammals	
Rate and extent of oral absorption	Rapid, C_{max} 2–8 h; extensive, > 80% excreted in the urine
Dermal absorption	4% concentrate, 13% for dilution in rats in vivo
Distribution	Extensive, highest concentrations in fat
Potential for accumulation	Low
Rate and extent of excretion	Rapid, > 80% in 24 h; enterohepatic recirculation in rats
Metabolism in animals	Hydroxylation, oxidation and conjugation. Some species differences.

Toxicologically significant compounds in animals, plants and the environment	Procymidone, hydroxy-procymidone
Acute toxicity	
Rat, LD_{50}, oral	> 5000 mg/kg bw
Rat, LD_{50}, dermal	> 2500 mg/kg bw
Rat, LC_{50}, inhalation	> 1.5 mg/L
Rabbit, skin irritation	Slight transient irritant
Rabbit, eye irritation	Not irritating
Guinea-pig, skin sensitization (test method used)	Negative (Magnusson & Kligman maximization test)
Short-term studies of toxicity	
Target/critical effect	Decreased body-weight gain, liver effects, testes
Lowest relevant oral NOAEL	25 mg/kg bw per day
Lowest relevant dermal NOAEL	1000 mg/kg bw per day
Lowest relevant inhalation NOAEC	No data
Genotoxicity	
	Not genotoxic
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	Body weight, liver effects
Lowest relevant NOAEL	14 mg/kg bw per day (rat)
Carcinogenicity	Liver tumours in mice; testes tumours in rats.
Reproductive toxicity	
Reproduction target/critical effect	Hypospadias; altered testes and epididymis weight
Lowest relevant reproductive NOAEL	12.5 mg/kg bw per day
Developmental target/critical effect	Hypospadias (rat)
Lowest relevant developmental NOAEL	12.5 mg/kg bw per day
Neurotoxicity/delayed neurotoxicity	
	No evidence in conventional studies
Special studies	
	Kinetic and metabolism studies in rats, monkeys, rabbits, mice and with human tissues showed differences between species. Rats having a relatively high area-under-the curve and a low capability to metabolize procymidone and hydroxy-procymidone.
	Receptor-binding assays showed that procymidone and hydroxy-procymidone could bind to rat and human androgen receptors. Both procymidone and hydroxy-procymidone were extensively bound (≥ 77%) to plasma proteins.
	Procymidone produced increases in luteinizing hormone and human chorionic gonadotrophin-stimulated production of testosterone in rats at 6000 ppm and ≥ 700 ppm respectively.
	Ejaculate mass was reduced in monkeys exposed to procymidone for 13 weeks at ≥ 100 mg/kg bw per day. NOAEL was 30 mg/kg bw per day

	Hydroxy-procymidone induced hypospadias in rats at ≥ 62.5 mg/kg bw per day; $BMDL_{10}$ was 43.8 mg/kg bw per day.
Medical data	
	No adverse findings reported

Summary

	Value	Study	Safety factor
ADI	0–0.1 mg/kg bw	Rat, studies of developmental and reproductive toxicity	100
ARfD	0.1 mg/kg bw	Rat, study of developmental toxicity	100

5.19 PROFENOFOS (171)

TOXICOLOGY

Profenofos is the ISO approved name for (*RS*)-*O*-4-bromo-2-chlorophenyl *O*-ethyl *S*-propyl phosphorothioate (IUPAC), CAS No. 41198-08-7. It is a broad-spectrum organophosphorus insecticide that is used to control insect pests in cotton, maize, sugar beet, soya bean, potato, vegetables and other crops. Its mode of action is by inhibition of acetylcholinesterase activity.

Profenofos was previously evaluated by JMPR in 1990 (Annex 5, reference *171*) and an ADI of 0–0.01 mg/kg bw per day was established. The ADI was based on the NOAEL of 20 ppm, equal to 1.0 mg/kg bw per day, the highest dose tested, in a three-generation study of reproduction in rats.

Profenofos was re-evaluated by the present meeting within the Periodic Re-evaluation Programme of the CCPR. All pivotal studies with profenofos were certified as complying with GLP.

Biochemical aspects

[Phenyl-^{14}C]profenofos was rapidly absorbed and eliminated after oral administration to rats. Total radioactivity eliminated via the urine and faeces exceeded 99% of the administered dose for a single dose of 1 or 100 mg/kg bw by gavage and repeated doses of 1 mg/kg bw by gavage. Elimination was rapid, with about of 95% of the total radiolabel being excreted in the urine within the first 24 h in all treated groups. For all doses, less than 4% of the radiolabel was excreted in the faeces. The concentration of radiolabel in tissues and organs reached a maximum after 2 h and remained at similar levels until 8 h after dosing. By 72 h, the tissue concentration of radiolabel was minimal. The absorption, distribution and excretion of ^{14}C-labelled profenofos was not sex- or dose-dependent in the range of 1 to 100 mg/kg bw and was unaffected by pre-treatment with unlabelled profenofos for 14 days. Unchanged profenofos was detected in the faeces, but the amount was very small (approximately 1–2% of the administered dose), and this was probably the proportion of the dose that was not absorbed. Four major metabolites were present in urine and no unchanged profenofos was detected. The major metabolites were the sulfate and glucuronide conjugates of 4-bromo-2-chloro-phenol that were formed by hydrolysis of the aryloxy–phosphorus bond followed by conjugation with sulfate or glucuronic acid. The other two metabolites were formed by cleavage of the phosphorus–sulfur bond either by loss of the propyl group or hydrolysis. The 4-bromo-2-chloro-phenol was detected in some urine samples, but probably arose as a result of hydrolysis of the conjugates after excretion.

Toxicological data:

The acute oral LD_{50} for profenofos ranged from 358 to 1178 mg/kg bw in rats. The acute oral LD_{50} for profenofos was 298 mg/kg bw in mice and 700 mg/kg bw in rabbits. The clinical signs detected in all

the studies of acute toxicity were typical of cholinergic poisoning, which appeared at doses greater than 100 mg/kg bw. Profenofos was of low toxicity when administered by the dermal route to rats (LD_{50}s, > 2000 and 3300 mg/kg bw). More varied results were obtained after dermal application to rabbits with LD_{50}s ranging from 131 to 2560 mg/kg bw depending on method of application (semi-occlusive, abraded skin or massaging). Profenofos was of low toxicity on exposure by inhalation, the LC_{50} being > 3.36 mg/L. Profenofos was moderately irritating to skin and mildly irritating to the eye and was shown to be a sensitizer under the conditions of the Magnusson & Kligman test and in the local lymph-node assay.

The primary effect of profenofos in studies of acute toxicity, short- and long-term studies of toxicity was inhibition of acetylcholinesterase activity and this was associated with signs of neurotoxicity at high levels of inhibition. Profenofos is a racemic mixture of the two optical isomers at the chiral phosphorus atom. The *S* (-) isomer is a markedly more potent inhibitor of acetyl cholinesterase in vitro than the *R* (+) isomer. The inhibited acetyl cholinesterase ages rapidly, an effect that prevents spontaneous reactivation. Rapid ageing would lead to a cumulative inhibitory effect after repeated exposures to profenofos, and would also render reactivation therapy with oximes ineffective (see item 2.4 under General considerations).

In a short-term repeat-dose study, no clinical signs of toxicity were observed in rats given diet containing profenofos at a concentration of 1000 ppm, equal to 85 mg/kg bw per day, for 8 weeks. Reduced food intake and body-weight gain were apparent at this dose and also at a dose of 100 ppm, equal to 8.4 mg/kg bw per day, which was given for 13 weeks. Inhibition of cholinesterase activity was the only other effect noted. Erythrocyte cholinesterase activity was inhibited by more than 20% at doses of 30 ppm, equal to 2.4 mg/kg bw per day, and greater. Brain acetylcholinesterase activity was inhibited at 1000 ppm, equal to 85 mg/kg bw per day. The NOAEL for inhibition of brain acetylcholinesterase activity was 300 ppm, equal to 22.0 mg/kg bw per day.

Inhibition of brain acetylcholinesterase activity and clinical signs consistent with neurotoxicity were observed in rats exposed to profenofos at a concentration of 0.07 mg/L per day by inhalation for 21 days.

In three studies of dermal toxicity in rabbits, the overall NOAEL for inhibition of brain acetylcholinesterase was 2.5 mg/kg bw per day on the basis of significantly reduced activity at 5 mg/kg bw per day.

Three studies were carried out in dogs given profenofos orally for 90 days, 6 months, or 1 year. Profenofos was given in the diet in the 90-day and 6-month studies, and daily in gelatin capsules in the 1-year study. No clinical signs of toxicity were recorded in these studies, the 6-month and 1-year studies including neurological examinations (NOAEL for clinical signs, 12.5 mg/kg bw per day). Brain acetylcholinesterase activity was significantly inhibited in males at 5 mg/kg bw per day in the 90-day study, but not in either sex at 2.9 or 14.4 mg/kg bw per day in the 6-month study, or at 1 or 12.5 mg/kg bw per day (the highest dose tested) in the 1-year study. Hence, for brain acetylcholinesterase inhibition, the overall NOAEL in these three studies in dogs was 2.9 mg/kg bw per day. Haematology parameters (erythrocyte count, haemoglobin concentration and erythrocyte volume fraction) were reduced; however, they were not considered to be toxicologically significant since there was no clear dose–response relationship, and the small changes observed were within the range for historical controls. Treatment of dogs with profenofos at 12.5 mg/kg bw per day for 1 year was also associated with an increase in binucleated perilobular hepatocytes, bile-duct hyperplasia and an increase in bile pigments in kidney tubules. These pathological findings were minimal in severity, were not observed in the 90-day or 6-month studies of toxicity.

Profenofos was not mutagenic in an adequate battery of studies of genotoxicity.

The Meeting concluded that profenofos is unlikely to be genotoxic.

In long-term studies, treatment of mice and rats with profenofos did not adversely affect survival; there were no clinical signs of toxicity, no increase in the incidence of tumour formation and no treatment-related changes in either gross pathology or histopathology. Plasma and erythrocyte cholinesterase activity were significantly reduced in mice given diet containing profenofos at 30 ppm,

equal to 4.5 mg/kg bw per day, and in rats at 100 ppm, equal to 5.7 mg/kg bw per day. In female mice, there was a statistically significant inhibition of brain acetylcholinesterase activity (25%) at termination of the group at 100 ppm, equal to 14.2 mg/kg bw per day, resulting in a NOAEL of 30 ppm, equal to 4.5 mg/kg bw per day. The NOAEL in the 2-year study of carcinogenicity in rats was 100 ppm, equal to 5.7 mg/kg bw per day, the highest dose tested. Profenofos was not carcinogenic in mice and rats up to the highest dose tested. Although overt toxicity was not observed in the study in rats, the Meeting considered that the available database was sufficient to evaluate the carcinogenic potential of profenofos.

In view of the lack of genotoxicity, the absence of carcinogenicity in mice and rats, and any other indication of carcinogenic potential, the Meeting concluded that profenofos is unlikely to pose a carcinogenic risk to humans.

Multigeneration studies have shown that profenofos has no effect on reproduction at doses of up to 400 ppm, equivalent to 35 mg/kg bw per day. The NOAEL for parental and pup toxicity was 100 ppm, equivalent to 7.0 mg/kg bw per day, on the basis of reduced body-weight gains and food consumption at 400 ppm, equivalent to 35 mg/kg bw per day, and the NOAEL for reproductive toxicity was 400 ppm, the highest dose tested.

Profenofos did not cause developmental effects in rats or rabbits. Clinical signs typical of cholinesterase inhibition were noted in rabbits given profenofos at 175 mg/kg bw per day and approximately 50% of the animals died. There were no treatment-related effects on the mean number of implantations, litter size, foetal body weight or embryolethality and there were no significant increases in variations or malformations in the foetuses. The NOAEL for maternal toxicity was 30 mg/kg bw per day and the NOAEL for developmental toxicity was 175 mg /kg bw per day, the highest dose tested. Studies of developmental toxicity in rats, maternal toxicity, which included clinical signs typical of cholinesterase inhibition, and deaths were observed at the highest dose of 120 mg/kg bw per day. There was no evidence for prenatal toxicity at either of these doses and the type and incidence of foetal malformations and variations was unaffected by treatment. The NOAEL for maternal toxicity was 90 mg/kg bw per day and the NOAEL for developmental toxicity was 120 mg/kg bw per day, the highest dose tested.

The Meeting concluded that profenofos is not teratogenic.

The potential for profenofos to cause developmental neurotoxicity had also been investigated in rats. In a preliminary range-finding study, rats were given diets containing profenofos at a concentration of 0, 4, 200, 400 or 600 ppm, equal to 0, 0.7, 33.9, 66.0 or 97.6 mg/kg bw per day. In this study, dose-dependent inhibition of the brain acetylcholinesterase activity was observed in dams at ≥ 200 ppm on postnatal day 22. The NOAEL for inhibition of brain acetylcholinesterase activity in dams was 4 ppm, equal to 0.7 mg/kg bw per day. A statistically significant inhibition of brain acetylcholinesterase activity of > 20% and 16% was found in female pups at ≥400 ppm and male pups at 600 ppm, respectively. In the main study of developmental neurotoxicity, rats were given diets containing profenofos at a concentration of 0, 3, 60 or 600 ppm (equal to 0, 0.3, 5.1 or 50.6 mg/kg bw per day). At 600 ppm in dams, brain acetylcholinesterase activity was decreased by 44% on day 22 of gestation, and by 26% (not statistically significant) on day 22 of lactation, and body weights and food consumption were reduced. A statistically significant inhibition of brain acetylcholinesterase activity was observed in female pups at 600 ppm compared with controls on day 5 (11% lower) but not at later times. At 600 ppm, there was a statistically significant reduction in pup body weights (11–12%). No effects on functional parameters or neurohistopathology were observed. The NOAEL for maternal toxicity was 60 ppm, equal to 5.1 mg/kg bw per day, on the basis of inhibition of brain acetylcholinesterase activity on day 22 of gestation and day 22 of lactation, reductions in body weight and food consumption at 600 ppm, equal to 50.6 mg/kg bw per day. The overall NOAEL for inhibition of brain acetylcholinesterase in pups was 60 ppm, equal to 5.1 mg/kg bw per day. The NOAEL for developmental neurotoxicity was 600 ppm, equal to 50.6 mg/kg bw per day, highest dose tested.

In two studies of acute neurotoxicity in rats, there were reversible signs typical of poisoning with acetylcholinesterase inhibitors (diarrhoea, meiosis, lacrimation, tremor), peaking 4 h after

administration of profenofos at 380 mg/kg bw by gavage. Lesser effects were seen at 200 mg/kg bw (hypoactivity, soft faeces), and there were no effects in the FOB at 190 mg/kg bw (the NOAEL for clinical signs). There was significant inhibition of brain acetylcholinesterase activity (by 37% in males and 43% in females) at 4 h after dosing at 400 mg/kg bw, with a NOAEL of 100 mg/ kg bw. Inhibition was absent after a recovery period of 14 days.

There were also no clinical signs of toxicity, and no adverse findings in a FOB or effects on motor activity in a 90-day study of neurotoxicity in rats. Pathological investigation revealed no evidence of treatment-related toxicity. At the highest dose of 600 ppm, equal to 36 mg/kg bw per day, there was a reduction of approximately 10% in body-weight gain. At 600 ppm, there was a statistically significant inhibition of brain acetylcholinesterase activity of 12% in males and 20% in females at week 13. The NOAEL for brain acetylcholinesterase inhibition was 135 ppm, equal to 7.7 mg/kg bw per day.

Profenofos did not induce delayed neuropathy in hens given two doses at 45.7 mg/kg bw (maximum tolerated dose) and then at 17.1 mg/kg bw, separated by an interval of 21 days (atropine protection being given as soon as clinical signs appeared).

No cases of adverse effects have been reported among workers involved in the manufacture of profenofos. In a biological monitoring study, whole-blood cholinesterase activity was inhibited by less than 30% in six workers who were monitored daily for 4 days during spraying of profenofos.

The Meeting concluded that the existing database on profenofos was adequate to characterize the potential hazards to foetuses, infants and children.

Toxicological evaluation

Erythrocyte acetylcholinesterase activity was found to be significantly more sensitive to profenofos than was brain acetylcholinesterase activity in rats, mice, rabbits, and dogs. However, in no species were any signs of toxicity seen at doses that did not also produce significant inhibition of brain acetylcholinesterase. The Meeting thus concluded that inhibition of brain acetylcholinesterase activity was the more appropriate end-point for risk assessment of profenofos.

The Meeting established an ADI of 0–0.03 mg/kg bw per day based on an overall NOAEL of 2.9 mg/kg bw per day identified on the basis of inhibition of brain acetylcholinesterase activity in three short-term studies in dogs and using a safety factor of 100. This ADI was supported by the NOAEL of 5.1 mg/kg bw per day identified on inhibition of maternal and pup brain acetylcholinesterase activity in a study of developmental neurotoxicity in rats and a NOAEL of 4.5 mg/kg bw per day identified on the basis of inhibition of brain acetylcholinesterase activity in a 2-year study in mice.

The Meeting established an ARfD of 1 mg/kg bw based on a NOAEL of 100 mg/kg bw in studies of acute neurotoxicity in rats, identified on the basis of clinical signs of neurotoxicity seen $\geq$ 200 mg/kg bw and inhibition of brain acetylcholinesterase activity at 400 mg/kg bw and using a safety factor of 100. The appropriate study for establishing the ARfD was the study of acute neurotoxicity since there was no evidence of developmental effects. This ARfD was considered to be protective against any clinical signs of acetylcholinesterase inhibition seen in studies of acute oral toxicity.

A toxicological monograph was prepared.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Mouse	Two-year studies of toxicity and carcinogenicity[a]	Toxicity	4.5 mg/kg bw per day	14.2 mg/kg bw per day
		Carcinogenicity	14.2 mg/kg bw per day[c]	—

Rat	Two-year studies of toxicity and carcinogenicity[a]	Toxicity	5.7 mg/kg bw per day[c]	—
		Carcinogenicity	5.7 mg/kg bw per day[c]	—
	Multigeneration study of reproductive toxicity[a]	Parental	7.0 mg/kg bw per day	35.0 mg/kg bw per day
		Reproductive toxicity	35.0 mg/kg bw per day[c]	—
		Offspring toxicity	7.0 mg/kg bw per day	35.0 mg/kg bw per day
	Developmental toxicity[b]	Maternal toxicity	90.0 mg/kg bw per day	120.0 mg/kg bw per day
		Embryo/fetotoxicity	120.0 mg/kg bw per day[c]	—
	Developmental neurotoxicity[a]	Parental toxicity	5.1 mg/kg bw per day	50.6 mg/kg bw per day
		Offspring toxicity	5.1 mg/kg bw per day	50.6 mg/kg bw per day
	Acute neurotoxicity[b,d]	Toxicity	100.0 mg/kg bw	400.0 mg/kg bw per day
Rabbit	Developmental toxicity[b]	Maternal toxicity	30.0 mg/kg bw per day	60.0 mg/kg bw per day
		Embryo/fetotoxicity	175.0 mg/kg bw per day[C]	—
Dog	Studies of toxicity[d]	Toxicity	2.9 mg/kg bw per day	12.5 mg/kg bw per day

[a] Dietary administration.
[b] Gavage administration.
[c] Highest dose tested.
[d] The results of two or more studies were combined.

Estimate of acceptable daily intake for humans

0–0.03 mg/kg bw

Estimate of acute reference dose

1 mg/kg bw

Information that would be useful for the continued evaluation of the compound

Results from epidemiological, occupational health and other such observational studies of human exposures

Critical end-points for setting guidance values for exposure to profenofos

Absorption, distribution, excretion and metabolism in mammals	
Rate and extent of oral absorption	About 94% within 24 h
Dermal absorption	Approximately 90%
Distribution	Widely distributed
Potential for accumulation	Low, no evidence of accumulation
Rate and extent of excretion	94% in urine within 24 h
Metabolism in animals	> 95% by conversion of the phosphorothiolate group to a variety of hydrolysis products

Toxicologically significant compounds in animals, plants and the environment	Parent
Acute toxicity	
Rat, LD_{50}, oral	358–1178 mg/kg bw
Rat, LD_{50}, dermal	3300 mg/kg bw
Rat, LC_{50}, inhalation	3.36 mg/L
Skin irritation	Moderately irritating
Eye irritation	Mildly irritating
Guinea-pig, skin sensitization (test method used)	Sensitizer (Magnusson & Kligman and local lymph-node assay)
Short-term studies of toxicity	
Target/critical effect	Inhibition of brain acetylcholinesterase activity
Lowest relevant oral NOAEL	2.9 mg/kg bw per day (dogs)
Lowest relevant dermal NOAEL	2.5 mg/kg bw per day
Lowest relevant inhalation NOAEC	< 0.07 mg/L
Genotoxicity	
	No genotoxic potential
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	Inhibition of brain acetylcholinesterase activity
Lowest relevant NOAEL	4.5 mg/kg bw per day (2-year study in mice)
Carcinogenicity	Not carcinogenic
Reproductive toxicity	
Reproduction target/critical effect	No reproductive effects
Lowest relevant reproductive NOAEL	400 ppm (35 mg/kg bw per day) (rats)
Developmental target/critical effect	No developmental effects
Lowest relevant developmental NOAEL	120 mg/kg bw per day (rats)
Neurotoxicity/delayed neurotoxicity	
Acute neurotoxicity	Inhibition of brain acetylcholinesterase activity, NOAEL was 100 mg/kg bw per day (rats)
Developmental neurotoxicity	Inhibition of brain acetylcholinesterase activity, NOAEL was 5.1 mg/kg bw per day (rats)
Delayed neuropathy	No delayed neurotoxicity, NOAEL was 45.7 mg/kg bw (chickens)
Medical data	
	No detrimental effects on agricultural workers

Summary

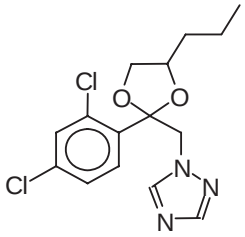
	Value	**Study**	**Safety factor**
ADI	0–0.03 mg/kg bw	Dog, studies of oral toxicity	100
ARfD	1 mg/kg bw	Rat, study of acute neurotoxicity	100

5.20 PROPICONAZOLE (160)

RESIDUE AND ANALYTICAL ASPECTS

Propiconazole, one of the triazole fungicides, was first evaluated by the JMPR in 1987 and has been reviewed for residues in 1991 and 1994. It was listed by the 2004 CCPR (36th session, ALINORM 01/24, Appendix XI) for periodic re-evaluation for residues by the 2007 JMPR. The toxicology of propiconazole was re-evaluated by the 2004 JMPR which estimated an ADI of 0-0.07 mg/kg bw and an ARfD of 0.3 mg/kg bw.

Propiconazole is a racemic mixture of four stereoisomers, which are separated into *cis*- and *trans*-diastereomers. All four stereoisomers of propiconazole provide biological activity. The intrinsic activity of each isomer is different from pathogen to pathogen. The broad spectrum and high level of activity of propiconazole is the result of the combined activity of all isomers.



The Meeting received a full data package including animal and plant metabolism studies (goats, hens, grape vines, carrots, celery, wheat, rice, peanuts, sugarcane), rotational crop studies, hydrolysis and photolysis studies in water and degradation in water/sediment systems, information on analytical methods, GAP information, supervised residue trial data from use as a foliar spray on a range of fruit, cereal and oil seed crops, sugar beets and sugarcane, nuts, coffee and tea, processing studies and livestock feeding studies. GAP information was also submitted by Australia and The Netherlands.

Metabolites mentioned in this appraisal are given in the table below.

Name used in this evaluation	Systematic chemical names, CAS numbers, and other abbreviations used in study reports
propiconazole (CGA-64250)	*1-{[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]methyl}-1H-1,2,4-triazole;*
β-hydroxy alcohol (CGA-118244)	*1-{[2-(2,4-dichlorophenyl)-4-(2-hydroxypropyl)-1,3-dioxolan-2-yl]methyl}- 1H-1,2,4-triazole;*
	2-(2,4-dichlorophenyl)-α-methyl-2-(1H-1,2,4-triazol-1-yl-methyl)-1,3-dioxolane-4-ethanol;
γ-hydroxy alcohol (CGA-118245)	*3-[2-(2,4-dichlorophenyl)-2-[1,2,4]triazol-1-yl-methyl-[1,3]dioxolan-4-yl]-propan-1-ol;*
	2-(2,4-dichlorophenyl)-2-(1H-1,2,4-triazol-1-yl-methyl)-1,3-dioxolane-4-propanol;
ketone (CGA-91304)	*CGA-58533;*
	1-(2,4-dichlorophenyl)-2-(1H-1,2,4-triazol-1-yl) ethanone;
	1-(2,4-dichlorophenyl)-2-[1,2,4]-triazol-1-yl-ethanone;
	ω-(1,2,4-triazole-1-yl)-2,4-dichloroacetophenone;
alkanol (CGA-91305)	*CGA-77502;*
	1-(2,4-dichlorophenyl)-2-[1,2,4]triazol-1-yl-ethanol;
	1-{[2-(2,4-dichlorophenyl)-2-hydroxy]ethyl}-1H-1,2,4-triazole;
	α-(2,4-dichlorophenyl)-1H-1,2,4-triazole-1-ethanol;
triazole (CGA-71019)	*1H-[1,2,4]-triazole*

Name used in this evaluation	Systematic chemical names, CAS numbers, and other abbreviations used in study reports
triazolyl alanine (CGA-131013)	*1,2,4-triazole-1-alanine; 2-amino-3-[1,2,4]triazol-1-yl-propionic acid; α-amino-1,2,4-triazole-1-propionic acid*
triazolyl acetic acid (CGA-142856)	*[1,2,4]triazol-1-yl-acetic acid*
triazolyl lactic acid (CGA-205369)	-
N-acetylated-1,2,4-triazole-1-alanine	-
2,4-DCBA (CGA-177291)	*2,4-dichloro-benzoic acid;*

Animal metabolism

The Meeting received information on the fate of orally dosed propiconazole in lactating goats and in laying hens. Experiments were carried out using uniformly ^{14}C- phenyl and uniformly ^{14}C-triazole labelled propiconazole. Metabolism in laboratory animals (mice, rats) was summarized and evaluated by the WHO panel of the JMPR in 2004.

Propiconazole is extensively metabolized in rats and mice and < 5% of the dose remains as the parent compound; however, many metabolites have not been identified. The primary metabolic steps involve oxidation of the propyl side-chain on the dioxolane ring to give hydroxy or carboxylic acid derivatives. Hydroxylation of the chlorophenyl and triazole rings followed by conjugation with sulfate or glucuronide was also detected. There is evidence for only limited cleavage between the triazole and chlorophenyl rings.

Three studies were performed on lactating goats. One lactating goat, orally treated once daily for 10 consecutive days with triazole-^{14}C-propiconazole at a calculated dose rate of 4.4 ppm in the feed, was sacrificed approximately 24 hrs after the last dose. The largest amount of radioactivity was found in the urine and faeces, which contained around 69% and 21% of the total dose, respectively. Tissues contained only 0.04%, while milk contained 0.18%. The radioactivity in the tissues did not exceed 0.02 mg/kg eq except for kidney (0.029 mg/kg eq) and liver (0.096 mg/kg eq). Radioactivity in milk reached a plateau on the sixth day of dosing at an average level of 0.015 mg/kg eq (range 0.015–0.016 mg/kg eq). The majority of the radioactivity in milk (> 74%) was associated with the whey fraction.

Radioactivity was characterized in goat milk and liver. Of the total radioactivity in milk, 3.0–5.6% could be identified as olefin, 13%–16% as ketone (CGA-91304) and 39% as triazole (CGA-71019). Sixteen to twenty percent remained unidentified. After a modified Kjeldahl digestion, 89% and 38% of the radiolabel in milk and liver, respectively, co-chromatographed with triazole.

In the second goat study, two lactating goats, orally treated once daily for four consecutive days with phenyl-^{14}C-propiconazole at calculated dose rates of 67 and 92 ppm in the feed, were sacrificed approximately 6 hrs after the last dose. Most of the administered [^{14}C] dose (86–96%) was eliminated in the urine (48–56%) and faeces including rumen contents at sacrifice (38–39%). Tissues and milk exhibited low levels of ^{14}C-residues. Highest levels were found in liver (average 3.8 mg/kg eq) and kidney (average 2.5 mg/kg eq), whereas muscle and fat were found to contain the lowest levels (average 0.08 mg/kg eq). Radioactivity in milk increased during the four day dosing period for both animals reaching an averaged maximum of 0.22 mg/kg eq on day 4.

In liver, kidney, tenderloin muscle and omental fat three major components of the residue were identified:

- parent propiconazole (liver 12%, kidney 4%, muscle 2%, fat 20% of the total radiolabel)

- a β-hydroxy alcohol (CGA-118244; liver 19%, kidney 9%, muscle 16%, fat 33%),
- and an alkanol (CGA-91305; liver 14%, kidney 17%, muscle 36%, fat 31%).

In liver, kidney and tenderloin muscle several other components were present at relatively low levels. They were not further characterized. Similar to tissue extracts, milk contained the relatively non-polar metabolites β-hydroxy alcohol (CGA-118244; 24%) and alkanol (CGA-91305; 24%). In addition, milk extracts were found to contain several other more polar residues at low levels. Unchanged parent propiconazole was not found in milk. Treatment with aryl sulfatase suggested the presence of sulfate conjugates of ring-hydroxylated species.

In the third goat study, two lactating Alpine goats, orally treated once daily for seven consecutive days with triazole-^{14}C-propiconazole at calculated dose rates of 44 and 40 ppm in the feed, were sacrificed approximately 20 hrs after the last dose. Approximately 92% of the administered dose was recovered. The majority of the radiolabelled material was found in the urine (66%) and faeces (21%). Tissues and milk exhibited low levels of ^{14}C-residues. Highest residue levels were found in liver (average 0.64 mg/kg eq) and kidney (average 0.28 mg/kg eq), whereas fat and muscle were found to contain the lowest levels (average 0.088 and 0.022 mg/kg eq, respectively). After 4 days radioactive residues in milk reached an average plateau concentration of 0.15 mg/kg eq (range 0.14–0.16 mg/kg eq) and 0.12 mg/kg eq (range 0.12–0.13 mg/kg eq) goats 1 and 2, respectively.

The most abundant residues were parent propiconazole in fat, alkanol (CGA-91305) in liver and kidney and triazole (CGA-71019) in kidney, muscle, fat and milk. Following enzyme hydrolysis of milk, triazole accounted for 40% of the total radiolabel and none of the unidentified components exceeded 6.1% (0.009 mg/kg). Parent was found at low levels in milk, but not in muscle.

Based on the above, it is proposed that the degradation of propiconazole in lactating goats proceeds primarily via the following pathways:

- Oxidation of the aliphatic side-chain of propiconazole to the alcohols CGA-118244 and CGA-118245.
- Further oxidation of the aliphatic side-chain to the carboxylic acid CGA-121676 observed in the urine and the hydroxy carboxylic acid metabolite SYN-542636 observed in the urine and kidney.
- Cleavage of the dioxolane ring to the ketone CGA-91304 followed by reduction of to the alkanol CGA-91305
- Cleavage of the alkyl bridge to release triazole CGA-71019, observed in muscle, milk and kidney.

Phase 1 metabolism products are then subject to phase 2 metabolism, i.e., glucuronide/sulphate conjugation. The metabolites triazolyl alanine (CGA-131013) and triazolyl acetic acid (CGA-142856), often observed in crop metabolism studies of triazole fungicides, were not present at detectable levels in lactating goats.

Two laying hens (Leghorn), orally treated once daily with ^{14}C-propiconazole for 16 consecutive days at calculated dose rates of 54 and 47 ppm in the feed, were sacrificed approximately 24 hrs after the last dose. One hen (HA) was dosed with ^{14}C-phenyl labelled and one hen (HB) with [^{14}C]triazole labelled propiconazole. Total recovered radioactivity was 94%–104%; most of the radioactivity (> 94%) was eliminated in the excreta.

Residue levels in egg yolk and white increased to a maximum level at days 11–15 and thereafter decreased; no real plateau was found. A maximum residue level was reached at day 11 at 1.2 and 0.98 mg/kg eq, respectively, for the triazole label and at days 13–15 at 0.87 and 0.90 mg/kg eq, respectively for the phenyl label. Levels of radioactive residues were different for the two labels in most of the tissues. The levels were generally higher for the triazole label, which was most pronounced for muscle (factor 7) and skin (1.5 fold). No significant label difference was found in the fat. These level differences indicate a cleavage between the phenyl and triazole ring and formation of label specific metabolites which are absorbed differently by different tissues.

In a second hen study, four laying hens (white Leghorn), orally treated once daily for 8 consecutive days with phenyl-^{14}C-propiconazole at a calculated dose rate of about 70 ppm in the feed, were sacrificed approximately 6 hrs after the last dose. Of the total dose, 73% to 87% was found to be eliminated in the excreta. Highest levels of radioactive residue were found in kidney (average 4.2 mg/kg eq) and liver (average 3.9 mg/kg eq). Levels of [^{14}C] residues in yolks for individual hens increased during the dosing period (average maximum 1.7 mg/kg eq), no plateau was reached. Average ^{14}C-residues for the four hens were found to be higher in yolks (reaching a maximum of 1.7 mg/kg at day 7) than in whites (reaching a maximum of 0.70 mg/kg at day 5). In tissues and eggs, three major components of the recovered radioactivity were parent propiconazole (1.5% in liver, 2% in kidney, 7% in muscle, 40% in skin/fat, 12% in egg yolk and 28% in egg white), β-hydroxy alcohol CGA-118244 (3% in liver, 2% in kidney, 2% in muscle, 4% in skin/fat, 9% in egg yolk and 52% in egg white) and alkanol CGA-91305 (59% in liver, 44% in kidney, 85% in muscle, 43% in skin/fat, 51% in egg yolk and 18% in egg white).

Based on the structures identified, it is proposed that the degradation of propiconazole in laying hens treated with phenyl-^{14}C-propiconazole proceeds primarily via the following pathways:

- hydroxylation of the propyl side-chain to form CGA-118244
- hydrolysis of the dioxolane ring to form the ketone CGA-91304, which is then reduced to the corresponding alcohol CGA-91305

In conclusion, although the metabolism of propiconazole in farm animals was qualitatively similar to that in laboratory animals, the level of the different metabolites could quantitatively be very different.

Plant metabolism

The Meeting received information on the fate of propiconazole after foliar spray treatment of fruits (grape vines), root crops (carrots), stem crops (celery), cereals (wheat, rice) and oilseeds (peanuts). In addition, the Meeting received information on the fate of propiconazole after dip treatment of sugarcane pieces. Further, the Meeting received information on the fate of 1,2,4-triazole after topical treatment of tomato fruits.

Four grapevine plants (variety Riesling and Sylvaner) were grown outdoors in Sisseln (Switzerland). One plant was treated with a phenyl-^{14}C-labelled and three plants were treated with a triazole-^{14}C-labelled EC-formulation of propiconazole. All plants were sprayed four times until run-off at a rate of 0.0025 kg ai/hl water at 14-18 day intervals. A first aliquot of grapes was harvested 30 days after the last application ('Aliquot' sample), and mature grapes were harvested 63 days after the final application ('Harvest' sample). For both labels, the content of radioactivity in grapes was low, i.e. < 0.05 mg/kg propiconazole equivalents. Unchanged propiconazole accounted only for 15% of [^{14}C] residues (0.006 mg/kg) in whole grapes; a number of metabolites were identified but at lower concentrations.

Eight green tomatoes were treated topically by surface streaking and injection with propiconazole metabolite [^{14}C]1,2,4-triazole at 20–30 mg ai/kg tomato and placed for two weeks in a greenhouse under a 12 hr dark/light cycle. Total radioactive residues amounted to 19 mg/kg eq. The major metabolite in tomatoes was identified as a 1,2,4-triazole-1-alanine conjugate (80% TRR). No free triazole was found.

Carrots, var. Danvers Half-Long, were grown in pots in the greenhouse. Phenyl-U-^{14}C-propiconazole formulated as a 3.6 EC was spray applied as foliar spray. Four equal applications were made at approximately one week intervals, with the final application 14 days before harvest. Carrots were harvested at maturity, and separated in tops (leaves) and roots. Residue levels in root were considerably lower than in leaves. Parent propiconazole was the major residue in roots, accounting for up to 75% TRR (0.62 mg/kg) in the roots. A number of metabolites were present in very low levels (< 3%).

Celery, var. Tall Utah 52/70, was grown in sandy loam soil in the greenhouse. Phenyl-U-^{14}C-propiconazole formulated as a 3.6 EC was applied as a foliar spray.

Unchanged parent propiconazole was the main component in mature celery (approximately 90% of the TRR).

The metabolism of propiconazole was investigated in field and greenhouse grown wheat (variety Svenno) after foliar application using phenyl-[^{14}C] and triazole-[^{14}C] radiolabelled test material.

Samples of upper plant parts harvested after 5 h, 11 and 25 days and of mature straw, husk and grain of triazole-^{14}C-propiconazole treated plants were extracted and partitioned.

The relative amount of parent propiconazole in the upper plant parts decreased from initially 93% at 5 h PHI to 28% and 9.8% at 11 and 25 days PHI, respectively. With degradation of parent propiconazole an increase in polar metabolites could be observed. At maturity, no parent propiconazole could be detected in the grains (< 0.01 mg/kg) whereas the straw still contained 0.18 mg/kg. Most of the radioactivity in grains was water-soluble (85%). A number of other metabolites at generally < 10% were identified in straw, husks and grains of triazole-[^{14}C] treated plants at maturity.

A very similar distribution of radioactivity as described above for triazole-^{14}C treated plants was found for the phenyl-^{14}C treated plants. However, [^{14}C] residues consisting of acidic compounds (not found in any other plant parts) were higher in grains of the triazole-[^{14}C]-experiment. This major (54% of radioactivity in grain) triazole-specific metabolite in the H_2O-phases of wheat grains was identified as 1,2,4-triazole-1-alanine.

Spring wheat, var. Butte 86, was grown in sandy loam soil in the greenhouse. Phenyl-U-^{14}C-propiconazole as a 3.6 EC formulation was spray applied to pots at a rate equivalent to the maximum recommended use rate (1 ×) and at a rate equivalent to five times the maximum recommended use rate (5 ×).

Parent propiconazole represented 0.4%–17% of the radiolabel in wheat samples, with the highest amounts in 50% mature wheat and very small amounts in mature grains (0.4–0.8%) of both 1 × and 5 × treated plants. The low amount of parent compound and phase 1 metabolites indicated extensive metabolism of propiconazole in greenhouse grown wheat. In the 50% mature wheat from the 5 × treatment four metabolites were identified as the glucose- and malonyl glucose conjugates of β-hydroxy alcohol CGA-118244 and γ-hydroxy alcohol CGA-118245. The 5 × mature wheat forage contained a metabolite that consisted of various isomers of the malonyl glucose conjugate of CGA-118244. A total of 83% of the non-extractable radioactivity from mature wheat forage was characterized and demonstrated to be similar to the extractable metabolites.

Rice, variety Labelle (Texas) was seeded in buckets on moist soil (silt loam) in the greenhouse at a density corresponding to 100 kg seeds/ha. A 2–3 cm paddy water layer was maintained in the buckets during the main growing period until 2 weeks before harvest. The plants were treated twice, under the practical conditions in the USA, first in the booting stage and again at full heading, 67 and 83 days after seeding, respectively. Applications were performed by over-top spraying with triazole-[^{14}C] labelled propiconazole formulated as EC 430, each at a rate of 580 mL formulated product/ha or 250 g ai/ha (in 500 L water/ha).

Overall losses from the first application up to harvest time amounted to about 63% of the effectively applied radioactivity. Autoradiography showed that almost no radioactivity was taken up by the young shoots. Total [^{14}C] residues at harvest were 5.2 mg/kg eq in stalks, 2.8 mg/kg eq in husks, 0.29 mg/kg eq in grains, 0.06 mg/kg eq in roots and 0.05 mg/kg eq in the upper 0–5 cm soil layer. Parent propiconazole was degraded in the shoots with a half life of about 15 days. Residual parent concentration at harvest time was highest in soil (78%) and roots (73%), husks (47%) and lowest in the stalks and grains (28% each).

The remaining organosoluble radioactivity in stalks, husks and grains was identified as mono-hydroxy-metabolites including CGA-118244 (all four β-isomers identified in stalks and grains) and CGA-91305. O-glycosides of CGA-118244 (all four β-isomers identified in stalks) and CGA-91305 amounted to 11% and 14% of the radioactivity in husks and stalks, whereas only 0.2% of the

radioactivity in grains was attributable to sugar conjugates. The two major fractions attributing to 35% and 6.7% of the radioactivity in grain extracts were identified as triazolyl acetic acid and triazolyl alanine, conjugates of triazole.

Two sets, one for each label (triazole-[^{14}C] and phenyl-[^{14}C] propiconazole), of a variety of Virginia peanut plants were grown in the greenhouse. Plant material was harvested at the equivalent of a 14 day PHI.

At maturity the triazole- and phenyl-label treated plants respectively, contained 2.9 and 4.4 mg/kg eq in the stalks, 0.33 and 0.05 mg/kg in the kernels, and 0.09 mg/kg in the shells for both labels. Despite the initially lower radioactivity in triazole-^{14}C-propiconazole treated plants, relatively higher amounts were translocated to the kernels.

In mature stalks unchanged parent propiconazole represented 18% of the total [^{14}C] residues for both labels. The nonpolar metabolites of the mature stalks from the two labels were the alkanol CGA-91305 and β-hydroxy alcohol CGA-118244. The [^{14}C] distribution in the mature kernels was significantly different for the two labels, reaching amounts of 0.33 mg/kg eq [^{14}C] residues for the triazole label and 0.05 mg/kg eq for the phenyl label. Most of the radioactivity (74%) in the triazole-labelled kernels was co-chromatographing with triazole.

In another study, peanut plants were sprayed eight times at two week intervals, with the first time 5 weeks after planting, each time at a rate of 28.3 g ai/ha. The soil in the plot was treated at a rate of 69 g ai/ha triazole-^{14}C labelled propiconazole at early pegging and again at the same rate 21 days later. The mature harvest was taken two weeks after the last application, approximately a 14 day PHI. Radioactivity was translocated from the leaves to the nuts.

At maturity two weeks after the last application, the plants contained 12, 2.4 and 14 mg/kg eq [^{14}C] residues in the stalks, shells and kernels respectively. These levels in the field study are much higher than those observed in the greenhouse, i.e., about a factor 40 for mature kernels, although the greenhouse plants received comparable amounts of the test substance as foliar treatment. It is therefore likely that the differences in the radioactive levels resulted from the additional soil applications in the field. Therefore, radioactivity was very likely translocated to the kernels not only from leaves but also from the roots.

The distribution of radioactivity was comparable in field and greenhouse grown plants, however the data indicate that metabolism of propiconazole in field grown peanuts is more extensive than in greenhouse grown peanuts.

Unchanged parent propiconazole, metabolites alkanol CG-91305, β-hydroxy alcohol CGA-118244 isomers, and their acidic sugar conjugates together constituted 44% of the total [^{14}C] residue in the mature peanut stalk. Of the total radioactivity in kernels 94% was co-chromatographing with the triazole standard. In a further (greenhouse) study based on TLC, HPLC, GC-MS and IR data, the major metabolite in mature peanut kernels was found to be the 1,2,4-triazole-1-alanine conjugate. This major metabolite also gives rise to other metabolites, most likely alterations of the alanine moiety.

The metabolism of propiconazole in seed piece dipped sugarcane was investigated in two field studies either using triazole-[^{14}C] or phenyl-[^{14}C] labelled propiconazole. The treated seed pieces were planted in the field. Plant samples were taken at 4, 8, 12, and 16 weeks after germination.

After 4 weeks, [^{14}C] residues were detected, indicating that translocation from the seed pieces to the plants occurred. At the recommended use rate ^{14}C-residue levels had decreased to 0.01 mg/kg by 8 weeks and to non-detectable levels (< 0.01 mg/kg) by 12 weeks. In conclusion, following dip treatment of sugarcane seed pieces, radioactive residues of all mature samples were below 0.01 mg/kg. This was confirmed by a second study.

Comparisons of the metabolic pathways in the different crops indicate that the biotransformation of propiconazole is qualitatively similar in all crops. Degradation takes place via hydroxylation of the propyl side-chain to form β-hydroxy alcohol CGA-118244 and γ-hydroxy alcohol CGA-118245; hydrolysis of the dioxolane ring and subsequent reduction leads to the alkanol CGA-91305. The various hydroxylated metabolites are effectively conjugated with sugars. The

phenyl-triazole bridge is cleaved primarily via conjugation of free 1.2.4-triazole with endogenous serine to give triazolyl alanine. This can then be converted to triazolyl acetic acid and triazolyl lactic acid. Radiolabelled propiconazole residues were able to translocate to other parts of the crops.

Environmental fate in soil

The Meeting received information on confined and field rotational crop studies. The uptake and distribution of triazole-^{14}C-propiconazole was investigated in field-grown rotational crops (lettuce, carrots, corn) following applications to peanuts. The uptake and distribution of [^{14}C] propiconazole was investigated in a greenhouse-grown rotational crop (peanut, winter wheat, field corn) following application to soil. Root uptake of **[**^{14}C] propiconazole and [^{14}C] triazole from soil was studied for spring wheat seedlings. Uptake of non-extractable aged soil residues of triazole-^{14}C-propiconazole was studied for spring wheat. Two sets of rotational crop studies were conducted with soya beans and rice as target crops.

As first rotational crop in the soya bean plots, winter wheat was planted in autumn following soya bean harvest. In the following spring, further rotational crops were planted into the soya bean plots including corn, sweet potatoes, sugar beets, lettuce and cabbage. A second rotation crop of winter wheat was planted one year after the soya bean harvest and was grown into the second year after soya bean harvest. Second crops of corn, sugar beets and lettuce were planted in the second spring after soya bean harvest. As first rotational crop in the rice plots, winter wheat was planted in autumn following rice harvest. Other rotational crops including sorghum, cabbage and sweet potatoes were planted in the following spring. A field rotational crop study was conducted with rape and sugar beet after application of propiconazole to bare soil.

From these studies it can be concluded that the metabolic pathway of propiconazole in rotational crops is similar to that in the target crop, differences being quantitative rather than qualitative. Metabolism was more extensive in rotational crops than in target crops. The major non-polar metabolites (β-hydroxy alcohol CGA-118244, γ-hydroxy alcohol CGA-118245, alkanol CGA-91305) and their conjugates found in the target crops were present only in very small quantities in the rotational crops. The major metabolites in rotational crops were polar and identified as conjugates of 1.2.4-triazole, i.e., triazolyl alanine and triazolyl acetic acid. As an example for spring wheat (uptake aged soil residues) 42% triazolyl alanine and 32% triazolyl acetic acid was found in grain and 40% triazolyl lactic acid and 22% triazolyl acetic acid in straw. It is concluded that more cleavage of the triazole-phenyl bridge occurred in rotational crops than in target crops, and that uptake of polar soil degradation products occurred in rotational crops.

Environmental fate in water-sediment systems

The Meeting received information on the hydrolysis and photolysis of propiconazole in sterile water, and degradation in water/sediment systems.

Propiconazole is hydrolytically stable under relevant environmental conditions. Although stable to photolysis in pure buffer solutions, propiconazole is rapidly degraded in natural waters, presumably via photosensitisation. Any degradation in the water phase by biotic processes is expected to be minimal. Propiconazole will however rapidly adsorb to sediments and 14 days after application 15–20% parent remained in the water; at the end of the study (175 days) only 0.9–2% was left. In the sediment it undergoes slow degradation. At the end of the study at 175 days, 77–82% of the residue in the sediment was still parent, with a small amount of carbon dioxide, alkanol CGA-91305, triazole and bound residues identified as end products.

Methods of analysis

The Meeting received information on methods of residue analysis for enforcement/monitoring and residue methods used in the various study reports. In the EU, the residue definition in commodities of plant and animal origin is parent propiconazole only. In the USA and Canada, residues are determined as total residues having the 2.4-dichlorobenzoic acid (DCBA) moiety. Therefore methods are divided into two groups: methods where only the parent compound propiconazole is determined and methods

where all residues containing the 2,4-DCBA (CGA-177291) moiety are determined ('total residue method').

Multi-method DFG S19 was shown to be sufficiently validated for post-registration monitoring and enforcement of parent propiconazole for commodities of plant and animal origin

In the parent-only methods for plant commodities, macerated samples are typically extracted with methanol and the extract is cleaned up by solvent partition and solid phase column chromatography. The final residue can then be determined by GLC with ECD or NPD or alternatively by LC-MS-MS. LOQs are typically in the 0.01–0.05 mg/kg range. The analytical methods for animal commodities are similar, but with extraction methods tailored for milk, eggs and animal tissues. The LOQ for milk, eggs and tissues is 0.01 mg/kg.

In the total residue methods, homogenized samples were extracted with methanol or acetonitrile and washed with hexane. Homogenized crops or aqueous extracts of oilseeds and nuts were typically refluxed for 16 h with 12 M HNO_3 to convert DCBA-containing residues to 2,4-DCBA. The refluxed solution was diluted with water and partitioned with dichloromethane. The dichloromethane layer was evaporated to dryness and derivatised with diazomethane. The derivative was cleaned-up using silica column chromatography. The 2,4-DCBA methyl ester derivative was determined by GC-MS (CI, at m/z 206) or GC-ECD. Calibration standards were prepared by in-situ derivatisation of 2,4-DCBA standards. Results were expressed as mg/kg eq, by using a factor 1.79. LOQs are typically in the 0.05–0.1 mg/kg range.

Stability of residues in stored analytical samples

The Meeting received information on storage stability of residues in extracts and frozen samples.

Parent propiconazole was stable in the following crop commodities for the intervals tested: soya bean fodder and soya bean grain 6 months at -15 °C, cereal straw and cereal grain 21 months at -20 °C. The Meeting considered these studies sufficient to cover the crops addressed by this Meeting. However, in future more storage stability studies would be desirable if further commodities are to be submitted in which the residue was measured as parent.

Total residues containing the 2,4-DCBA moiety were stable in the following crop commodities for the intervals tested:

- corn silage 8 months at 4 °C,
- soya beans 3.5 months at 4 °C,
- soya bean fodder and grain 6 months, peanut fodder, peanut shell, peanut nutmeat 25 months at -15 °C,
- rye and tall fescue grass (straw and seeds) 38 months at -20 °C, peaches, bananas, corn meal, wheat grain, peanut hay, peanut hulls, peanut nutmeat, celery, corn oil and carrots 3 years at -20 °C.

The stability of propiconazole in products of animal origin was investigated in addendum studies to metabolism studies in hens and goats. Propiconazole residues were found to be stable for up to 223 days in animal tissue when stored frozen.

Definition of the residue

Propiconazole is efficiently degraded in farm animals and is only found in significant amounts in goat liver and fat and hen skin/fat and eggs. Lower amounts are also present in other edible tissues and milk. The major metabolites are the alkanol (CGA-91305) in goat liver and kidney and triazole (CGA-71019) in goat kidney, muscle, fat and milk. In hen edible tissues and eggs, the major metabolites were the alkanol CGA-91305 and the β-hydroxy alcohol CGA-118244. Triazole, the major residue in milk, is not specific for propiconazole since it can be derived from conazole pesticides and is therefore not a good indicator for propiconazole use. Therefore parent is considered to be a suitable residue for enforcement in animal products.

The metabolites containing the dichlorophenyl-moiety were also found in laboratory animals and are therefore included in the toxicological evaluation of JMPR 2004. The Meeting concluded that these metabolites will not be of greater toxicity than the parent and could well be of lower toxicity. However, because of the lack of more specific data, the Meeting decided that all metabolites containing the dichlorophenyl-moiety (=metabolites convertible to 2,4-DCBA) should be taken into consideration for the dietary risk assessment.

The metabolism of propiconazole is qualitatively similar in all plant species tested and resembles that of other fungicides of the triazole family.

Parent propiconazole, although effectively degraded, is still a major component of the total recovered residue in the edible portion of most crops over a longer period following application. The Meeting decided that parent propiconazole is a suitable analyte for enforcement purposes in plant commodities.

In grapes, 33% of the radiolabel was composed of the ketone (CGA-91304) moiety and 5% the alkanol (CGA-91305) moiety, while triazolyl alanine accounted for 10%. In carrots β-hydroxy alcohol CGA-118244, alkanol CGA-91305 and α-hydroxy alcohol CGA-136735 were the most significant metabolites.

Three plant-specific metabolites - triazolyl alanine, triazolyl acetic acid and triazolyl lactic acid - were mainly found in wheat grain, rice grain and rotational crops. They are derived from triazole, which is also found in animal metabolism. These triazole metabolites are of toxicological concern, but are not specific for propiconazole since they are formed from all conazole pesticides. Therefore they should not be part of the propiconazole residue definition for dietary risk assessment. Although national authorities may wish to conduct a separate cumulative risk assessment for these metabolites; in the case of propiconazole, the levels of the triazole metabolites are low under practical conditions.

The Meeting recommended the following as residue definitions for propiconazole.

For plants:

Definition of the residue for compliance with the MRL: propiconazole

Definition of the residue for estimation of dietary intake: propiconazole plus all metabolites convertible to 2.4-dichlorobenzoic acid, expressed as propiconazole

For animals:

Definition of the residue for compliance with the MRL: propiconazole

Definition of the residue for estimation of dietary intake: propiconazole plus all metabolites convertible to 2.4-dichlorobenzoic acid, expressed as propiconazole

The residue is fat soluble.

Results of supervised trials on crops

The propiconazole residues in cranberries were evaluated by the 2006 JMPR. That Meeting estimated a maximum residue of 0.3 mg/kg, an HR of 0.13 mg/kg and STMR of 0.058 mg/kg for cranberries, based upon the residue definition for enforcement, i.e. propiconazole. The present Meeting endorsed those recommendations. As a result of the residue definition for dietary risk assessment, in order to convert from propiconazole to total residue, the STMR and HR values were then multiplied by a factor of 3 to yield 0.39 and 0.174 mg/kg, respectively.

Supervised trials were reported to the present Meeting on apricots, cherries, nectarines, peaches, plums, blackberry, blueberries, raspberry, bananas, pineapples, sugar beets, barley, rye, sorghum, wheat, corn, popcorn, rice, sugarcane, almond, pecan, peanuts, rapeseed, canola seed, soya bean, coffee and tea.

The residues were analysed either as the parent compound or as total residues measured as 2,4-dichlorobenzoic acid (2,4-DCBA) and calculated back to parent compound. The total residues

listed hereunder are the parent compound equivalent of residues measured as 2,4-DCBA. The performance of the analytical methods was within the parameters expected, based on the validation data. The untreated samples contained detectable 2,4-DCBA in several cases. The results reported were not corrected for analytical recoveries or blank values.

The definition of residues specifies the parent propiconazole as the residue for enforcement purposes. Therefore the maximum residue estimates should be based on the parent residues. Residue data on parent compound was available for bananas, sugar beet, barley, rye, wheat, rape and canola seed, soya bean, coffee and tea. For dietary intake calculation purposes, the Meeting estimated in each case what the STMR and HR would be taking into account all residues convertible to 2,4-DCBA.

The Meeting decided (based on the metabolism studies available) to apply a conservative default factor of 3 to food commodities. This would convert parent-only residues to total residues convertible to 2,4-DCBA, except when additional data were available to make a more realistic assessment. For cereal straw a conversion factor of 10 is applied based on metabolism studies.

The Meeting could recommend maximum and median residue levels based on the LOQs of the parent compounds because the maize, corn, pineapple, sugar cane, and pecan residues were measured as total residues based on the determination of 2,4-DCBA. This also took into account that the total residues were below or at the LOQ in all samples.

As the proportion of parent residues and the total residues based on the determination of 2,4-DCBA varied significantly among various crops, the Meeting could not use the residue data for estimation of maximum residue levels for stone fruits, prunes, berries, rice, sorghum, almonds and peanuts. The Meeting withdraws its previous recommendations of maximum residue levels for almonds, peanuts and stone fruits.

No residue data were provided for grapes, mango, oats, and whole peanut, and consequently the Meeting withdraws its previous recommendations for maximum residue levels for these crops.

Residue trials based on the determination of the parent compound

Banana

Field trials were performed on bagged bananas in Honduras applying propiconazole at both the maximum and double rate. Samples were taken between 0 and 9 days after last application (GAP in Honduras for both bagged and non-bagged bananas): 8–10-cycle programme at every 18–21 days. PHI=0). The parent propiconazole was measured in peel and pulp separately. The peel/pulp weight ratio was not reported. The pulp contained non-detectable residues in all bagged samples ($10 \times < 0.02$ mg/kg) regardless of the PHI, and number of applications. Two peel samples out of 10 contained detectable residues (0.024, 0.03 mg/kg).

The compound was also applied 7 or 13 times on non-bagged banana. The banana pulp contained detectable residues in two samples (0.025 and 0.029 mg/kg), while the other pulp samples contained non-detectable residues < 0.02 (12). Following the treatments at the recommended rate (0.1 kg ai/ha) the peel contained residues of < 0.02 (3) 0.021, 0.026, 0.032, 0.044, 0.045, 0.046, 0.07, < 0.072, 0.075, 0.1 mg/kg.

The Meeting took into account that the peel amounts to about 30% of the weight of the whole banana; consequently the calculated maximum residue level in whole banana would be ($0.3 \times 0.1+0.7 \times 0.029=0.052$): 0.02, 0.021, 0.021, 0.022, 0.027, 0.028, 0.044, 0.052 mg/kg.

The Meeting confirmed its previous recommendation of 0.1 mg/kg for whole banana and using the default conversion factor of 3 estimated a median residue of 0.06 mg/kg and an HR of 0.087 (3×0.029) mg/kg in banana pulp.

Sugar beet

Twelve trials were performed in France, Germany and UK applying EC formulation of propiconazole at a rate of 3 times 0.1–0.125 kg ai/ha. The GAP in Denmark (0.125 kg ai/ha PHI 30 days) and

Germany (0.1125 kg ai/ha, PHI 28 days) are very similar. Even after three applications the parent propiconazole residues were below the LOQ (< 0.01 to < 0.05 mg/kg) of the methods in all root samples. The LOQ of the method was 0.01 or 0.02 mg/kg in the more recent trials.

Based on the Danish and German GAP, the Meeting estimated a maximum residue level of 0.02 mg/kg for sugar beet roots. The Meeting withdrew its previous recommendation of 0.05 mg/kg for the maximum residue level. Using the default conversion factor of 3 the Meeting estimated a median residue of 0.06 mg/kg.

Cereals

Barley

Field trials were performed in France, Germany and Switzerland applying propiconazole in accordance with the GAP in France (2 × 0.12 kg ai/ha with 42 days PHI). The parent propiconazole residues in barley grains were: < 0.02 (7), 0.02 (4), 0.025, 0.03, 0.03, 0.03, 0.03, 0.03, 0.04, 0.04, 0.05, 0.1, and 0.11 mg/kg.

Based on the GAP in France, the Meeting estimated a maximum residue level of 0.2 mg/kg, and an STMR of 0.0675 (3 × 0.0225) mg/kg for barley. The Meeting withdrew its previous recommendation of 0.05 mg/kg for barley.

Rye

Two trials were performed with 2 × 0.125 kg ai/ha application rate. Grain samples taken 48–50 days after the second application did not contain detectable parent residues (< 0.01, < 0.02 mg/kg).

Wheat

Field trials were performed in France Germany and UK applying propiconazole in accordance with the GAP in France (2 × 0.12 kg ai/ha with 42 days PHI). The parent propiconazole residues in wheat grains were below the LOQ (< 0.01, < 0.02 mg/kg) in all samples (12).

As the GAP for wheat rye and triticale are the same, and in both commodities the residues were below the LOQ, the Meeting decided to combine residues in wheat and rye.

The Meeting estimated a maximum residue level of 0.02 mg/kg and an STMR of 0.06 (3 × 0.02) mg/kg for wheat and rye and triticale.

The Meeting withdrew its previous recommendation of 0.05 mg/kg for wheat and rye.

Rape and Canola seed

Five trials were conducted in Canada during 2 years applying double rate. The GAP is maximum 3 applications at 0.125 kg ai/ha with a PHI of 60 days. None of the samples (one rape and four canola) contained detectable parent propiconazole residues (0.02 mg/kg). Triazolylalanine (which is not part of the residue definition) was determined separately ranging from 0.38 mg/kg to 2.2 mg/kg.

The Meeting estimated a maximum residue level of 0.02 mg/kg and an STMR residue of 0.06 (3 × 0.02) mg/kg for canola and rape seed.

The Meeting withdrew its previous recommendation of 0.05 mg/kg for rape seed.

Soya bean

Field trials on soya bean were performed in 16 states in the USA. The GAP of the USA allows 2 applications at 0.12–0.18 kg ai/ha at a 21 day interval up to growth stage R6 (first flowers opened). Propiconazole was applied twice by post foliar broadcast spray at 0.19 kg ai/ha. Dried soya bean samples were collected 30 days after the last application. The parent propiconazole residues in dried seed were: < 0.01 (12), 0.01 (3)0.02 (3), 0.04 and 0.05 mg/kg.

The Meeting estimated a maximum residue level of 0.07 mg/kg and an STMR of 0.03 (3 × 0.01) mg/kg.

Coffee

Four trials were performed in Brazil and Mexico at the recommended and double rates. The parent propiconazole residues were below the LOQ of 0.02 and 0.04 mg/kg in the three samples taken 30–40 days after last application.

Based on the Brazilian GAP (apply at 30–60 days interval with 0.15–0.175 kg ai/ha) and Costa Rican GAP (apply at a rate of 0.19–0.25 kg ai/ha maximum 5 times PHI 30 days) the Meeting estimated a maximum residue level of 0.02 mg/kg and an STMR of 0.06 (3 × 0.02) mg/kg for coffee beans.

The Meeting withdrew its previous recommendation of 0.1 mg/kg for coffee.

Tea

Six trials were conducted in Bangladesh and Indonesia following approximately the Indonesian GAP (0.15 kg ai/ha at 10–14 days) in three trials. The green tea leaves 14 days after last application contained the parent propiconazole at the following concentrations: 0.05, 0.08 and 0.11 mg/kg.

As the sampled and analysed commodities did not correspond to the Codex Commodity description, the Meeting could not recommend maximum residue limits.

Recommendations based on total residue

Maize, Sweet corn and popcorn

Numerous field trials were performed in the USA with EC and WP formulation at the recommended maximum and exaggerated rates (1.5 × maximum seasonal rate). The total residue was measured as 2,4-DCBA.

In 19 field corn grain samples the residues were below the LOQ (< 0.05 mg/kg) except in two trials (0.05 and 0.06 mg/kg) regardless of the PHI and the application rate.

Two of eleven popcorn samples contained 0.06, 0.065 (1.2 × rate) mg/kg residue.

Ear samples from four sweet corn trials did not contain any detectable residues (< 0.05 mg/kg).

The Meeting took into account that the parent compound is not the major part of the residues, and estimated a maximum residue level and an STMR value of 0.05 mg/kg for field, sweet and popcorn.

Pineapple

Propiconazole is authorised for seed pieces treatment. No measurable residues of propiconazole, determined as 2,4-dichlorobenzoic acid, were detected (< 0.05 mg/kg) in pineapple fodder, shells, bran or cores from any of the three locations at the exaggerated treatment rates (1.5–3 × label rates).

The Meeting concluded that the registered use of propiconazole does not lead to detectable residues, and estimated a maximum residue level of 0.02* mg/kg and an HR and STMR of 0.02 mg/kg for pineapple.

Sugarcane

Propiconazole is registered for use on sugarcane as a cold and hot dip treatment. A radio-label study indicated that following treatment of seed pieces at 5 × and 10 × rate, there were no measurable residues in cane six months after planting. Furthermore, no TRR (< 0.01 mg/kg) was detected in any plant parts (chopped cane, bagasse, raw sugar, molasses) grown from the seed treated at 5 ×, 10 × and 20 × rates.

The Meeting concluded that the registered use of propiconazole does not lead to detectable residues, and estimated a maximum residue level of 0.02* mg/kg and an STMR of 0 mg/kg in sugar.

The Meeting withdrew its previous recommendation of 0.05 mg/kg for sugar cane.

Pecan

Eight trials were carried out at about 1.5–3 × the registered rate at different locations in the USA during 1980–1984. Samples were collected 7–21 days after last application which is much shorter than the permitted minimum 45 days. The total residues were determined as 2,4-dichlorobenzoic acid (2,4-DCBA). None of the 38 pecan nut samples contained residues above the LOQ of 0.05–0.1 mg/kg.

The Meeting concluded that the registered use of propiconazole does not lead to detectable residues, and estimated a maximum residue level of 0.02* mg/kg and an HR and STMR of 0.02 mg/kg for pecan nuts.

The Meeting withdrew its previous recommendation of 0.05 mg/kg for pecan.

Trials providing data on total residues

As the residues measured do not match the residue definition, the Meeting was unable to estimate residue levels for the following commodities.

Stone fruits

Trials carried out in typical growing areas of the USA were reported to the meeting. The total residues were measured as 2,4-dichlorobenzoic acid (2,4-DCBA).

Apricots

Three trials performed at the maximum recommended rate (0.12 kg ai/ha) resulted in total residues at day 0: 0.08, 0.23 and 0.29 mg/kg.

Nectarines

Sixteen trials were performed in seven States of the USA applying 3–5 times 0.123 kg ai/ha. Samples taken at day 0 (GAP) contained total propiconazole residues of: 0.05, 0.06, 0.12, 0.12, 0.12, 0.12, 0.15, 0.24, 0.26, 0.29, 0.33, 0.4, 0.42, 0.45, 0.65, and 1 mg/kg.

Peaches

Sixteen samples taken at day 0 from trials performed in seven states of the USA where propiconazole was applied 1–5 times at 0.123 kg ai/ha (GAP) contained total propiconazole residues of: 0.05, 0.07, 0.08, 0.14, 0.14, 0.18, 0.24, 0.25, 0.27, 0.27, 0.29, 0.3, 0.32, 0.42, 0.57, and 0.72 mg/kg.

Cherries

Fourteen trials on cherry, tart cherry and sweet cherry were conducted with EC, gel and WP formulations applying propiconazole 5 times at 0.123 kg ai/ha. Samples taken at day 0 contained total residues of: 0.15, 0.18, 0.18, 0.28, 0.36, 0.4, 0.41, 0.46, 0.5, 0.5, 0.66, 0.74, 0.82, and 0.99 mg/kg.

Plums

Eight samples taken at day 0, from trials performed in three states of the USA applying propiconazole 5 times at 0.123 kg ai/ha, contained total propiconazole residues of: < 0.05(4), 0.09, 0.09, 0.12, and 0.17 mg/kg.

Prunes

Four samples taken at day 120, from trials performed in three States of USA applying propiconazole 3 times at 0.123 kg ai/ha, contained total propiconazole residues of: < 0.05(3) mg/kg. Residues in dry prunes were: < 0.05(3) and 0.07 mg/kg.

Berries

Seven field trials were performed in the USA on blueberries and raspberry at the maximum recommended rate. Samples taken 30 days after last application (GAP) contained residues of: 0.16, 0.23, 0.29, 0.31, 0.4, 0.44, and 0.62 mg/kg.

Rice

Twenty two trials were conducted in various states of the USA in 1998 according to US GAP (0.19–0.32 kg ai/ha, 2 application before head emergence). The total residues in rice grain were: 0.09, 0.14, 0.14, 0.41, 0.48, 0.74, 0.86, 0.94, 0.99, 1, 1.15, 1.6, 1.68, 1.75, 1.95, 2, 2.4, 3.6, 3.7, 3.9, 5, and 6.3 mg/kg.

Sorghum

Trials were performed according to the US GAP (0.09–0.12 kg ai/ha with maximum 0.5 kg ai/ha/season) in several states of the USA. The total residues, measured as 2,4-DCBA, found in samples taken at around 21 days were: 0.71, 0.93, 1, 1, 1.3, 1.45, 1.65, 2.05, 2.15, and 2.25 mg/kg.

Almonds

Trials were conducted with concentrate and dilute spray applications of EC and WP formulations in the USA. Following 4 applications at the maximum recommended rate and PHI (0.25 kg ai/ha with 60 day PHI), the total propiconazole residues in almonds were: < 0.05 (8), 0.05, 0.05, 0.06, 0.06, 0.06, 0.06, 0.07, 0.09, 0.09, and 0.1 mg/kg.

Peanut

Six trials were performed at the recommended maximum rate and another 13 trials at about double that rate. The label specifies 14 days PHI for the lower rate and 21 days PHI for the high rate.

The total propiconazole residues at about 21 days after the last application were: < 0.05, 0.05, 0.07, 0.07, 0.08 and 0.08 mg/kg.

Residues at 14 days were: < 0.05, < 0.05, 0.05, 0.06, 0.06, and 0.1 mg/kg.

There was no significant difference between the residues in peanut at 14 and 21 days.

Residues in animal feed

The residues in animal feed resulting from the trials described above are summarized below.

Trials providing data on residues of parent compound

Sugar beet leaves

Following treatments according to the GAP in Denmark and Germany (0.1125–0.125 kg ai/ha and PHI of 28–30 days) propiconazole residues in sugar beet leaves were: 0.01, 0.01, 0.02, 0.04, < 0.1, < 0.1, 0.1, 0.1, 0.2, 0.22, 0.25, 0.25, 0.25, and 0.32 mg/kg.

The Meeting estimated a highest residue level of 0.96 (3 × 0.32) mg/kg and a median residue level of 0.3 (3 × 0.1) mg/kg for sugar beet leaves.

Barley straw

Following applications according to French GAP (2 × 0.125 kg ai/ha with a PHI of 42 days) the residues in barley straw were: 0.03, < 0.04 (4), 0.05, 0.05, 0.07, 0.07, 0.12, 0.14, 0.15, 0.15, 0.22, 0.3, 0.32, 0.36, 0.41, 0.42, 0.68, 0.83, and 0.97 mg/kg.

Wheat straw

Following applications according to French GAP (2 × 0.125 kg ai/ha with PHI of 42 days) the residues in wheat straw in ranked order, median underlined, were: < 0.04, < 0.04, < 0.04, 0.06, 0.1, 0.13, 0.15, 0.19, 0.3, 0.3, 0.32, 0.41, 0.43, 0.49, 0.54, 0.58, 0.65, 0.77, 0.8, 0.81, 0.82, and 0.89 mg/kg.

The Meeting considered that the residue distribution in barley and wheat straw is the same and combined the two data sets. Residue found, in ranked order were: 0.03, < 0.04 (7), 0.05, 0.05, 0.06, 0.07, 0.07, 0.1, 0.12, 0.13 0.14, 0.15, 0.15, 0.15, 0.19, 0.22, 0.3 (3), 0.32, 0.032, 0.36, 0.41, 0.41, 0.42, 0.43, 0.49, 0.54, 0.58, 0.65, 0.68, 0.77, 0.8, 0.81, 0.82, 0.83, 0.89 and 0.97 mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg for barley, rye, triticale and wheat straw. For cereal straw a conversion factor of 10 is applied to convert to total residue based on metabolism studies. The Meeting estimated a highest residue of 9.7 (10 × 0.97) and an STMR of 2.6 (10 × 0.26) mg/kg for barley, rye, triticale and wheat straw.

Soya bean

Soya bean forage

Following the US GAP (2 × 0.12–0.18 kg ai/ha at 21 days intervals up to growth stage R6) the residues 14 days after second application were: 0.1, 0.13, 0.165, 0.2, 0.45, 0.46, 0.5, 0.5, 0.75, 0.77, 0.78, 0.8, 0.8, 0.8, 0.84, and 1.15 mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg, and using the default conversion factor of 3 a highest residue of 3.45 (3 × 1.15) mg/kg, and an STMR of 1.875 (3 × 0.625) mg/kg.

Soya bean fodder

Following the US GAP (2 × 0.12–0.18 kg ai/ha at 21 days intervals up to growth stage R6) the residues 14 days after second application were: 0.12, 0.15, 0.17, 0.335, 0.4, 0.48, 0.65, 0.65, 0.7, 0.77, 1.1, 1.15, 1.2, 1.4, 1.5, and 3.2 mg/kg.

The Meeting estimated a maximum residue level of 5 mg/kg, and using the default conversion factor of 3 a highest residue of 9.6 (3 × 3.2) mg/kg, and an STMR of 2.025 (3 × 0.675) mg/kg.

Trials providing data on total residues based on 2,4-DCBA measurement

Following the corresponding GAPs the residues measured are listed below.

Sorghum forage (total residue): 2.45, 3.1, 3.6, 4.3, 4.55, 4.65, 5, 6.6, 6.9, 7.95, and 8.1 mg/kg.

Sorghum stover (total residue): 4.35, 5.05, 6.25, 6.6, 6.85, 7.3, 7.7, 8, 9.5, and 13.5 mg/kg.

Rice straw (total residue): 0.98, 1.1, 1.15, 1.4, 1.6, 1.65, 1.75, 2, 2.35, 2.35, 2.8, 3.3, 3.45, 3.7, 4, 7.75, 10, 11.5, 13.5, and 16.5 mg/kg.

*Corn forage (*total residue): < 0.05, 0.08, 0.1, 0.35, 0.4, 0.58, 0.69, 1, 1.55, 2.05, 2.1, 2.76, 2.9, and 5.0 mg/kg.

Corn stover and fodder (total residue): < 0.02, 0.02, 0.075, 0.09, 0.46, 0.68, 1.3, 1.5, 1.9, 2.2, 2.4, 2.42, 2.6, 2.65, 3.4, 3.7, 3.72, 3.8, 3.9, 4.1, 4.2, 5, 6.9, 7.7, 8.2, 10, 12.5, 16, and 17 mg/kg.

Almond hull contained total propiconazole residues of: 0.74, 0.75, 0.86, 1.5, 1.75, 1.9, 2.2, 2.6, 2.75, 2.8, 2.9, 3.1, 4.0, 4.7, 6.75, 6.8, 7.2, and 7.4 mg/kg.

Peanut hay contained total propiconazole residues of: 1.7, 2.49, 6.5, 8.7, 13.4 and 14 mg/kg.

As the residues measured do not match the residue definition, the Meeting was not able to estimate residue levels for sorghum forage and stover; rice straw; corn forage, stover and fodder; almond hull and peanut hay.

Fate of residues during processing

The Meeting received information on the fate of radiolabelled propiconazole in grapes processed to grape juice and sugarcane processed to chopped cane, bagasse, raw sugar and molasses. Furthermore the fate of incurred residues of propiconazole during the processing of sugar beet, corn grain, rice, sorghum, wheat, sugarcane, peanut and tea was reported. The processing factors (PF) shown below were calculated from the residues for the commodities for which maximum residue levels, STMRs and HRs were estimated.

In all trials, except for those on grape, sugarcane and tea, residues were measured as 2,4-DCBA and expressed as propiconazole equivalents. Since the Meeting decided that the residue definition is propiconazole, these trials cannot be used for the estimation of MRL, STMR, HR or in calculations of animal dietary burden.

RAC	Processed product	No.	PF	Median PF (or best estimate)
Grape[1]	Grape juice Grape presscake	1	0.05 0.95	0.05 0.95
Tea[2]	Brewed green tea	9	0.03, 0.02, 0.02, 0.03, 0.02, 0.03, 0.02, 0.02, 0.02	0.02

[1] radioactive parent propiconazole; [2] residue measured as parent propiconazole

Grape juice (from grapes in the metabolism study) contained < 0.001 mg/kg unchanged parent propiconazole. The major metabolite in grape juice is 1,2,4-triazole-l-alanine.

Freshly cut sugarcane seed pieces were treated by dipping for one minute in triazole-labelled propiconazole. The seed pieces were then planted and mature sugarcane was collected at 58 weeks after treatment. Sugarcane was processed into chopped cane, bagasse (fibre), raw sugar and molasses. No radioactive residues (< 0.01 mg/kg eq) were found in the raw agricultural commodity or any of the processed commodities. Based on the STMR value of 0 mg/kg for sugar cane, the Meeting decided to estimate an STMR-P of 0 mg/kg for sugar.

Homogenised green tea leaves were extracted with 200 mL boiling water for 2 minutes. The processing factor for brewed green tea was 0.02. Since no MRL and STMR recommendation could be made, the Meeting was unable to recommend an STMR-P for brewed green tea.

Residues in animal commodities

Farm animal feeding

The meeting received a lactating dairy cow feeding study and a laying hen feeding study, which provided information on likely residues resulting in animal commodities, milk and eggs from propiconazole residues in the animal diet.

Lactating dairy cows

Groups of three lactating Holstein dairy cows were dosed once daily either in the feed (low dose) or via gelatin capsule or intra-rumen injection with propiconazole at 15 ppm (1 ×), 75 ppm (5 ×) and 150 ppm (10 ×) in the dry-weight diet for 14–28 consecutive days. Milk samples for analysis were taken at 0, 1, 4, 7, 12, 14, 21 and 28 days and samples of muscle, liver, kidney and fat were collected on 14, 21 and 28 days. Both total residues containing the 2,4-DCBA moiety and parent propiconazole *per se* were determined.

No parent propiconazole (< 0.01 mg/kg) was found in any of the milk samples at all feeding levels. In muscle and kidney, no parent propiconazole (< 0.05 mg/kg) was detectable at all feeding levels. The maximum level in liver was 0.14 mg/kg at the 15 ppm feeding level (average 0.08 mg/kg), 0.34 mg/kg in the 75 ppm feeding level (average 0.22 mg/kg) and 0.66 mg/kg at the 150 ppm feeding level (average 0.42 mg/kg); in fat it was < 0.05 mg/kg at the 15 ppm and 75 ppm feeding levels and 0.08 mg/kg at the 150 ppm feeding level (average 0.06 mg/kg).

No 'total DCBA-residue' (< 0.01 mg/kg) was found in any of the milk samples at the 15 ppm feeding level. At the 75 ppm feeding level, the average total residue in milk was 0.044 mg/kg eq, while the maximum total residue found was 0.08 mg/kg eq. At the 150 ppm feeding level, the average total residue in milk was 0.10 mg/kg eq, while the maximum total residue found was 0.11 mg/kg eq.

In muscle, no 'total DCBA-residue' (< 0.05 mg/kg) was detectable at the 15 ppm feeding level. The maximum level in muscle was 0.11 mg/kg at the 75 ppm feeding level (average 0.08 mg/kg) and 0.18 mg/kg at the 150 ppm feeding level (average 0.14 mg/kg). The maximum level in liver was 0.81 mg/kg at the 15 ppm feeding level (average 0.63 mg/kg), 4.3 mg/kg in the 75 ppm feeding level (average 3.7 mg/kg) and 5.6 mg/kg at the 150 ppm feeding level (average 5.2 mg/kg); in kidney it was 0.63 mg/kg at the 15 ppm feeding level (average 0.60 mg/kg), 4.7 mg/kg in the 75 ppm feeding level (average 3.8 mg/kg) and 6.5 mg/kg at the 150 ppm feeding level (average 5.7 mg/kg); in fat it was < 0.05 mg/kg at the 15 ppm feeding level, 0.23 mg/kg at the 75 ppm feeding level (average 0.15 mg/kg) and 0.26 mg/kg at the 150 ppm feeding level (average 0.21 mg/kg).

Laying hens

Groups of 15 mature white Leghorn hens were fed propiconazole at 7.5 (1 × rate), 37.5 (5 × rate) and 75 (10 × rate) ppm in the feed. Eggs were sampled on 0, 1, 3, 7, 10, 14, 17, 21 and 28 days and pooled by treatment and sampling day. Three birds per treatment group were sacrificed on days 7, 14, 21, and 28. Both total residues containing the 2,4-DCBA moiety and parent propiconazole *per se* were determined. No propiconazole residues (< 0.05 mg/kg) were found in the eggs or the tissue sample analysed regardless of feeding level.

In eggs, no 'total DCBA-residue' (< 0.05 mg/kg) was detectable at the 7.5 ppm feeding level. At the 37.5 ppm feeding level a maximum total residue of 0.18 mg/kg was found (average 0.11 mg/kg). At the 75 ppm feeding level a maximum total residue of 0.37 mg/kg was found (average 0.27 mg/kg).

In muscle, no 'total DCBA-residue' (< 0.05 mg/kg) was detectable at the 7.5 and 37.5 ppm feeding level. The highest average level in muscle was 0.07 mg/kg at the 75 ppm feeding level. In liver, no 'total DCBA-residue' (< 0.1 mg/kg) was detectable at the 7.5 ppm feeding level. The highest average level in liver was 0.16 mg/kg at the 37.5 ppm feeding level and 0.47 mg/kg at the 75 ppm feeding level. In fat, no 'total DCBA-residue' (< 0.05 mg/kg) was detectable at the 7.5 ppm feeding level. The highest average level in fat was 0.05 mg/kg at the 37.5 ppm feeding level and 0.07 mg/kg at the 75 ppm feeding level.

Livestock dietary burden

The Meeting estimated the dietary burden of propiconazole in farm animals on the basis of the diets listed in Annex 6 of the 2006 JMPR Report (OECD Feedstuffs Derived from Field Crops). Calculation from highest residue, STMR (some bulk commodities) and STMR-P values provides the levels in feed suitable for estimating MRLs, while calculation from STMR and STMR-P values for feed is suitable for estimating STMR values for animal commodities. The percentage dry matter is taken as 100% when the highest residue levels and STMRs are already expressed as dry weight.

Estimated maximum and mean livestock dietary burdens

Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are provided in Annex 6. The calculations were made according to the animal diets from US-Canada, EU and Australia in the OECD Table (Annex 6 of the 2006 JMPR Report).

	Animal dietary burden, propiconazole, ppm of dry matter diet					
	US-Canada		EU		Australia	
	max	mean	max	mean	max	mean
Beef cattle	3.0	1.35	4.14	1.18	10.0 [1]	3.35 [2]
Dairy cattle	3.0	1.34	4.55	1.02	4.70 [3]	1.96 [4]
Poultry - broiler	0.07	0.07	0.06	0.06	0.06	0.06

Poultry - layer	0.07	0.07	1.98 [5]	0.75 [6]	0.05	0.05

1 Highest maximum beef or dairy cattle dietary burden suitable for MRL estimates for mammalian meat.

2 Highest mean beef or dairy cattle dietary burden suitable for STMR estimates for mammalian meat.

3 Highest maximum dairy cattle dietary burden suitable for MRL estimates for milk

4 Highest mean dairy cattle dietary burden suitable for STMR estimates for milk.

5 Highest maximum poultry dietary burden suitable for MRL estimates for poultry meat and eggs.

6 Highest mean poultry dietary burden suitable for STMR estimates for poultry meat and eggs.

Animal commodities, MRL estimation

In a feeding study where lactating cows were dosed at 15 ppm dry feed, no parent propiconazole residues were detected in tissues and milk. Therefore no residues are to be expected at the maximum calculated dietary burden of 10 ppm feed for beef cattle and 4.7 ppm for dairy cattle.

In the feeding study where laying hens were dosed at 7.5 ppm feed, no parent propiconazole residues were detected in tissues and eggs. Therefore no residues are to be expected at the maximum calculated dietary burden of 1.98 ppm feed for poultry.

The Meeting estimated a maximum residue level of 0.01* mg/kg in mammalian meat, offal and milk. The Meeting estimated a maximum residue level of 0.01* mg/kg in poultry meat and eggs.

STMRs and HRs are derived from the measurements of total DCBA-containing residues. The mean calculated dietary burden for dairy cattle is 1.96 ppm. No 'total DCBA-residue' (< 0.01 mg/kg) was found in any of the milk samples at the 15 ppm feeding level. Therefore the Meeting estimated an STMR of 0.01 mg/kg in milk.

The highest calculated dietary burden for cattle is 10 ppm. In muscle and fat, no 'total DCBA-residue' (< 0.05 mg/kg) was detectable at the 15 ppm feeding level. The Meeting estimated STMRs and HRs of 0.05 mg/kg in muscle and fat.

In liver and kidney, at the 15 ppm feeding level the maximum total residues were 0.81 and 0.63 mg/kg respectively while the mean values were 0.63 and 0.60 mg/kg, respectively. Because of all the uncertainties involved in the calculation of the dietary burden based on total residue, the Meeting did not extrapolate down but decided to use an STMR of 0.6 mg/kg and an HR of 0.8 mg/kg for edible offal.

The highest calculated dietary burden for poultry is 2 ppm. In eggs, muscle and fat no 'total DCBA-residue' (< 0.05 mg/kg) was detectable at the 7.5 ppm feeding level. The Meeting estimated STMRs and HRs of 0.05 mg/kg in eggs, muscle and fat.

DIETARY RISK ASSESSMENT

Refer to general item on common triazole metabolites.

Long term intake

The evaluation of propiconazole has resulted in recommendations for MRLs and STMRs for raw and processed[1] commodities. Consumption data were available for 21 food commodities and were used in the dietary intake calculation. The results are shown in Annex 3.

The International Estimated Daily Intakes in the 13 GEMS/Food cluster diets, based on the estimated STMRs were in the range 0–2% of the maximum ADI of 0.07 mg/kg bw (Annex 3). The Meeting concluded that the long-term intake of residues of propiconazole from uses that have been considered by the JMPR is unlikely to present a public health concern.

[1] Banana pulp

Short-term intake

The international estimated short-term intake (IESTI) for propiconazole was calculated for the food commodities (and their processing fractions) for which maximum residue levels, STMRs and HRs were estimated and for which consumption data were available. The results are shown in Annex 4.

The IESTI varied from 0–1 % of the ARfD (0.3 mg/kg bw) for the general population. The IESTI varied from 0–3% of the ARfD for children 6 years and below. The Meeting concluded that the short-term intake of residues of propiconazole from uses considered by the Meeting was unlikely to present a public health concern.

5.21 PYRIMETHANIL (226)

TOXICOLOGY

Pyrimethanil is the approved ISO name for *N*-(4,6-dimethylpyrimidin-2-yl)aniline (IUPAC), also known as 4,6-dimethyl-*N*-phenyl-2-pyrimidinamine (CAS; CAS No. 53112-28-0). Pyrimethanil is an anilinopyrimidine fungicide that inhibits the secretion of fungal enzymes. It is a fungicide that is intended for the control of *Botrytis cinerea* on grapes and strawberries.

Pyrimethanil has not been evaluated previously by JMPR and was evaluated by the present Meeting at the request of the 39th Session of the CCPR.[43] All pivotal studies with pyrimethanil were certified as complying with GLP.

Biochemical aspects

In rats given radiolabelled pyrimethanil orally, about 80% of the administered dose was absorbed (for the lower dose, 11.8 mg/kg bw, and for the higher dose, 800 mg/kg bw) on the basis of urinary excretion (cage-wash included) in 96 h. About 72% of the dose was absorbed after pre-treatment with pyrimethanil at a dose of 10 mg/kg bw per day for 14-days, on the basis of urinary excretion (cage-wash included). Pyrimethanil was rapidly excreted at both doses, with more than 95% of the lower dose and 63–67% of the higher dose being excreted within the first 24 h. At the lower dose, plasma concentrations of radioactivity peaked at 1 h after dosing. At the higher dose, plasma concentrations of radioactivity initially peaked at 1 h after dosing. After an initial decline, a second peak of plasma radioactivity was observed at 5 h after dosing. The elimination half-life was about 4.8 h and 11.8 h at the lower and higher dose, respectively. Most of a radiolabelled dose was eliminated in the urine (79–81%) with the remainder in faeces (15–23%) at the lower and higher doses. No bioaccumulation of pyrimethanil was observed. A similar excretion pattern was observed in mice and dogs.

Systemically absorbed pyrimethanil was extensively metabolized. The major metabolites of pyrimethanil in the urine and faeces resulted from aromatic oxidation to form phenols in either or both rings and conjugation with glucuronic acid and sulfate. A minor pathway included oxidation of the methyl group on the pyrimidine ring to produce alcohol. The same six metabolites were identified in the urine and faeces. Unchanged pyrimethanil was isolated only in the faeces of males and females (0.3% and 2.1% of the faecal radioactivity at 10 and 1000 mg/kg bw, respectively). Distribution, metabolite profiles and excretion were essentially independent of pre-treatment with unlabelled compound and of sex.

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[43] Codex Alimentarius Commission. *Report of the 39th Session of the Codex Committee on Pesticide Residues, 7–12 May 2007, Beijing, China* (ALINORM07/30/24).

Toxicological data

Pyrimethanil has low acute toxicity when administered by oral, dermal or inhalation routes. The LD_{50} in rats treated orally was 4149 mg/kg bw in males and 5971 mg/kg bw in females. The LD_{50} in rats treated dermally was > 5000 mg/kg bw. The LC_{50} in rats treated by inhalation (nose only) was > 1.98 mg/L (dust). Pyrimethanil was minimally irritating to the eyes of rabbits and not irritating to the skin of rabbits. Pyrimethanil was not a skin sensitizer as determined by Buehler and Magnusson & Kligman (maximization) tests in guinea-pigs. Clinical signs after oral administration consisted of reduced activity, reduced muscle tone, urogenital soiling, coolness to touch, which generally resolved within 1 day. There were no pathological findings.

In short-term and long-term studies in mice, rats and dogs, the major toxicological findings included decreased body weight and body-weight gains, often accompanied by decreased food consumption. The major target organs in mice and rats were liver and thyroid organs as evidenced by organ-weight changes, histopathological alterations, and clinical chemistry parameters (including increased cholesterol, and gamma-glutamyl transferase levels).

In a 90-day dietary study of toxicity in mice, decreased body-weight gains, slightly increased cholesterol and total bilirubin concentrations, an increase in liver weights and histopathological findings in thyroid, kidney and kidney stones were seen at 10000 ppm, equal to1864 mg/kg bw per day. Increases in thyroid weights were associated with exfoliative necrosis and pigmentation of follicular cells. The NOAEL was 900 ppm, equal to 139 mg/kg bw per day).

In a 90-day dietary study of toxicity in rats, decreased body weights, body-weight gains (28–33%) and decreased food consumptions, brown urine and increased urinary proteins, decreased organ weights (heart, adrenal, spleen, thymus), increased liver, kidney, gonad weights, and hypertrophy in liver and thyroid were seen at 8000 ppm, equal to 529.1 mg/kg bw per day, in both sexes. Thyroid effects in rats were manifested as increased incidence and severity of follicular epithelial hypertrophy and follicular brown pigment. The NOAEL was 800 ppm, equal to 54.5 mg/kg bw per day.

Gavage administration of pyrimethanil at > 600 mg/kg bw per day, the highest dose tested, induced vomiting in dogs within 4 h after dosing, suggesting local gastrointestinal tract irritation. This was not considered to be a toxicologically relevant effect for establishing an ARfD. In a 90-day study of toxicity in dogs, diarrhoea, salivation hypoactivity (within 3 h after dosing) and slightly decreased water consumption was observed at 800 mg/kg bw per day. The NOAEL was 80 mg/kg bw per day. In a 52-week study of toxicity in dogs, decreases in body-weight gains (6% and 17% in males and females, respectively), food consumption and feed-conversion efficiency, water consumption, reduced clotting time and increased count of neutrophils were observed at 250 mg/kg bw per day. The NOAEL was 30 mg/kg bw per day. The overall NOAEL was 80 mg/kg bw per day when results of 90-day and 1-year studies of toxicity in dogs were combined.

Pyrimethanil was not mutagenic in an adequate battery of studies of genotoxicity in vitro and in vivo.

The Meeting concluded that pyrimethanil is unlikely to be genotoxic.

The carcinogenicity potential of pyrimethanil was studied in mice and rats. In a study of carcinogenicity in mice, an increased incidence of urinary tract lesions including bladder distension and thickening were observed in male mice during the first weeks at 1600 ppm, equal to 210.9 mg/kg bw per day. The NOAEL was 160 ppm, equal to 20.0 mg/kg bw per day. There were no treatment-related neoplastic findings in the bioassay in mice.

In the study of carcinogenicity in rats, decreased body-weight gains, increased serum cholesterol and GGT levels, necropsy (dark thyroids), and histopathological findings (increases in centrilobular hepatocyte hypertrophy, and increased incidence of colloid depletion and hypertrophy of the follicular epithelium in thyroids) were observed at 5000 ppm, equal to 221 mg/kg bw per day). The NOAEL was 400 ppm, equal to 17 mg/kg bw per day. In rats given pyrimethanil, the thyroid was the only tissue to show a higher incidence of tumours than the controls. The number of benign follicular

cell adenomas in both sexes at the highest dose was higher than in concurrent controls and historical controls.

Special studies were conducted to evaluate the toxicity seen in the liver and thyroid. Mechanistic data suggest that thyroid hormone imbalance caused by increased thyroid hormone clearance by the induction of liver enzymes resulted in increased thyroid-stimulating hormone (TSH) activity and persistent stimulation of the thyroid. Such effects may lead to changes in thyroid homeostasis and alterations in morphology. Rodent thyroid tumours induced by this mode of action are not relevant to humans because rats are much more sensitive to thyroid hormone imbalance and elevations in TSH levels. Thus, the results of bioassays in rats do not raise a cancer concern for humans.

In view of the lack of genotoxicity and the absence of relevant carcinogenicity in rats and mice, the Meeting concluded that pyrimethanil is unlikely to pose a carcinogenic risk to humans.

In a two-generation study of reproduction in rats, reproductive parameters were not affected at the highest dose tested (5000 ppm, equal to 293.4 mg/kg bw per day). The NOAEL for parental systemic toxicity was 400 ppm (equal to 23.1 mg/kg bw per day) on the basis of decreases in body-weight (11–13%) and body-weight gains (11–17%). Offspring toxicity was manifested as a decrease in pup body weights (17%) on postnatal day 21 at 5000 ppm, equal to 293.3 mg/kg bw per day. The NOAEL for offspring toxicity was 400 ppm, equal to 23.1 mg/kg bw per day. Pyrimethanil was not embryotoxic, fetotoxic or teratogenic at doses of up to 1000 mg/kg bw per day in rats. Pyrimethanil was not teratogenic in rabbits. Decreases in foetal body weights were observed at 300 mg/kg bw per day. These decreases in foetal weights (described as “runts” in the study report) were observed in the presence of severe maternal toxicity manifested as a significant decrease in body-weight gain and food consumption, reduced production and size of faecal pellets and death of three rabbits (moribund condition) at 300 mg/kg bw per day. The NOAEL for maternal toxicity in rabbits was 45 mg/kg bw per day and the NOAEL for developmental toxicity was 300 mg/kg bw per day, the highest dose tested.

The Meeting concluded that pyrimethanil is not teratogenic.

In a study of acute neurotoxicity in rats, transient functional observational battery (FOB) effects (gait, ataxia, decreased hind limb-grip strength in males, decreased body temperature) were observed at 1000 mg/kg bw on day 1. Total motor activity was also decreased by $\geq 52\%$ at 1000 mg/kg on day 1 in both sexes compared with controls. All animals appeared normal on days 8 and 15. As these transient and non-specific effects occurred at a high dose administered by gavage, the Meeting concluded that they were not an appropriate basis for establishing an ARfD. The NOAEL was 100 mg/kg bw. In a short-term study of neurotoxicity in rats, no treatment-related changes in mortality, clinical signs, FOB, motor activity, brain measurements (weight, length, and width), gross necropsy, or neurohistopathology were observed at doses of up to 6000 ppm, equal to 391.9 mg/kg bw per day. In females, an overall decrease in body-weight gain of 21% was observed at 6000 ppm, equal to 429.9 mg/kg bw per day. The NOAEL in females was 600 ppm, equal to 38.7 mg/kg bw per day, and 6000 ppm, equal to 319.9 mg/kg bw per day, in males.

The Meeting considered that pyrimethanil is not neurotoxic on the basis of the available data.

No significant adverse effects were reported in personnel working in production plants.

The Meeting concluded that the existing database on pyrimethanil was adequate to characterize the potential hazards to foetuses, infants and children.

Toxicological evaluation

The Meeting established an ADI of 0–0.2 mg/kg bw based on a NOAEL of 400 ppm (equal to 17.0 mg/kg bw per day) on the basis of increased cholesterol and GGT levels, and histopathological changes in the liver and thyroid at 5000 ppm (equal to 221 mg/kg bw per day) in a 2-year study in rats, and using a safety factor of 100. This ADI is supported a by two-generation study of reproduction in rats in which the NOAEL for parental systemic toxicity was 400 ppm, equal to 23.1 mg/kg bw per

day, on the basis of decreased body weights and body-weight gains at 5000 ppm, equal to 293.3 mg/kg bw per day. This ADI is also supported by the NOAEL of 160 ppm, equal to 20.0 mg/kg bw per day, in males in a 2-year study of toxicity in mice; this NOAEL was identified on the basis of increased incidences of urinary tract lesions including bladder distension and thickening seen at 1600 ppm, equal to 210.9 mg/kg bw per day.

The Meeting concluded that it was not necessary to establish an ARfD for pyrimethanil because no toxicity could be attributable to a single exposure in the available database, including a study of developmental toxicity in rats and rabbits. Observations in the study of acute toxicity in rats and clinical signs of toxicity in the pyrimethanil database appeared at doses of 640 mg/kg bw per day and greater were not considered to be relevant for establishing an ARfD since they were transient, non-specific and occurred at high doses. The Meeting also considered clinical signs (vomiting) in several studies of toxicity in dogs; these were considered to be local effects and therefore not relevant in establishing an ARfD.

A toxicological monograph was prepared.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Mouse	Eighty-week study of toxicity and carcinogenicity[a]	Toxicity	160 ppm, equal to 20.0 mg/kg bw per day	1600 ppm, equal to 210.9 mg/kg bw per day
		Carcinogenicity	1600 ppm, equal to 210.9 mg/kg bw per day[c]	—
Rat	Two-year study of toxicity and carcinogenicity[a]	Toxicity	400 ppm, equal to 17 mg/kg bw per day	5000 ppm, equal to 221 mg/kg bw per day
		Carcinogenicity	5000 ppm, equal to 221 mg/kg bw per day[c]	—
	Multigeneration study of reproductive toxicity[a]	Parental toxicity	400 ppm, equal to 23.1 mg/kg bw per day	5000 ppm, equal to 293.3 mg/kg bw per day
		Offspring toxicity	400 ppm equal to 23.1 mg/kg bw per day	5000 ppm, equal to 293.3 mg/kg bw per day
	Developmental toxicity[b]	Maternal toxicity	85 mg/kg bw per day	1000 mg/kg bw per day
		Embryo/fetotoxicity	1000 mg/kg bw per day[c]	____
Rabbit	Developmental toxicity[b]	Maternal toxicity	45 mg/kg bw per day	300 mg/kg bw per day
		Embryo/fetotoxicity	45 mg/kg bw per day	300 mg/kg bw per day
Dog	Ninety-day and 1-year study of toxicity[b]	Toxicity	80 mg/kg bw per day	400/250 mg/kg bw per day

[a] Dietary administration.
[b] Gavage administration.
[c] Highest dose tested.

Estimate of acceptable daily intake for humans

0–0.2 mg/kg bw per day

Estimate of acute reference dose

Unnecessary

Information that would be useful for continued evaluation of the compound

Results from epidemiological, occupational health and other such observational studies of human exposure

Critical end-points for setting guidance values for exposure to pyrimethanil

Absorption, distribution, excretion, and metabolism in mammals	
Rate and extent of oral absorption	Rapid and nearly complete absorption; maximum plasma concentration reached by 1 h
Distribution	Widely distributed in tissues
Potential for accumulation	Low, no evidence of accumulation
Rate and extent of excretion	Approximately 97% (77% in urine and 20% in faeces) within 24 h at 11.8 mg/kg bw per day
Metabolism in animals	Extensive; metabolic pathways include aromatic oxidation to form phenols and conjugation with glucuronic acid and sulfate, minor pathway included oxidation of methyl group to produce alcohol
Toxicologically significant compounds in animals, plants and the environment	Pyrimethanil
Acute toxicity	
Rat, LD_{50}, oral	4149 mg/kg bw for males
Rat, LD_{50}, dermal	> 5000 mg/kg bw
Rat, LC_{50}, inhalation	> 1.98 mg/L dust (4-h exposure, nose only)
Rabbit, skin irritation	Not an irritant
Rabbit, eye irritation	Minimal irritation
Guinea-pig, skin sensitization	Not a sensitizer (Magnussen & Kligman and Buehler test)
Short-term studies of toxicity	
Target/critical effect	Liver and thyroid hypertrophy
Lowest relevant oral NOAEL	54.5 mg/kg bw per day (90-day-rat)
Lowest relevant dermal NOAEL	No data
Lowest relevant inhalation NOAEC	No data
Genotoxicity	
	No genotoxic potential
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	Liver and thyroid
Lowest relevant NOAEL	17 mg/kg bw per day (2-year study of carcinogenicity in rats)
Carcinogenicity	No relevant carcinogenicity in mice and rats
Reproductive toxicity	
Reproduction target/critical effect	No toxicologically relevant effects
Lowest relevant reproductive NOAEL	239.9 mg/kg bw per day (rats; highest dose tested)

Developmental target/critical effect	No developmental toxicity in rats and rabbits
Lowest relevant developmental NOAEL	300 mg/kg bw per day (highest dose tested; rabbits)
Neurotoxicity/delayed neurotoxicity	
Acute neurotoxicity	No sign of specific neurotoxicity
Mechanistic data	
	Studies on hepatic clearance and thyroid hormone perturbations
Medical data	
	No significant adverse health effects reported

Summary

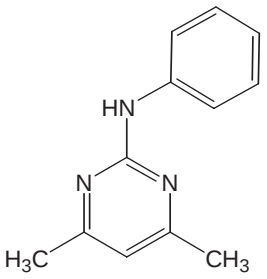
	Value	Study	Safety factor
ADI	0–0.2 mg/kg bw per day	Rats, 2-year study of toxicity	100
ARfD	Unnecessary	—	—

RESIDUE AND ANALYTICAL ASPECTS

Pyrimethanil is an anilinopyrimidine fungicide that inhibits the secretion of hydrolytic enzymes by the fungi that are needed during the infection process. Pyrimethanil blocks the ability of fungi to degrade and digest the plant tissues, thus stopping penetration and development of the disease.

At the 37th session of the CCPR (ALINORM 04/27/24), pyrimethanil was listed as a candidate for evaluation of a new compound by the 2007 JMPR.

Chemical name: N-(4,6-dimethylpyrimidin-2-yl) aniline



Animal metabolism

The Meeting received results of an animal metabolism study in lactating dairy cows. A lactating dairy cow was orally dosed for seven consecutive days with [^{14}C]pyrimethanil at a daily dose rate of 10 ppm in the diet, which corresponds to 0.4 mg/kg bw per day for a 600 kg cow. Residues in muscle and fat were too low to isolate and identify (0.02–0.04mg/kg total radioactive residue, TRR). The TRR in milk reached a plateau on about day 5 (0.07 mg/kg). No pyrimethanil was found in the milk from any day of the treatment. The major metabolite present in milk (64% TRR) was identified 2-anilino-4,6-dimethylpyrimidin-5-ol. Also present in milk were metabolites (27% TRR) characterized as highly polar.

Parent pyrimethanil was not found in kidney or liver. The TRR in kidney was identified as 46% 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine, 5% 2-anilino-4,6-dimethylpyrimidin-5-ol, and 7% 2-(4-hydroxyanilino)-4-hydroxymethyl-6-methylpyrimidine. Again, 42% TRR was characterized as

highly polar. No metabolite was identified in liver, but the TRR was characterized as 48% protein, 9% lipid, 7% ribonucleic acid and 6% sulfurated glycoamino-glycans.

Metabolism in the rat was quite similar to that of the cow. In the rat, only small amounts of the administered pyrimethanil were found in faeces and none was found in urine. The major metabolite in urine and faeces was 2-(4-hydroxyanalino)-4,6-dimethylpyrimidine and its sulfate, 13–52%. Other metabolites, generally < 10% of total extracted radioactivity in the excreta, were 2-anilino-4,6-dimethylpyrimidin-5-ol, 2-(4-hydroxyanilino)-4-hydroxymethyl-6-methylpyrimidine, 2-(4-hydroxyanilino)-6-dimethyl-pyrimidin-5-ol and 2-anilino-6-methylpyrimidine-4-methanol.

The Meeting concluded that pyrimethanil is very extensively metabolised in cattle, forming monohydroxy and dihydroxy derivatives in milk and kidney, and being incorporated into biological substrates in liver. No accumulation occurs in muscle or fat.

Plant metabolism

The Meeting received plant metabolism studies for the foliar application of [^{14}C]pyrimethanil, radiolabelled either on the aniline ring or at C-2 of the pyrimidine ring, for apples, grapes, carrots, tomato, leaf lettuce and strawberry. Generally the majority of the radioactivity was removed in a dichloromethane surface wash (56% grapes, 90% tomato). In all instances, the major component of the TRR was pyrimethanil (apple fruit, 70–77%; carrot root, 70–89%; tomato fruit, 95–96%; leaf lettuce 44%; strawberry fruits, no identifications made). Minor metabolites identified included hyrdoxylated and conjugated derivatives of pyrimethanil 2% TRR, and the ß-O-glucoside of 2-anilino-4-hydroxymethyl-6-hydroxymethylpyrimidine 3% TRR in apples; malonyl-β-O-glucoside of 2-anilino-hydroxymethyl-6-methylpyrimidine 6% TRR, and the β-glucoside of 2-anilino-4-hydroxymethyl-6-methylpyrimidine 6% TRR on carrot foliage (< 1% TRR each on carrot root); hydroxylated and conjugated compounds of pyrimethanil 6–28% TRR on tomato leaves; conjugate of 2-(4-hydroxyanilino)-4,6-dimethylpyridine 5% TRR and conjugate of 2-anilino-4,6-dimethylpyrimidin-5-ol, 8% TRR on leaf lettuce. Where both radiolabels were tested on the same crop, no significant differences were found in the compositions of the TRRs.

The Meeting concluded that the metabolism of pyrimethanil had been adequately defined via studies on three distinct crop types: fruit, root and leafy. Very little metabolism occurs, and the major portion of the residue is the parent pyrimethanil. The similarity in metabolic profiles between studies conducted with the radiolabel in either the aniline ring or the pyrimidine ring indicates no cleavage at the ring junction (aniline amino group). Minor metabolites identified are hydroxylated and conjugated derivatives of pyrimethanil, and are generally less than 10% TRR.

Environmental fate

The Meeting received studies on aqueous hydrolysis, aerobic and anaerobic degradation in soil, photolysis in water and residues in succeeding crops. Pyrimethanil is stable to hydrolysis in water at pH 5, 7 and 9 at 20 °C.

Under aerobic conditions, pyrimethanil slowly degraded in soil with about 80% remaining after 130 days. This was followed by a rapid decline in both extractable radioactivity and pyrimethanil levels. At higher soil treatment rates (500 mg/kg) differences were seen in the apparent degradation of the pyrimidine and aniline labels. With the pyrimidinyl label, about 60% of the extractable radioactivity was identified as 2-amino-4,6-dimethylpyrimidine. Cleavage of the aniline linkage is indicated.

Pyrimethanil does undergo photolytic degradation in water (sterile buffer) at pH 4 and pH 7 with estimated half-lives of 1 and 80 days, respectively. In a separate experiment using in sterile water containing humic acids, the half-life was reduced to less than 2 days at pH 7.

The Meeting concluded that pyrimethanil is stable under aqueous hydrolysis at pH 2–9 and is relatively stable on soil under aerobic conditions. It was also concluded that pyrimethanil is not stable in water under photolysis.

The uptake of 2-[^{14}C]pyrimidinyl-labelled pyrimethanil in *rotational crops* under confined conditions was reported to the Meeting. The pyrimethanil was applied to soil at a rate of 2.4 kg ai/ha. Substantial residues were found in crops planted 30 days after the treatment, 0.23 to 8.2 mg/kg TRR as pyrimethanil. Pyrimethanil comprised 1% (radish top) to 45% (wheat forage) of the TRR. The major identified metabolite (> 10% TRR) was 2-anilino-4-hydroxymethyl-6-methylprimidine in wheat forage and lettuce. Pyrimethanil was < 0.05 mg/kg in all rotational crops at the 30 day plantback interval, *except* for wheat grain (73 day, 0.41 mg/kg TRR, < 0.001 mg/kg pyrimethanil), forage (35 day immature, 1 mg/kg TRR, 1.1 mg/kg pyrimethanil), and straw (73 day, 8.2 mg/kg TRR, 0.22 mg/kg pyrimethanil). At a 130 day plantback interval, total residues in the crops declined to 0.01 to 0.03 mg/kg, with parent comprising 1–26% of the TRR. No extractable metabolite exceeded 10% TRR.

Three field rotational crop studies with a single crop, wheat, were conducted. Using a 30 day plantback interval following harvest of treated potatoes (3 applications at 0.8 kg ai/ha), residues of pyrimethanil and 2-anilino-4-hydroxymethyl-6-methylprimidine were below the limits of detection (< 0.012 mg/kg for pyrimethanil and < 0.015 mg/kg for 2-anilino-4-hydroxymethyl-6-methylprimidine), except for one wheat forage sample (< 0.05 mg/kg LOQ). The intervals from plantback to harvest were 128–232 days for forage and 190–316 days for straw.

The Meeting concluded that residues of pyrimethanil, in rotational crops planted 30 days or more after the final application of pyrimethanil to the primary crop, will most likely be below the LOQ (< 0.05 mg/kg), with the possible exception of forages and straws.

Methods of Analysis

The Meeting received information for analytical methods on the quantitative determination of pyrimethanil in a variety of crops and for the determination of pyrimethanil and metabolites 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine and 2-anilino-4,6-dimethylpyrimidine in bovine commodities.

The plant commodity methods consist of organic solvent extraction (acetone or methanol), clean-up, and analysis by either gas chromatography, with a mass spectrometer detector (GC/MS, m/z 198), or by high performance liquid chromatography with an ultraviolet detector (HPLC). The HPLC method was validated for apples, tomatoes, grapes, green beans, wine, grape juice, and grape pomace. The validated limits of quantitation (LOQs) are 0.05, 0.05, 0.02, 0.05, 0.02 and 0.02 mg/kg, respectively. The GC/MS method was validated for potatoes, carrots, tomatoes, green beans, lettuce, sweet peppers, strawberries, raspberries, apples, peaches, plums and oranges. A LOQ of 0.05 mg/kg was demonstrated for all of these commodities.

A radiovalidation study was conducted for the GC/MS procedure. Lettuce from the metabolism study was subjected to the extraction and analysis procedures of the method. Extraction efficiency was 97%.

A GC/MS method was described for the determination of pyrimethanil and metabolites 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine and 2-anilino-4,6-dimethylpyrimidin-5-ol in milk, fat, muscle, liver and kidney. The metabolites are converted to methylated derivatives prior to analysis. The demonstrated LOQs are 0.01 mg/kg for each of the analytes in milk and 0.05 mg/kg in each of the analytes in the various tissues. The independent laboratory validation encountered considerable problems and did not achieve acceptable validation for precision for pyrimethanil in meat at 0.05 mg/kg and overall at levels of 0.05 and 0.5 mg/kg. No radiovalidation of the method was reported.

Multiresidue methods (US FDA and DFG S 19) were reported for pyrimethanil in various plant commodities.

The Meeting concluded that adequate analytical methods exist for both data collection and enforcement purposes for pyrimethanil residues in plant commodities and for pyrimethanil, 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine (SN 614276), and 2-anilino-4,6-dimethylpyrimidin-5-ol (SN 614277) in milk and bovine tissues.

Stability of pesticide residues in stored analytical samples

The Meeting received information on the stability of pyrimethanil in a variety of crop matrices, but no information on stability in livestock commodities. Pyrimethanil is stable (< 30% loss) in apples, grapes, tomatoes, lettuce, carrots, peas (dried), peaches and plums for at least 365 days when the commodities are stored frozen at about -20 °C.

The Meeting concluded that pyrimethanil is stable on frozen plant commodities for at least one year. No conclusions are possible on the stability of pyrimethanil or its metabolites in livestock commodities.

Residue definition

The major component of the residue on numerous plant commodities, from the foliar application of pyrimethanil, is pyrimethanil. Minor amounts of hydroxylated pyrimethanil derivatives are found, generally < 10% each of the total residue. The two analytical methods determine only pyrimethanil.

In livestock (cow) commodities, pyrimethanil is not found following oral administration of the compound. The major metabolites are 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine and 2-anilino-4,6-dimethylpyrimidin-5-ol, in kidney and milk, respectively. The analytical method provided determines the parent and the two named metabolites.

The log of the octanol/water partition coefficient is 2.8. In the cow feeding study, no pyrimethanil (< 0.05 mg/kg) was found in either fat or muscle at a 50 ppm feeding level. In the same study, the milk fat contained 0.031 mg/kg of 2-anilino-4,6-dimethylpyrimidin-5-ol, and the skim milk contained 0.064 mg/kg of 2-anilino-4,6-dimethylpyrimidin-5-ol and 0.015 mg/kg 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine. Thus, the total residue concentrated slightly in the non-fat portion of milk.

The Meeting concluded that the residue definition for both enforcement and dietary exposure considerations for plant commodities is pyrimethanil. The Meeting further concluded that the residue definition for both enforcement and dietary exposure considerations for milk is the sum of pyrimethanil and 2-anilino-4,6-dimethylpyrimidin-5-ol, expressed as pyrimethanil and for livestock tissues (excluding poultry) is the sum of pyrimethanil and 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine, expressed as pyrimethanil.

The Meeting also decided that pyrimethanil is not fat-soluble.

Results of supervised trials on crops

The Meeting received supervised trials data for the foliar application of pyrimethanil as a suspension concentrate formulation (SC) to a variety of fruit, vegetable, and nut crops. Additionally, supervised trial data reports were received for the post-harvest treatment of citrus, pome fruit and cherries.

Citrus

Various post-harvest treatments of lemon, orange, tangelo, tangerine, and grapefruit were reported for 45 trials from the USA. The USA GAP is: 204 g/L pyrimethanil + 263 g/L imazalil SC, dip or wash at 0.08 kg ai/hL or drench at 0.08 kg ai/hL or aqueous line spray at 0.1 kg ai/hL or wax line spray/storage and pack wax at 0.2 kg ai/hL, with a maximum of two treatments (of all types); 400 g/L pyrimethanil SC, dip or wash at 0.1 kg ai/hL or drench at 0.05 kg ai/hL or aqueous line spray at 0.2 kg ai/hL or wax line spray/storage and pack wax at 0.2 kg ai/hL, with a maximum of 2 or 3 treatments. Additionally, eight trials for the post-harvest treatment of oranges and mandarins in Spain were reported. No GAP was supplied, and the GAP of the USA was utilized. Thirty-three USA trials (9 × lemon, 10 × orange, 5 × grapefruit, 4 × tangelo and 4 × tangerines) were at maximum GAP. No Spanish trials matched the USA GAP.

Residues in the 32 trials in ranked order (median underlined) were: 1.2 (3), 1.4, 1.5 (2), 1.7 (2), 1.9, 2.1, 2.2, 2.3, 2.6, 2.7 (3), 2.8 (3), 2.9, 3.1, 3.3, 3.4 (2), 3.6, 4.1 (2), 4.2, 4.3, 4.6, 5.5,

5.8 mg/kg. No data were provided on the analysis of the edible portion (pulp). The Meeting estimated a maximum residue level of 7 mg/kg (Po) and an STMR of 2.8 mg/kg.

Pome fruit

Pre-harvest apple trials were reported from Europe and the USA. Pear trials were reported from the USA.

Two apple trials were conducted in Germany, two in northern France, and one in the UK. None of the trials matched the GAP of Belgium, 400 g/L SC, 0.45 kg ai/ha, 0.22 kg ai/hL, 5 applications, 28 day PHI. Two apple trials were conducted in southern France, two in Italy and one in Spain. One trial matched the GAP of Italy, 400 g/L SC, 0.04 kg ai/hL, 5 applications, 14 day PHI. The residue (Italy) was 0.56 mg/kg.

Twelve apple trials were conducted in the USA at the GAP, 400 g/L SC, 0.45 kg ai/ha, 1.8 kg ai/ha per season, 72 day PHI. The residues in ranked order are: < 0.05 (7), 0.06, 0.10, 0.12, 0.15, 0.16 mg/kg.

Six pear trials were conducted in the USA under the same USA GAP as apples. The residues found were: < 0.05 (6) mg/kg.

Post-harvest treatment of apples was reported from Spain and France and the USA. The GAP of Belgium is 200 g/L pyrimethanil + 200 g/L imazalil SC, spray or dip at 0.04 kg ai/hL, one treatment. Two of nine European trials were at the maximum GAP, and residues are 0.57 and 1.7 mg/kg. An additional trial matched the GAP of Chile, 3.78 mg/kg.

The GAP of the USA is dipping, drenching or aqueous line spray at 0.1 kg ai/hL or wax line spray at 0.2 kg ai/hL. Up to 2 treatments (of any combination) may be used. The GAP of Chile is identical, but only one treatment is permitted. Using the GAP of the USA, no trials are at GAP. Using the GAP of Chile, 10 of 32 trials were at maximum GAP. The residues in ranked order on apples were: 0.27, 0.28, 0.33, 0.39, 0.64, 0.70, 1.1 (2), 1.2, 1.5 mg/kg. Studies on the post-harvest treatment of pears in the USA were also reported. The GAPs of Chile and the USA are the same as for apples. Using the GAP of the USA, the residues of two trials are at GAP 1.01 and 1.18 mg/kg. Using the GAP of Chile, an additional eight of 35 trials were at the maximum GAP. Residues of pyrimethanil in ranked order were: 0.13, 0.18, 0.32, 0.45, 0.56, 0.86, 1.1 (2) mg/kg. Six post-harvest treatment trials on pears were reported from France, Spain and Belgium. No trials matched the GAPs of Chile or the USA. Two trials (BE, FR) matched the GAP of Belgium (200 g/L pyrimethanil + 200 g/L imazalil SC, spray or dip at 0.04 kg ai/hL, one treatment), and the residue values are 0.32 and 0.55 mg/kg.

Studies on the thermofogging post-harvest treatment of apples and pears in Europe was reported. However, the only GAP supplied (Chile) has yet to be approved by the national government. The Meeting noted that the maximum residue under the proposed GAP was 3.5 mg/kg on pears in Italy.

The residue values for post-harvest treatment of apples and pears in the USA and Europe at the GAPs of Chile or the USA are from the same population and may be combined. Residues in the 21 trials in ranked order (median underlined) were: 0.13, 0.18, 0.27, 0.28, 0.32, 0.33, 0.39, 0.45, 0.56, 0.64, 0.70, 0.86, 1.0, 1.1 (4), 1.2 (2), 1.5, 3.8 mg/kg. Based on the post-harvest treatments, the Meeting estimated an STMR of 0.70 mg/kg and a maximum residue level of 7 mg/kg for pome fruit (Po).

Stone fruit

Apricot, peach and plum trials were reported from the USA. The GAP is identical for all: 600 g/L SC, 0.8 kg ai/ha, 2.4 kg ai/ha/season, 2 day PHI. Five apricot trials were at maximum GAP: 0.61, 0.64, 1.2, 1.3, 1.7 mg/kg. Twelve peach trials were at maximum GAP: 0.38, 0.54, 0.94, 1.1, 1.2, 1.3 (3), 1.5, 1.6, 2.6 mg/kg. Eight plum trials were at maximum GAP: 0.05, 0.44, 0.58, 0.59 (2), 0.61, 0.62, 1.2 mg/kg.

The Meeting considered the apricot, peach and plum trials not to be from the same population. The Meeting estimated an STMR of 1.2 mg/kg and a maximum residue level of 3 mg/kg for apricots.

The meeting estimated an STMR of 1.3 mg/kg and a maximum residue level of 4 mg/kg for peaches and for nectarines. The Meeting estimated an STMR of 0.59 mg/kg and a maximum residue level of 2 mg/kg for plums.

Reports on the post-harvest treatment of peaches and plums in the USA were reported, but no GAP was provided.

Reports on the post-harvest treatment of cherries in Germany were reported. A GAP was supplied for Chile (400 g/L SC, dipping, 0.04 kg ai/hL, 1 application. Eight trials were at maximum GAP, and the values in ranked order were: 0.82, 1.0, 1.1, 1.2, 1.4(3), 2.5 mg/kg. The Meeting estimated an STMR of 1.3 mg/kg and a maximum residue level of 4 mg/kg (Po) for cherries.

Berries and other small fruits

Supervised trials for the foliar application of pyrimethanil to grapes were reported from the EU and the USA. Five trials in northern Europe (two from Germany and three from France) were evaluated against the GAP of France (400 g/L SC, 1 kg ai/ha, 1 application, 21 days PHI: 0.37, 0.44, 0.59, 0.97, 1.1 mg/kg); and 10 trials in southern Europe (2 Spain, 6 France, 2 Italy: 0.28, 0.48, 1.0, 1.5 mg/kg) were evaluated against the GAP of Spain (400 g/L SC, 0.08 kg ai/hL, one application, 21 day PHI). Nine trials were at maximum GAP, and the residues in ranked order were: 0.28, 0.37, 0.44, 0.48, 0.59, 0.92, 1.0, 1.1, 1.5 mg/kg.

Twelve trials were reported from the USA (USA GAP: 600 g/L SC, 0.8 ka ai/ha, 1.6 kg ai/ha/season, 7 day PHI). All trials were at maximum GAP, and the residues found were: 0.12, 0.44, 0.49, 0.64, 0.66, 0.71, 0.89, 1.2, 1.5, 1.6, 2.0, 2.5 mg/kg.

The Meeting considered the EU and USA trials to be from the same population and combined the results. Residues in the 21 trials in ranked order (median underlined) were: 0.12, 0.28, 0.37, 0.44(2), 0.48, 0.49, 0.59, 0.64, 0.66, 0.71, 0.89, 0.92, 1.0, 1.1, 1.2, 1.5 (2), 1.6, 2.0, 2.5 mg/kg. The Meeting estimated an STMR of 0.71 mg/kg and a maximum residue level of 4 mg/kg for grapes.

Eight trial were conducted on the foliar application of pyrimethanil to strawberries in the USA, where the GAP is 600 g/L SC, 0.8 kg ai/ha, 2.4 kg ai/ha/season, 1 day PHI. All trials were at maximum GAP, and the residues in ranked order (median underlined) were: 0.79, 0.93, 0.99, 1.1, 1.2, 1.3(2), and 2.3 mg/kg. The Meeting estimated an STMR of 1.2 mg/kg and a maximum residue level of 3 mg/kg for strawberries.

Bananas

Eleven trials each on the foliar treatment of bagged and unbagged bananas with pyrimethanil were reported from Costa Rica (3), Ecuador (3), Colombia (3) and Guatemala (2). The GAP is identical in all these countries: 600 g/L SC, 0.3 kg ai/ha, 6 applications, 0 day PHI (constant harvesting). All residues were below the LOQ except one bagged banana sample in Ecuador. The residues in ranked order were: < 0.05 (21), 0.09 mg/kg. All pulp samples were < 0.05 mg/kg. The Meeting estimated an STMR of 0.05 mg/kg and a maximum residue level of 0.1 mg/kg for bananas.

Bulb Vegetables

Nine trials were conducted on the foliar application of pyrimethanil to dry bulb onions and spring onions in the USA, where the GAP is: 600 g/L SC, 0.8 kg ai/ha, 2.4 kg ai/ha/season, 7 days PHI. All trials were conducted at maximum GAP, and the residues in ranked order on bulb onions were: < 0.05 (3), 0.075, 0.087, 0.095 mg/kg. Residues on green onions in ranked order are: 0.26, 0.38, 1.6 mg/kg. The Meeting estimated an STMR of 0.062 mg/kg and a maximum residue level of 0.2 mg/kg for bulb onions (dry). The Meeting estimated an STMR of 0.38 mg/kg and a maximum residue level of 3 mg/kg for spring onions.

Fruiting Vegetables, Other than Cucurbits

Sixteen trials were conducted on the foliar application of pyrimethanil to tomatoes in the USA, where the GAP is: 600 g/L SC, 0.3 kg ai/ha, 1.6kg ai/ha/season, 1 day PHI. All trials were at maximum

GAP, and the residues in ranked order were: 0.06, 0.07 (3), 0.10, 0.13, 0.14 (2), 0.15, 0.16, 0.17, 0.20, 0.22, 0.23, 0.35, 0.37 mg/kg.

Eight glasshouse trials were conducted in Europe, 2 in France and 6 in the Netherlands. The GAP of France is 400 g/L SC, 0.8 kg ai/ha, 2 applications, 3 day PHI. All trials were at maximum GAP, and the residues in ranked order (median underlined) were: 0.26 (2), 0.31 (2), 0.33 (2), 0.36 (2) mg/kg.

The USA and EU trials were not considered to be from the same population, and the Meeting used the EU trials to estimate an STMR of 0.32 mg/kg and a maximum residue level of 0.7 mg/kg for tomatoes.

Leafy Vegetables

Trials were conducted on both head lettuce and leaf lettuce in Europe. The GAP of France (400 g/L SC, 0.8 kg ai/ha, 2 applications, 21 day PHI) was applied to field trials in the UK (4), the Netherlands (1), France (North, 2), and Germany (2): < 0.05 (5), 0.11, 0.13, 0.28, 0.43 mg/kg. The GAP of Italy (400 g/L SC, 0.8 kg ai/ha, 2 applications, 14 day PHI) were applied to trials in Italy (2), Greece (1), France (South, 1), and Spain (1): 0.05, 0.14, 0.31, 0.77, 1.2 mg/kg. The residues in ranked order for head lettuce were: < 0.05 (5), 0.05, 0.11, 0.13, 0.14, 0.28, 0.31, 0.43, 0.77, 1.2 mg/kg.

Glasshouse trials were also reported from Europe (UK, Netherlands and Germany) for head lettuce. The GAP of Italy is 400 g/L SC, 0.8 kg ai/ha low volume, 0.08 kg ai/hL high volume, 2 applications, 14 day PHI. All trials were at maximum GAP, using high volume, and the residues in ranked order were: 0.37, 0.41, 0.49, 0.61, 0.85, 0.97 (2), 1.4, 1.6 mg/kg.

The Meeting considered the field and glasshouse trials in Europe not to be from the same population and used the glasshouse trials to estimate an STMR of 0.85 mg/kg and a maximum residue level of 3 mg/kg for head lettuce.

Field trials were also conducted in France, Greece, Italy and Portugal for leaf lettuce. Using the GAP of Italy (400 g/L SC, 0.8 kg ai/ha, 2 applications, with a 14 day PHI), three of the four trials were at maximum GAP. The residues in ranked order are 0.62, 0.68, 7.5 mg/kg. The Meeting considered three trials an insufficient number for the estimation of an STMR and a maximum residue level for leaf lettuce.

Legume Vegetables

Trials for the application of pyrimethanil to common beans (green beans) were reported from France (4) and Germany (3). The GAP in France is 400 g/L SC, 0.6 kg ai/ha, 1 application, 14 day PHI. Residues in ranked order were: < 0.05 (3), 0.05, 0.07, 0.08, 0.09.

Trials were also reported for the treatment of green beans in glasshouses in France (2), Italy (1), Spain (3), and Greece (2). The GAP of France is 400 g/L SC, 0.6 kg ai/ha, 14 day PHI. The residues in ranked order (median underlined) were: < 0.05, 0.12, 0.13, 0.20, 0.25, 0.28, 0.91, 1.9 mg/kg.

The Meeting considered the field and glasshouse trials on green beans not to be from the same population and used the glasshouse trials to estimate an STMR of 0.22 mg/kg and a maximum residue level of 3 mg/kg for common beans.

Root and tuber vegetables

Trials were reported on the foliar application of pyrimethanil to carrots in Brazil and Europe. Two trials in Brazil did not match the GAP of Brazil (300 g/L SC, 0.6 kg ai/ha, with a 14 day PHI). Nine trials, conducted in Northern Europe were received from the UK, France, Germany and the Netherlands. Eight trials were at the maximum GAP of France, i.e., 400 g/L SC, 0.8 kg ai/ha × 2 applications, with a 21 day PHI. Residues in rank order were: < 0.05 (2), 0.07 (2), 0.24, 0.28, 0.35, 0.36 mg/kg. Nine trials were conducted in Southern Europe in Spain, France, Greece, Italy and Portugal, and all were conducted at the maximum GAP of Italy (400 g/L SC, 0.8 kg ai/ha × 2

applications, with a 7 day PHI), residues in rank order were: < 0.05, 0.05, 0.08, 0.09, 0.14, 0.21, 0.33, 0.44, 0.54 mg/kg. Residues in the two areas were comparable, and the combined residue values in ranked order (median underlined) were: < 0.05 (3), 0.07 (3), 0.08, 0.09, 0.13, 0.14, 0.21, 0.24, 0.28, 0.33, 0.35, 0.36, 0.44, 0.54 mg/kg. The Meeting estimated an STMR of 0.14 mg/kg and a maximum residue level of 1 mg/kg for carrots.

Supervised trials for the foliar application of pyrimethanil to potatoes were reported from the USA where the GAP is 0.3 kg ai/ha (600 g/L SC), with a maximum of 1.6 kg ai/ha/season, with a 7 day PHI. The ranked order of residue values for 16 trials at maximum GAP was: < 0.05(16). The Meeting estimated an STMR of 0.05 mg/kg and a maximum residue level of 0.05* mg/kg for potatoes.

Tree Nuts

The Meeting received a report on supervised field trials on almonds in the USA, where the GAP is 0.8 kg ai/ha (600 g/L SC), with a maximum of 2.4 kg ai/ha/season, and a 30 day PHI. Six trials were at the maximum GAP and the ranked order of residue values on almond hulls were: 1.9, 2.4, 2.6, 2.7, 3.6, 9.2 mg/kg. The ranked order of values on almond nutmeat was: < 0.05(4), 0.06, 0.10 mg/kg. The Meeting estimated an STMR of 2.6 mg/kg and a maximum residue level of 12 mg/kg for almond hulls. The Meeting also estimated an STMR of 0.05 and a maximum residue level of 0.2 mg/kg for almond nutmeats.

Legume Animal Feeds

Thirteen supervised trials were carried out in Europe (France, Germany and the UK) for the foliar application of pyrimethanil to fodder peas (field peas, combining peas, protein peas). The GAP in France is 400 g/L SC, 0.6 kg ai/ha, with a 28 day PHI. Eleven trials were conducted at this maximum GAP, and the values in ranked order for dry seeds were: < 0.05 (4), 0.08, 0.09, 0.11, 0.12, 0.22, 0.25, 0.30 mg/kg. The highest residue was 0.30 mg/kg. The values in ranked order for straw were: < 0.05 (3), 0.15(2), 0.24, 0.28, 0.64, 0.66, 1.0 mg/kg. The highest residue was 1.0 mg/kg. The Meeting estimated an STMR of 0.09 mg/kg and a maximum residue level of 0.5 mg/kg for fodder pea seed (dry) and an STMR of 0.20 mg/kg and a maximum residue level of 3 mg/kg for fodder pea straw.

Fate of residues during processing

The Meeting received processing studies for oranges, apples, grapes, tomatoes, green beans and carrots. No information was supplied on the fate of radiolabelled pyrimethanil under general processing conditions.

Oranges with incurred residues of pyrimethanil from post-harvest treatment (2.9 mg/kg; 7.5 mg/kg) were processed by a commercial process into juice, dried pulp and citrus oil. The average processing factors were 0.01 for juice, 0.45 for pulp (dried), and 20 for citrus oil. Applying these factors to the STMR for citrus (2.8 mg/kg), the Meeting estimated the following STMR-Ps for citrus juice, citrus pulp (dried) and citrus oil, respectively: 0.028 mg/kg; 1.3 mg/kg; 56 mg/kg.

Apple processing studies were conducted in Germany (four trials) and the USA (one trial). The median processing factor for juice was 0.45 (n=5), the average factor for puree (n=2) was 0.37, and the factor for wet pomace (n=1) was 4.1. Applying these factors to the STMR, the Meeting estimated: STMR-P of 0.32 mg/kg for juice; a STMR-P of 2.9 mg/kg for wet apple pomace, and a STMR-P of 0.26 mg/kg for apple puree. The STMR-P and maximum residue limit estimates for dry apple pomace are 7.2 mg/kg (0.7 mg/kg × 4.1/0.40) and 40 mg/kg (3.8 mg/kg × 4.1/0.4), respectively, assuming that wet apple pomace contains 40% dry matter (*Table of OECD Feedstuffs Derived from Field Crop).*

A plum to prune processing study was conducted in the USA. The processing factor of 0.81 applied to the STMR of fresh plums (0.59 mg/kg) yields an STMR-P of 0.48 mg/kg for (dried) prunes.

Processing studies for the conversion of grapes to white wine was reported from Italy. The median processing factor (n=11, one value > 1 with all others < 1) was 0.48. Applying this factor to the STMR for grapes of 0.71 mg/kg yields a STMR-P of 0.34 mg/kg for wine.

A processing study for the conversion of grapes to juice and raisin (USA) was reported to the Meeting. The processing factors for juice, wet pomace and raisins are 0.7, 2.4 and 1.6, respectively (n=1). Applying these factors to the appropriate STMRs or HR levels the Meeting estimated the following: STMR-P for juice 0.50 mg/kg; STMR-P for wet grape pomace 1.7 mg/kg; STMR-P for grape raisins 1.1. The Meeting also estimated a maximum residue level of 5 mg/kg for grape raisins.

A tomato processing study was conducted in the USA in which tomatoes with incurred residues were processed by a commercial-type method into puree and paste, with processing factors (n=1) of 0.31 and 1.1, respectively. Applying these factors to the STMR for tomatoes (0.32 mg/kg) yields STMR-Ps of 0.10 mg/kg and 0.35 mg/kg for tomato puree and tomato paste, respectively.

Samples of green beans with incurred pyrimethanil residues (Europe) were processed utilizing commercial canning and freezing techniques (n=4). The median processing factor was 0.40 for canning and the median factor for freezing was 0.50. Using the freezing factor, the STMR-P for processed green (common) beans was estimated as 0.11 mg/kg (0.50 × 0.22).

Samples of carrot from four locations in Southern Europe with incurred residues of pyrimethanil were processed by commercial-type procedures into canned carrots, frozen carrots, carrot juice and carrot puree. The median processing factors (n=4) for canned carrots and frozen carrots were 0.59 and 0.45, respectively. The median processing factors (n=4) for juice and puree were 0.20 and 0.45, respectively. Using these factors, STMRs were derived for canned carrots, 0.083 mg/kg, and frozen carrots, 0.063 mg/kg; the average STMR for canned/frozen carrots, 0.073 mg/kg; carrot juice 0.028 mg/kg; and carrot puree 0.063 mg/kg. The HR for canned/frozen carrots is 0.28 mg/kg (the average of 0.59 × 0.54 mg/kg and 0.45 × 0.54 mg/kg).

Livestock dietary burden

Based on the *Table of OECD Feedstuffs Derived from Field Crops*, Annex 4, ENV/JM/MONO (2006) 32, also published as Annex 6 of the 2006 JMPR *Report*, the following feed items are potentially available: pea hay (straw), carrot culls, potato culls, pea seed, almond hulls, apple pomace (wet), citrus (dried pulp), potato (processed waste), grape pomace (wet). Calculation from highest residue, STMR (some bulk commodities) and STMR-P values provides the levels in feed suitable for estimating MRLs, while calculation from STMR and STMR-P values for feed is suitable for estimating STMR values for animal commodities. The percentage dry matter is taken as 100% when the highest residue levels and STMRs are already expressed as dry weight.

Estimated maximum and mean livestock dietary burdens

Dietary burden calculations for beef cattle and dairy cattle are provided below. The calculations were made according to the animal diets from US-Canada, EU and Australia in the *Table of OECD Feedstuffs Derived from Field Crop* (Annex 6 of the 2006 JMPR Report).

Poultry metabolism, poultry analytical methods and poultry feeding studies were not provided. The manufacturers noted a lack of poultry feed items. However, the *Table of OECD Feedstuffs Derived from Field Crop* indicates several poultry feeding items that potentially contain pyrimethanil residues: carrot culls (10% Australia); pea seed (20% US, EU), pea hay (straw) (10% Europe) and potato culls (10% Europe).

	Animal dietary burden, pyrimethanil, ppm of dry matter diet					
	US-Canada		EU		Australia	
	max	mean	max	mean	max	mean
Beef cattle	2.42	1.90	2.49	1.70	3.52[1]	2.76
Dairy cattle	1.69	1.18	1.76	0.93	3.52[1]	2.86[2]

[1] Highest maximum beef or dairy cattle dietary burden suitable for MRL estimates for mammalian meat and milk.

[2] Highest mean beef or dairy cattle dietary burden suitable for STMR estimates for mammalian meat and milk.

Animal commodity maximum residue levels

The Meeting received a report on the feeding of Holstein lactating cattle for 28 days with pyrimethanil. Dosing was made on a daily basis at the nominal dose rates of 1, 3, 10 and 50 ppm in the diet. The total residue (pyrimethanil + 2-(4-hydroxyanilino-4,6-dimethylpyrimidine + 2-anilino-4,6-dimethylpyrimidin-5-ol) reached a plateau in milk between day 15 and day 22 at the 50 ppm dosing level.

Residues in milk (final day 27) were below the LOQ (0.01 mg/kg per compound) at the 50 ppm dosing level for each of pyrimethanil and 2-(4-hydroxyanilino-4,6-dimethylpyrimidine. The metabolite 2-anilino-4,6-dimethylpyrimidin-5-ol had a maximum concentration of 0.088 mg/kg and an average concentration of 0.069 mg/kg in final milk from the 50 ppm dosing regimen. The same metabolite was found at a maximum concentration of 0.017 mg/kg in milk at the 10 ppm feeding level and was absent (< 0.01 mg/kg) at the 3 ppm dosing level.

A milk sample from day 27 was separated into skim milk and milk fat. The residue in skim milk consisted of 0.015 mg/kg 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine and 0.064 mg/kg 2-anilino-4,6-dimethylpyrimidin-5-ol. Milk fat contained 0.031 mg/kg 2-anilino-4,6-dimethylpyrimidin-5-ol. Thus, the residue is not fat soluble.

At the 50 ppm level, each of the parent and metabolite 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine was absent at the LOQ (0.05 mg/kg) in all tissues except kidney. Pyrimethanil was absent in kidney (at the 50 ppm feeding level). The average concentration of 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine in kidney was 0.63 mg/kg and the maximum residue was 0.88 mg/kg. At the 3 ppm feeding level, the average concentration of 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine in kidney was 0.066 mg/kg and the maximum was 0.08 mg/kg. At the 10 ppm feeding level, the average concentration of 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine in kidney was 0.12 mg/kg and the maximum was 0.13 mg/kg.

In the table below, dietary burdens are shown in round brackets (), feeding levels and residue concentrations from the feeding study are shown in square brackets [] and estimated concentrations related to the dietary burdens are shown without brackets.

Pyrimethanil total residues[1], mg/kg

Dietary burden (ppm) Feeding level [ppm]	Milk	Muscle	Liver	Kidney	Fat
MRL					
	Mean	Highest	Highest	Highest	Highest
MRL, beef cattle (3.52) [3.0]		(< 0.1) [< 0.1]	(< 0.1) [< 0.1]	(0.09[2] + < 0.05[3]) [0.08[2] + < 0.05[3]]	(< 0.1) [< 0.1]
MRL, dairy cattle (3.52) [3.0]	(< 0.03) [< 0.03[4]]	(< 0.1) [< 0.1]	(< 0.1) [< 0.1]	(0.09[2] + < 0.05[3]) [0.08[2] + < 0.05}	(< 0.1) [< 0.1]
STMR					
	Mean	Mean	Mean	Mean	Mean
STMR beet cattle (2.76) [3.0]		(< 0.1) [< 0.1]	(< 0.1) [< 0.1]	(0.058 [2]+ < 0.05[3]) [0.066[2] + < 0.05[3]]	(< 0.1) [< 0.1]
STMR dairy cattle (2.86) [3.0]	(< 0.02) [< 0.02]	(< 0.1) [< 0.1]	(< 0.1) [< 0.1]	(0.060 + < 0.05[3]) [0.066 [2]+ < 0.05[3]]	(< 0.1) [< 0.1]

[1]The LOQ is 0.05 for each of pyrimethanil and 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine, in animal tissues. The LOQ is 0.01 mg/kg for each of pyrimethanil, 2-anilino-4,6-dimethylpyrimidin-5-ol, 2-anilino-4,6-dimethylpyrimidin-5-ol in milk.
[2] 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine.
[3] Pyrimethanil. At a 50 ppm pyrimethanil feeding level, pyrimethanil was < 0.05 mg/kg. By extrapolation, at the 3 ppm feeding level, the pyrimethanil concentration would be < 0.005 mg/kg.
[4] pyrimethanil + 2-(4-hydroxyanilino-4,6-dimethylpyrimidine + 2-anilino-4,6-dimethylpyrimidin-5-ol. At a 50 ppm feeding level only 2-anilino-4,6-dimethylpyrimidin-5-ol had quantifiable residues.

The Meeting estimated an STMR of 0.01 mg/kg for milk and estimated a maximum residue level of 0.01 mg/kg for milk. The Meeting estimated STMRs of 0.0 mg/kg for each of meat and fat and maximum residue levels of 0.05 (*) mg/kg for meat. The Meeting estimated an STMR of 0.065 mg/kg for edible offal based on the STMR value for dairy cow kidney. The Meeting estimated a maximum residue level of 0.1 mg/kg for edible offal (mammalian) based on the value of kidney.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes (IEDI) of pyrimethanil based on the STMRs estimated for 32 commodities for the thirteen GEMS/Food cluster diets were in the range of 0% to 5% of the maximum ADI (0.2 mg/kg bw). The Meeting concluded that the long-term intake of residues of pyrimethanil resulting from its uses that have been considered by JMPR is unlikely to present a public health concern.

Short-term intake

The 2007 JMPR decided that an ARfD is unnecessary. The Meeting therefore concluded that the short-term intake of pyrimethanil residues is unlikely to present a public health concern.

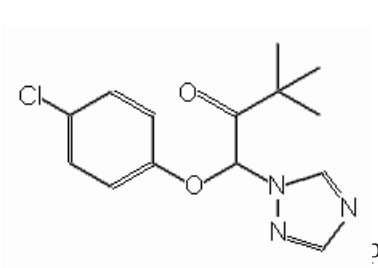
5.22 TRIADIMEFON (133)/ TRIADIMENOL (168)

RESIDUE AND ANALYTICAL ASPECTS

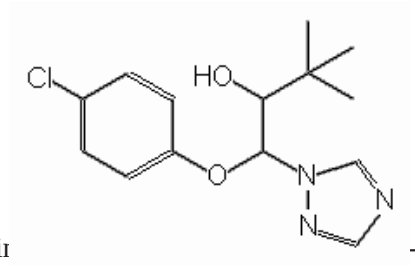
Triadimenol and triadimefon are related substances and follow the same metabolic pathways in all matrices investigated. Both compounds were evaluated by JMPR several times since 1978 and the last time in 2004, when an ADI of 0–0.03 mg/kg bw and an ARfD of 0.08 mg/kg bw were established for triadimefon and triadimenol each. The residue evaluation of the compounds was completed by the current Meeting within the periodic re-evaluation program.

Data submitted by the manufacturer and evaluated at this Meeting include metabolism in animal and plants, degradation in soil, residues in succeeding crops, analytical methods, supervised residue trials and processing studies.

The following appraisal includes the evaluation of the residue behaviour for both triadimefon and triadimenol.



ophenoxy)-3,3-dir



-butanone

Triadimenol β-(4-chlorophenoxy)-α-(1,1-dimethylethyl)-1H-1,2,4-triazole-1-ethanol

Triadimefon and triadimenol are structurally related systemic fungicides with registered uses in many countries. Their main mode of action is inhibitors of ergosterol biosyntheses in fungi.

The following abbreviations are used for the metabolites discussed below:

M02	γ-(4-chlorophenoxy)-β-hydroxy-α,α-dimethyl-1H-1,2,4-triazole-1-butanoic acid

M09	1-(4-chlorophenoxy)-4-hydroxy-3,3-dimethyl-1-(1H-1,2,4-triazol-1-yl)-2-butanone
M10	β-(4-chlorophenoxy)-α-(1,1-dimethylethyl)-1H-1,2,4-triazole-1-ethanol

Animal metabolism

The Meeting received results of animal metabolism studies in rats, lactating goats and laying hens.

Rats

The metabolism of triadimefon and triadimenol in rats was evaluated within the toxicological assessment by the JMPR in 2004. In the following paragraphs the summaries of the metabolism for both active substances in rats from the 2004 Report are presented.

Triadimefon

In a study on the absorption, distribution, metabolism and excretion of triadimefon in rats, the dose given and pre-treatment with non-labelled triadimefon did not significantly affect excretion and metabolism patterns. In males about one-third and in females about two-thirds of the administered dose was excreted in the urine and vice versa in the faeces. After 96 h, 2% of the radioactivity remained in females and 9% in males, with the highest residue levels found in liver and kidneys.

The metabolism of triadimefon starts either by direct oxidation of a t-butyl methyl group to the hydroxy or the carboxy compound with subsequent glucuronidation, or these steps are preceded by reduction of the keto group of triadimefon to the putative intermediate, triadimenol. As a consequence, many of the metabolites found in triadimenol metabolism studies are also found with triadimefon. Nevertheless, the metabolism of triadimefon in rats provides a pathway for demethylation of the t-butyl group, which is not seen with triadimenol. This might be a result of the very low biotransformation of triadimenol via triadimefon as an intermediate.

Triadimenol

In rats, radiolabelled triadimenol is rapidly absorbed from the gastrointestinal tract, with radioactivity reaching peak concentrations in most tissues between 1 and 4 h after dosing. Up to 90% of the administered dose was excreted, with an elimination half-life for the radiolabel of between 6 and 15 h. Excretion was essentially complete within 96 h. After 5–6 days, radioactivity in most organs was below the limits of quantification.

Renal excretion accounted for up to 21% of the orally administered dose in males and up to 48% in females. The remainder was found in the faeces. In bile-duct cannulated males, 93% of the administered dose was recovered in the bile and only 6% in the urine, indicating that a substantial amount of the administered dose undergoes enterohepatic recycling. Radioactivity in expired air was negligible.

Triadimenol was extensively metabolized, predominantly by oxidation of one of the t-butyl methyl groups to give hydroxy or carboxy derivatives. The putative intermediate triadimefon has not been isolated. Cleavage of the chloro-phenyl and the triazole group was of minor significance. In the urine and faeces most of the metabolites were not conjugated, but in bile the metabolites were found to be extensively glucuronidated.

Goats

One lactating goat was dosed with [phenyl-UL-^{14}C]triadimefon at a rate of 2.6 mg ai/kg body weight for three consecutive days. Approximately 83% of the total radioactivity administered was excreted until sacrifice. At sacrifice the total radioactive residues (TRR) in the edible tissues were 3.5 mg/kg in kidney, 1.6 mg/kg in liver, 0.29 mg/kg in fat and 0.07 mg/kg in muscle. For milk TRR values of 0.027 to 0.029 mg/kg were detected.

Triadimefon was rapidly metabolised in the lactating goat. It was not identified in urine (0–24 h), kidney, liver and muscle and was present at low amounts in milk (1% of the TRR, < 0.001 mg/kg) and in fat (4% of the TRR, 0.013 mg/kg). Triadimenol as a metabolite of triadimefon was only identified in relevant amounts in the liver (20% of the TRR). In the fat, muscle and milk only minor amounts, 1–3% of the TRR, were detected. No triadimenol could be found in the kidney. The majority of the radioactive residues (57–82% of the TRR) in the tissues, milk and urine were identified as glucuronic acid or sulfate conjugates of the metabolites M02, M09 and M10. Unconjugated M02 accounted for 0.039–0.3 mg/kg or 4–17% of the TRR in kidney, liver, muscle, fat and urine. Unconjugated M09, unconjugated M10, and p-chlorophenol sulfate and triadimenol glucuronide were minor metabolites.

It was concluded that the metabolism of triadimefon in the goat is comparable to the metabolism in the rats.

Hens

A group of ten laying hens was fed with [phenyl-UL-^{14}C]triadimefon for three consecutive days at a dose rate of 2.5 mg/kg bw each. Data for the rate of absorption in hens was not presented in the study. At sacrifice the TRR in the edible tissues were 0.73 mg/kg in liver, 0.17 mg/kg in fat, 0.12 mg/kg in muscle and up to 0.09 mg/kg in whole eggs.

Triadimefon was rapidly metabolised in laying hens. It was not identified from liver and muscle and was detected in fat (0.038 mg/kg or 22% of the TRR) and in eggs (0.004–0.007 mg/kg or 4–9% of the TRR). For triadimenol in fat and eggs amounts of about 20% of the TRR were detected. In liver about 5% of the TRR was identified as triadimenol, while in muscle no detectable triadimenol residues could be found. As with the metabolism in lactating goats, a wide spectrum of metabolites could be identified, mostly in quantities below 10% of the TRR. The major metabolites detected were M10 in eggs (18% of the TRR; 0.016 mg/kg) and desmethyl-hydroxyl triadimenol (M31) in liver (13% TRR), muscle (24% TRR) and eggs (23% TRR).

The metabolism of triadimefon in hens is comparable to the metabolism in the rats.

Plant metabolism

The Meeting received plant metabolism studies for triadimefon following foliar application on grapes, barley and wheat. The metabolism of triadimenol was investigated after foliar application on grapes, wheat and sugar beets as well as after seed dressing application on barley and wheat. For tomatoes and cucumbers additional studies comparing foliar and soil treatment with triadimenol were conducted.

In each crop tested, triadimefon and triadimenol were found to be the main residue remaining (grapes: 55–61% TRR, barley: 30–36% TRR, wheat: 52–62% TRR, sugar beets: 26–73% TRR, cucumber: 61–98% TRR and tomato: 76–92% TRR). After foliar application, triadimefon was metabolised to triadimenol. After 14 to 28 days a higher level of triadimenol compared to triadimefon could be observed (except for tomatoes). The investigation of the metabolic pattern showed that the biochemical transformation processes involved consist mainly of conjugation reactions of the parent compound and to a lesser degree in the partial oxidation of the tertiary butyl group of the parent. The product M10 from this oxidation is also subsequently conjugated. A complete cleavage of the triadimenol and triadimefon chemical structure leading to formation of 4-chlorophenol and 1,2,4-triazole is observed in soil only. The 1,2,4-triazole is taken up by the plant via the roots and is conjugated through an enzymatic reaction with serine to form triazole alanine. Subsequent transformation into triazole hydroxy propanoic acid and triazole acetic acid also occurred. The other part of the active substance molecule, 4-chlorophenol, is conjugated in the plants into 4-chlorophenyl-glucoside.

Environmental fate in soil

The Meeting received information on the environmental fate of triadimefon and triadimenol in soil, including aerobic soil metabolism, field dissipation and crop rotational studies. In addition soil photolysis studies with both triadimefon and triadimenol were submitted.

The soil photolysis studies conducted with [phenyl-UL-^{14}C]triadimefon and [phenyl-UL-^{14}C]triadimenol showed that no accelerated degradation occurs under irradiation. Metabolites were identified only in small amounts mainly consisting of 1,2,4-triazole and p-chlorophenol.

In a confined rotational crop study, soil was treated with [phenyl-UL-^{14}C] triadimenol or [triazole-3,5-^{14}C] triadimenol. Over three subsequent years wheat was treated with a seed dressing application (corresponding to 0.038 kg ai/100 kg seeds) followed by an additional foliar treatment with identically labelled triadimefon at a rate of 0.25 kg ai/ha. In this part of the study most of the radioactivity identified in grain consisted of triazole alanine (approximately 50% of the TRR, 0.46-1.06 mg/kg) and triazole -lactic-acid (approximately 30% of the TRR, 0.24–0.72 mg/kg). Triazole acetic acid was only identified in traces at the level of the LOQ (< 0.01 mg/kg). No parent triadimefon or triadimenol could be identified in the harvested wheat grain.

In the fourth year wheat and sugar beets were planted as rotational crops without additional treatment. In grain, low amounts of TRR (0.03 mg/kg) could be identified for the phenyl-labelled substance. For the triazole-label, higher residues of 1.18 mg/kg were detected in grain. In grain most of the residues identified consisted of triazole-alanine (0.33 mg/kg) and triazole -lactic-acid (0.12 mg/kg). The rest of the plant showed comparable amounts of radioactivity between both labels ranging from 0.33 mg/kg (roots) up to 0.78 mg/kg (straw). The identification of the total radioactivity showed no triadimefon/triadimenol-residues above 0.01 mg/kg in grain. In straw and glumes triadimefon and triadimenol residues were detected at levels up to 0.14 mg/kg.

In four field rotational crop studies barley was treated with a dose rate of unlabelled triadimenol corresponding to 0.125–0.25 kg ai/ha. Fourteen days after harvesting the barley, turnips and oilseed rape were planted and grown to maturity. In barley no residues above the LOQ of 0.1 mg/kg were detected in all matrices. Further identification of the residues was not performed. The sampling of the rotational crops was conducted 103 (turnips) to 167 days (oilseed rape) after planting. In all plant matrices and in analysed soil layers of 0–10 cm and 10–20 cm no triadimenol residues above the LOQ of 0.1 mg/kg were detected.

The Meeting concluded that residues from the use of triadimefon and triadimenol under field conditions are unlikely to occur in concentrations above 0.01 mg/kg in succeeding crops.

Methods of analysis

The Meeting received description and validation data for analytical methods of triadimefon and triadimenol in plant and animal matrices. All enforcement methods are based on variations of the DFG S19 multi-residue method. The samples are extracted using acetone/water (2:1 v/v) and a subsequent clean-up by GPC or solid phase extraction. The residue of triadimefon and triadimenol is analysed on a gas chromatograph using an alkali-flame ionisation detector (GC-FID(N)). A mass selective detector (MS) is used for confirmatory purposes. MS detection was done at a mass charge ratio of m/z=208 for triadimefon and m/z=168 for triadimenol. For plant matrices an LOQ of 0.05 mg/kg for all commodities was achieved.

In animal matrices the enforcement methods follow the same scheme as in plant matrices and are validated with an LOQ of 0.01 mg/kg for all commodities. The recovery rates were within the range of 70% to 110%.

In addition the Meeting received information on various specialised methods. Most methods include only minor variations in the extraction technique according to the matrix analysed. In these specialised methods LOQs for triadimefon and triadimenol in plant matrices of 0.01 mg/kg up to 0.05 mg/kg were achieved with recovery rates above 70%. For animal matrices specialised methods to measure the total residues of all compounds containing 4-chlorophenyl were reported. Treatment with hypochloric acid resulted in complete transformation of the residues into 4-chlorophenyl. After

derivatisation with 2,4-dinitrofluorobenzene the total amount of residue is detected using GC-MS techniques.

The Meeting concluded that adequate analytical methods exist for the determination of triadimefon and triadimenol in crops and livestock commodities both for data collection and MRL enforcement purposes.

Stability of pesticide residues in stored analytical samples

The Meeting received information on the stability of triadimefon and triadimenol in wheat, grapes, tomatoes, apples, cucumbers, pineapples, sugar beets, asparagus and coffee beans. All samples were stored at -20 °C for up to 24 months. Animal matrices eggs, fat, liver, muscle and milk were fortified with triadimenol and stored from 432 days (milk) up to 873 days (liver). In all matrices the remaining triadimenol and triadimefon levels were above 70% of the initial fortification concentrations.

The Meeting concluded that triadimefon and triadimenol are stable in plant and animal matrices under frozen storage conditions.

Residue definition

The plant metabolism studies with triadimefon used in foliar applications and triadimenol in seed dressing and foliar treatments show that a large part of the remaining residues consist of triadimefon and/or triadimenol. Further metabolites were identified in all matrices, but the amounts were much lower than for the active substances.

In rotational crop studies on barley and in a 3 year study on wheat with radiolabelled triadimefon and triadimenol, the triazole-metabolites triazole-alanine, triazole-lactate and triazole-acetic-acid were found in the grain. Triazole acetic acid was detected in traces at the limit of detection only. Triazole-alanine (0.33 mg/kg) and triazole-lactic-acid (0.12 mg/kg) formed the major part of the total radioactivity found in grain.

The available analytical enforcement methods for plant matrices determine triadimefon and triadimenol. Additional methods for M09 and M10 are available.

The Meeting concluded that the residue definition for plant matrices is the sum of triadimefon and triadimenol for both enforcement and risk assessment purposes.

The animal metabolism studies conducted with triadimefon show a substantial degradation for triadimefon as well as for triadimenol. Although the metabolic pathways for goats and hens are similar, significant residues of triadimefon and triadimenol were only detected in goat liver and poultry fat and eggs. Goat muscle, fat and milk as well as poultry liver contained both active substances of between 1 and 5% of the TRR. In goat kidney and poultry muscle no triadimefon or triadimenol was detected. The main part of the radioactivity found consisted of glucuronide- and sulphate-conjugates of M09 and M10. No 1,2,4-triazole metabolites were identified in the animal matrices.

The available analytical enforcement methods determine triadimefon and triadimenol. Specialised methods for the measurement of all structures containing 4-chlorophenyl were submitted.

4-chlorophenyl is a common moiety in various pesticides and has a broad spectrum of other uses. The Meeting decided that the total residue based on 4-chlorophenyl would not be a specific marker for triadimefon and triadimenol and concluded the residue definition for enforcement of animal matrices to be the sum of triadimefon and triadimenol. As triadimefon and triadimenol were identified as the only compounds of toxicological concern, the Meeting concluded that the sum of triadimefon and triadimenol is also an appropriate residue definition for risk assessment purposes for animal matrices.

The log of the octanol/water partition coefficients for triadimefon and triadimenol are 3.1 and 3.3 respectively. In ruminant as well as in poultry metabolism studies, fat tissues contained much higher triadimefon and triadimenol residues than the corresponding muscle matrices (muscle: non-detect up to 0.001 mg/kg, fat: 0.009 mg/kg up to 0.043 mg/kg).

Based on the above, the Meeting agreed:

Definition of the residue in plant and animal commodities (for the estimation of dietary intake and for compliance with MRLs): sum of triadimefon and triadimenol

The Meeting also decided that triadimefon and triadimenol are fat-soluble.

Results of supervised residue trials on crops

The Meeting received supervised trials data for the application of triadimefon and triadimenol to a variety of crops, including apples, grapes, strawberries, currants, bananas, pineapples, sugar beets, cucumbers, courgettes, melons, watermelons, tomatoes, peppers, artichoke, barley, oats, wheat, oats and coffee.

Apples

Field trials involving triadimenol foliar applications to apples are available from France, Germany, Israel, Italy, New Zealand, Spain, South Africa and United Kingdom.

In Cyprus, triadimenol may be applied at a rate of 0.0025 kg ai/hL with a PHI of 14 days. The residues from trials in Germany and the United Kingdom, matching this GAP, were: < 0.05, 0.06(3) and 0.08(3) mg/kg (sum of triadimefon and triadimenol) in apples.

The GAP of Algeria consists of an application rate of 0.005 kg ai/hL and a PHI of 7 days. From one supervised residue trial on apples matching this GAP from Israel the corresponding residue in was 0.4 mg/kg (sum of triadimefon and triadimenol).

From Italy a GAP using 0.004 kg ai/hL and a PHI of 14 days was reported. The corresponding residues from trials in France, Germany, Italy, Spain and United Kingdom matching this GAP were < 0.05(3), 0.05, 0.06, 0.06, 0.07, 0.09, 0.1, 0.11, 0.14 and 0.18 mg/kg (sum of triadimefon and triadimenol) in apples.

The GAP of Spain for apples is 0.013 kg ai/hL with a PHI of 15 days. The residues from trials in Germany matching this GAP were: < 0.05(3), 0.07, 0.09 and 0.1 mg/kg (sum of triadimefon and triadimenol) in apples.

The Meeting decided to pool the data from all GAPs with the exception of the supervised trial data from Israel, as the PHI of 7 days results in a different residue population and insufficient data for an evaluation of that GAP was submitted. The combined residue trial results (n=25) for apples from the other GAPs in ranked order (median underlined) were: < 0.05(7), 0.05, 0.06(5), 0.07, 0.07, 0.08(3), 0.09, 0.09, 0.1, 0.1, 0.11, 0.14 and 0.18 mg/kg (sum of triadimefon and triadimenol).

The Meeting estimated an STMR value of 0.06 mg/kg, an HR value of 0.18 mg/kg and a maximum residue level of 0.3 mg/kg for the sum of triadimefon and triadimenol in apples.

The Meeting withdraws both of its previous recommendations for triadimefon and for triadimenol in pome fruits of 0.5 mg/kg.

Grapes

Field trials involving the foliar applications of triadimefon and triadimenol to grapes were made available from Australia, Chile, France, Germany, Greece, Italy, South Africa, Spain, Turkey and the United States. In several supervised residue trials the analysed commodities referred to grape bunches rather than grape berries. The Meeting decided that both results may be used for the evaluation as the differences are likely to have a negligible influence on the residue levels.

Triadimefon

The GAP of Croatia and Macedonia consists of an application rate of 0.0025 kg ai/hL with a PHI of 35 days. Residues from trials in Germany matching this GAP were: < 0.04, < 0.04, 0.09, 0.25 and 3.2 mg/kg (sum of triadimefon and triadimenol).

The GAP of Russia is 0.005 kg ai/hL with a PHI of 30 days. The residues from trials in Germany matching this GAP were: 0.21, 0.33, 0.43 and 0.69 mg/kg (sum of triadimefon and triadimenol).

The GAP of Belarus and Kazakhstan is 0.0075 kg ai/hL with a PHI of 30 days. The residues from trials in Germany matching this GAP were: < 0.05, < 0.05, 0.07, 0.07, 0.09, 0.15, 0.15, 0.28 and 1.7 mg/kg (sum of triadimefon and triadimenol).

The maximum GAP in South Africa is 0.095 kg ai/ha (0.0063 kg ai/hL) with a PHI of 7 days. The residues from trials in South Africa matching this GAP were: 0.11, 0.27, 0.36 and 0.37 mg/kg (sum of triadimefon and triadimenol).

The GAP of the United States is 0.21 kg ai/ha with a PHI of 14 days. The residues from trials in the US matching this GAP were: 0.03, 0.08, 0.15, 0.27, 0.59, 0.78 and 0.78 mg/kg (sum of triadimefon and triadimenol).

Triadimenol

The GAP of Australia and New Zealand is 0.0025 kg ai/hL with a PHI of 7 days. The residues from trials in Australia and New Zealand matching this GAP were: < 0.05, 0.05, 0.16, 0.18 and 0.6 mg/kg (sum of triadimefon and triadimenol).

The GAP of Bulgaria is 0.0025 kg ai/hL with a PHI of 30 days. The residues from trials in Germany matching this GAP were: < 0.05(3), 0.06, 0.07, 0.09, 0.1 and 0.15 mg/kg (sum of triadimefon and triadimenol).

The GAP of Cyprus and Italy is 0.005 kg ai/hL with a PHI of 14 days. The residues from trials in Germany, Italy, Israel and Turkey matching this GAP were: 0.04, 0.05, 0.06, 0.07, 0.08 and 0.6 mg/kg (sum of triadimefon and triadimenol).

The GAP of France is 0.075 kg ai/ha with a PHI of 15 days. The residues from trials in France, Greece and Spain matching this GAP were: < 0.02, < 0.02, 0.04, 0.04, 0.1 and 0.11 mg/kg (sum of triadimefon and triadimenol).

The GAP of Georgia, Moldova and the Ukraine is 0.013 kg ai/ha with a PHI of 30 days. The residue from one trial in France matching this GAP was < 0.02 mg/kg (sum of triadimefon and triadimenol).

The GAP of South Africa is 0.12 kg ai/ha (0.0075 kg ai/hL) with a PHI of 14 days. The residues from trials in South Africa matching this GAP were: 0.17, 0.3, 0.32, 0.46, 0.54, 0.58, 0.8, 1.4 and 1.9 mg/kg (sum of triadimefon and triadimenol).

The Meeting decided to pool the data from all GAPs for triadimefon and triadimenol in grapes. The combined results (n=63) in grapes in ranked order (median underlined) were: < 0.02(3), 0.03, < 0.04, < 0.04, 0.04(3), < 0.05(5), 0.05, 0.05, 0.06, 0.06, 0.07(4), 0.08, 0.08, 0.09(3), 0.1, 0.1, 0.11, 0.11, <u>0.15</u>(4), 0.16, 0.17, 0.18, 0.21, 0.25, 0.27, 0.27, 0.28, 0.3, 0.32, 0.33, 0.36, 0.37, 0.43, 0.46, 0.54, 0.58, 0.59, 0.6, 0.6, 0.69, 0.78, 0.78, 0.8, 1.4, 1.7, 1.9 and 3.2 mg/kg (sum of triadimefon and triadimenol).

Based on the uses of both triadimefon and triadimenol the Meeting estimated an STMR value of 0.15 mg/kg, an HR value of 3.2 mg/kg and estimated a maximum residue level of 5 mg/kg for the sum of triadimefon and triadimenol in grapes. The IESTI calculation indicates that the consumption of grapes at the HR level of 6.1 mg/kg will lead to an exceedance of the ARfD, but no residue data was available from an alternative GAP to estimate a lower HR value.

The Meeting withdraws both of its previous recommendations for triadimefon in grapes of 0.5 mg/kg and for triadimenol in grapes of 2 mg/kg.

Strawberries

Field trials involving foliar application of triadimenol to glasshouse <u>strawberries</u> are available from Belgium, Italy, Netherlands and Spain.

A GAP for protected strawberries is only available from Spain, with a spray concentration of 0.013 kg ai/hL and a PHI of 3 days. The residues from trials matching this GAP in ranked order (median underlined) were: 0.08, 0.09, 0.13, 0.24, 0.26, 0.27, 0.29, 0.3, 0.31 and 0.41 mg/kg (sum of triadimefon and triadimenol).

Based on the use of triadimenol in strawberries the Meeting estimated an STMR value of 0.265 mg/kg, a HR value of 0.41 mg/kg and a maximum residue level of 0.7 mg/kg for the sum of triadimefon and triadimenol in strawberries.

The Meeting withdraws both of its previous recommendations for triadimefon and triadimenol in strawberries of 0.1 mg/kg each.

Currants

Field trials involving foliar application of triadimenol to currants were reported from Germany, Netherlands and the United Kingdom.

The GAP from the Netherlands consists of a spray concentration of 0.0075 kg ai/hL with a PHI of 14 days. The residues from trials matching the GAP of the Netherlands in ranked order (median underlined) were: 0.06, 0.07, 0.19, 0.19, 0.23, 0.23, 0.25, 0.39 and 0.49 mg/kg (sum of triadimefon and triadimenol).

Based on the use of triadimenol in currants the Meeting estimated an STMR value of 0.23 mg/kg, a HR value of 0.49 mg/kg and a maximum residue level of 0.7 mg/kg for the sum of triadimefon and triadimenol in currants.

The Meeting withdraws both of its previous recommendations for triadimefon in currants (black, red) of 0.2 mg/kg and for triadimenol in currants (red, black) of 0.5 mg/kg.

Raspberries

GAP information for the use of triadimefon and triadimenol on raspberries was reported from Belarus and the United States. Field trials involving either active substance were not made available.

The Meeting withdraws both of its previous recommendations for triadimefon in raspberries (red, black) of 1 mg/kg and for triadimenol in raspberries (red, black) of 0.5 mg/kg.

Bananas

Field trials involving triadimenol in foliar application to bananas are available from Cameroon, Costa Rica, Honduras, Ivory Coast, Martinique, Puerto Rico, South Africa and the USA.

The GAP of Cuba is 0.14 kg ai/ha with a PHI of 7 days. The residues from trials matching this GAP were: < 0.01, < 0.04, < 0.04, 0.1, 0.11, 0.18 and 0.8 mg/kg (sum of triadimefon and triadimenol) in whole bananas (unbagged). In banana pulp (unbagged) the corresponding residues were: < 0.01, < 0.04, < 0.04, 0.09, 0.14, 0.18 and 0.3 mg/kg (sum of triadimefon and triadimenol).

The GAP of Brazil is 0.1 kg ai/ha with a PHI of 14 days. The residues from trials matching this GAP were: < 0.01, < 0.02, < 0.05, < 0.05, 0.08 and 0.14 mg/kg (sum of triadimefon and triadimenol) in whole bananas (unbagged). In banana pulp (unbagged) the corresponding residues were: < 0.01, < 0.02, < 0.05, < 0.05, 0.07 and 0.14 mg/kg (sum of triadimefon and triadimenol).

Field trials involving triadimenol a broadcast application of granules in bananas are available from Cameroon, Costa Rica, Ecuador and Ivory Coast.

Maximum GAPs in Guatemala and Nicaragua reported for the spreading of triadimenol in bananas is 1 kg ai/ha with a PHI of 21 days. The residues from trials matching the GAP were: < 0.01, 0.01, < 0.04, < 0.04, 0.04 and < 0.05 mg/kg (sum of triadimefon and triadimenol) in whole bananas. In banana pulp the corresponding residues were: < 0.01(4), 0.02, < 0.04, < 0.04, 0.04 and < 0.05 mg/kg (sum of triadimefon and triadimenol).

The Meeting decided to pool the data from all GAPs for foliar and spreading applications of triadimenol in bananas. The combined results (n=19) in whole banana fruits were: < 0.01(3), 0.01, < 0.02, < 0.04(4), 0.04, < 0.05(3), 0.08, 0.1, 0.11, 0.14, 0.18 and 0.8 mg/kg (sum of triadimefon and triadimenol). In banana pulp the combined result (n=22) were: < 0.01(6), < 0.02, 0.02, < 0.04(4), 0.04, < 0.05(3), 0.07, 0.09, 0.14, 0.14, 0.18 and 0.3 mg/kg (sum of triadimefon and triadimenol).

Based on the residue data on banana pulp the Meeting estimated an STMR value of 0.04 mg/kg and an HR of 0.3 mg/kg (sum of triadimefon and triadimenol) for bananas.

Based on the use of triadimenol in bananas the Meeting estimated a maximum residue level of 1 mg/kg for the sum of triadimefon and triadimenol in bananas.

The Meeting withdraws its previous recommendation for triadimenol in bananas of 0.2 mg/kg.

Mango

GAP information for the use of triadimefon and triadimenol on mangoes was reported from a number of countries. Field trials involving either active substance were not made available.

The Meeting withdraws both of its previous recommendations for triadimefon and triadimenol in mangoes of 0.05* mg/kg.

Pineapples

Field trials involving triadimefon in post-harvest dipping of pineapples are available from Ivory Coast and the United States.

The GAP of the Ivory Coast consists of a dipping solution of 0.01 kg ai/hL with a 0 days PHI. The residues from trials matching this GAP were: 0.1, 0.46 and 0.56 mg/kg (sum of triadimefon and triadimenol) in whole fruits. In pineapple pulp the corresponding residues were: < 0.06, < 0.06 and 0.1 mg/kg (sum of triadimefon and triadimenol).

The GAP of Costa Rica, Dominican Republic, Guatemala and Honduras involves a dipping solution of 0.05 kg ai/hL with a 0 days PHI. The residues from trials matching the GAP were: 0.82, 0.85, 0.97, 1.1, 1.1, 1.4, 1.5, 1.6, 1.6, 1.8, 2.0, 2.2 and 2.5 mg/kg (sum of triadimefon and triadimenol) in whole fruits. In pineapple pulp the corresponding residues in ranked order (median underlined) were: 0.07, 0.07, 0.09, 0.1, 0.1, 0.11, 0.11, 0.13, 0.13, 0.14, 0.14, 0.15 and 0.16 mg/kg (sum of triadimefon and triadimenol).

Based on the residue data on pineapple pulp complying with the GAPs of Costa Rica, the Dominican Republic, Guatemala and Honduras the Meeting estimated an STMR value of 0.11 mg/kg and a HR of 0.16 mg/kg (sum of triadimefon and triadimenol) for pineapples.

Based on the use of triadimenol in pineapples according to the GAPs from Costa Rica, the Dominican Republic, Guatemala and Honduras the Meeting estimated a maximum residue level of 5 mg/kg (Po) for the sum of triadimefon and triadimenol in pineapples.

The Meeting withdraws both of its previous recommendations for triadimefon in pineapples of 2 mg/kg and for triadimenol in pineapples of 1 mg/kg.

Sugar beets

Field trials involving triadimenol in sugar beets are available from Germany and the United Kingdom. The GAP of the United Kingdom for sugar beets consists of an application rate of 0.13 kg ai/ha with a PHI of 14 days. The residues from trials matching the GAP were: < 0.05(9) mg/kg (sum of triadimefon and triadimenol) in sugar beet roots.

Based on the use of triadimenol in sugar beets the Meeting estimated an STMR value of 0.05 mg/kg, an HR value of 0.05 mg/kg and a maximum residue level of 0.05* mg/kg for the sum of triadimefon and triadimenol in sugar beets.

The Meeting withdraws both of its previous recommendations for triadimefon and triadimenol in sugar beets of 0.1* mg/kg.

Onion, spring and welsh

GAP information for the use of triadimefon and triadimenol on onions was reported from Columbia, Japan and Korea. Field trials involving either active substance were not made available.

The Meeting withdraws all of its previous recommendations for triadimefon and triadimenol in onion, spring and onion, welsh of 0.05* mg/kg.

Fruiting vegetables, cucurbits

Triadimefon

Field trials involving triadimefon in cucumbers are available from Australia, Japan and the United States. The GAP of New Zealand for the field application on cucumbers is 0.005 kg ai/hL with a PHI of 1 day. The residue from one trial matching the GAP was < 0.2 mg/kg (sum of triadimefon and triadimenol) in fruits.

Maximum GAP in Mexico, for the field application of triadimefon to cucumbers consists of an application rate of up to 0.13 kg ai/ha with a PHI of 0 days. The residues from United States trials matching this GAP were < 0.02, 0.02, 0.02, 0.03(3), 0.04, 0.04, 0.05, 0.08(3) and 0.11 mg/kg (sum of triadimefon and triadimenol) in fruits.

The GAP of the Ukraine for the application of triadimefon in glasshouse cucumbers is 0.0025 kg ai/hL with a PHI of 5 days. The residues from Japanese trials matching this GAP were: < 0.02, < 0.02 mg/kg (sum of triadimefon and triadimenol) in fruits.

Field trials involving triadimefon in melons are available from Mexico and the United States. Maximum GAP in Mexico for triadimefon in field application to melons is 0.15 kg ai/ha with a PHI of 0 days. The residues from trials in Mexico and the United States, matching this GAP, were: < 0.02, < 0.02, 0.03, 0.04, 0.05(4), 0.11, 0.11, 0.13 and 0.13 mg/kg (sum of triadimefon and triadimenol) in whole fruits. In melon pulp the corresponding residues were: 0.03, 0.03, 0.04 and 0.04 mg/kg (sum of triadimefon and triadimenol).

Triadimenol

Field trials involving triadimenol in cucumbers were made available from Australia and the United States. GAP in Australia involves the field application to cucumbers at a rate of 0.1 kg ai/ha with a PHI of 1 day. The residue from one trial matching this GAP was 0.1 mg/kg (sum of triadimefon and triadimenol) in fruits.

The GAP of Greece and Italy for triadimenol applications to glasshouse cucumbers is 0.005 kg ai/hL with a PHI of 14 to15 days. The residues from trials matching this GAP were: < 0.05(4) mg/kg (sum of triadimefon and triadimenol) in fruits.

In Spain the GAP for the application of triadimenol to glasshouse cucumbers is 0.013 kg ai/hL with a PHI of 3 days. The residues from trials matching this GAP were: < 0.05(5), 0.06, 0.06, 0.07, 0.08, 0.1, 0.1 and 0.12 mg/kg (sum of triadimefon and triadimenol) in the fruits.

Field trials involving triadimenol in melons are available from France, Greece, Italy and Spain. GAP from Morocco for triadimenol in field application to melons is 0.075 kg ai/hL with a PHI of 3 days. The residues from trials matching the GAP were: < 0.05(6), 0.05 and 0.06 mg/kg (sum of triadimefon and triadimenol) in whole fruits. In melon pulp the corresponding residues were < 0.05 and < 0.05 mg/kg (sum of triadimefon and triadimenol). GAP in Spain for triadimenol applications to glasshouse melons is 0.013 kg ai/hL with a PHI of 3 days. The residues from trials in Italy matching this GAP were: < 0.05(3), and 0.13 mg/kg (sum of triadimefon and triadimenol) in whole fruits. In melon pulp the corresponding residues were < 0.05(4) mg/kg (sum of triadimefon and triadimenol).

Field trials involving triadimenol in watermelons were made available from Italy and Spain. The GAP of Greece for the field application of triadimenol to watermelons is 0.005 kg ai/hL with a

PHI of 15 days. The residue from one trial in Italy matching this GAP was < 0.05 mg/kg (sum of triadimefon and triadimenol) in whole fruits. In melon pulp the corresponding residue was < 0.05 mg/kg (sum of triadimefon and triadimenol).

The GAP for triadimenol in glasshouse application to watermelons (as a GAP for cucurbits) was reported from Chile at 0.13 kg ai/ha with a PHI of 3 days. The residues from glasshouse trials in Italy matching this GAP were < 0.05(3), 0.05 mg/kg (sum of triadimefon and triadimenol) in whole fruits. In melon pulp the corresponding residues were < 0.05(4) mg/kg (sum of triadimefon and triadimenol).

The Meeting decided to pool the data for triadimefon and triadimenol from all GAPs for field and glasshouse application in cucurbits. The combined results (n=61) in whole fruits were: < 0.02(5), 0.02, 0.02, 0.03(4), 0.04(3), < 0.05(22), 0.05(7), 0.06(3), 0.07, 0.08(4), 0.1(3), 0.11(3), 0.12, 0.13(3) and < 0.2 mg/kg (sum of triadimefon and triadimenol). In the edible part (whole fruit or pulp) the combined results (n=48) in ranked order (median underlined) were: < 0.02(3), 0.02, 0.02, 0.03(5), 0.04(4), < 0.<u>05</u>(20), 0.05, 0.06, 0.06, 0.07, 0.08(4), 0.1(3), 0.11, 0.12 and < 0.2 mg/kg (sum of triadimefon and triadimenol).

The Meeting estimated an STMR value of 0.05 mg/kg and a HR of 0.2 mg/kg (sum of triadimefon and triadimenol) for cucurbits, including melons and watermelons.

Based on the uses of both triadimefon and triadimenol the Meeting estimated a maximum residue level of 0.2 mg/kg for the sum of triadimefon and triadimenol in fruiting vegetables, cucurbits.

The Meeting withdraws both of its previous recommendations for triadimefon in fruiting vegetables, cucurbits of 0.1 mg/kg and for triadimenol in fruiting vegetables, cucurbits of 2 mg/kg.

Fruiting vegetables other than cucurbits, except fungi and except sweet corn

Triadimefon

Field trials involving triadimefon in <u>peppers</u> were made available from Australia. The GAP of Japan for the field application of triadimefon to peppers is 0.005 kg ai/hL with a PHI of 1 day. The residues from trials matching the GAP were < 0.05 and < 0.05 mg/kg (sum of triadimefon and triadimenol).

Field trials involving triadimefon in <u>tomatoes</u> were made available from Australia and Japan. GAP in Belarus for triadimefon in glasshouse application to tomatoes is 0.5 kg ai/ha with a PHI of 10 days. The residues from Japanese trials matching the GAP were: 0.14, 0.15, 0.43 and 0.68 mg/kg (sum of triadimefon and triadimenol).

Triadimenol

Field trials involving triadimenol in <u>peppers</u> were made available from Germany and Spain. The GAP of Spain for triadimenol in glasshouse peppers is 0.013 kg ai/hL with a PHI of 3 day. The residues from trials matching the GAP were 0.11, 0.16, 0.21, 0.21, 0.23, 0.33, 0.33 and 0.38 mg/kg (sum of triadimefon and triadimenol).

Field trials involving triadimenol in <u>tomatoes</u> are available from Belgium, France, Germany, Greece, Italy and Spain.

The GAP of Italy for the field application of triadimenol to tomatoes is 0.005 kg ai/hL with a PHI of 14 days. The residues from trials matching this GAP were < 0.05(4) mg/kg (sum of triadimefon and triadimenol).

The GAP of Morocco and Spain for the field application of triadimenol to tomatoes is 0.013 kg ai/hL with a PHI of 3 days. The residues from trials matching this GAP were < 0.05 and 0.21 mg/kg (sum of triadimefon and triadimenol).

The GAP of Italy for the glasshouse application of triadimenol to tomatoes is 0.005 kg ai/hL with a PHI of 14 days. The residues from trials matching this GAP were < 0.05(3) and 0.08 mg/kg (sum of triadimefon and triadimenol).

The GAP of Morocco and Spain for triadimenol in glasshouse application to tomatoes is 0.013 kg ai/hL with a PHI of 3 days. The residues from trials matching this GAP were 0.05, 0.05, 0.11, 0.12, 0.13, 0.15, 0.25, 0.27 and 0.29 mg/kg (sum of triadimefon and triadimenol).

The Meeting decided to pool the data for triadimefon and triadimenol from all GAPs for application in glasshouse for tomatoes and peppers. The combined results (n=25) in whole fruits in ranked order (median underlined) were: < 0.05(3), 0.05, 0.05, 0.08, 0.11, 0.11, 0.12, 0.13, 0.14, 0.15, 0.15, 0.16, 0.21, 0.21, 0.23, 0.25, 0.27, 0.29, 0.33, 0.33, 0.38, 0.43 and 0.68 mg/kg (sum of triadimefon and triadimenol).

The Meeting estimated an STMR value of 0.15 mg/kg and an HR of 0.68 mg/kg (sum of triadimefon and triadimenol) for fruiting vegetables other than cucurbits, except fungi and except sweet corn.

Based on the uses of both triadimefon and triadimenol the Meeting estimated a maximum residue level of 1 mg/kg for the sum of triadimefon and triadimenol in fruiting vegetables other than cucurbits, except fungi and except sweet corn.

The Meeting withdraws its previous recommendations for the triadimefon in peppers, sweet of 0.1 mg/kg and for tomatoes of 0.2 mg/kg. The Meeting also withdraws its previous recommendations for triadimenol in peppers, sweet of 0.1 mg/kg and in tomatoes of 0.5 mg/kg.

Peas and chick-peas

GAP information for the use of triadimefon and triadimenol on peas and chick-peas were reported from various countries. Field trials involving either active substance were not made available.

The Meeting withdraws its previous recommendations for triadimefon in chick-peas and in peas of 0.05(*) mg/kg. The Meeting also withdraws its previous recommendations for triadimenol in chick-peas of 0.05(*) mg/kg and in peas of 0.1 mg/kg.

Artichoke, globe

Field trials involving triadimenol in globe artichoke were made available from Italy and Spain. The GAP of Cyprus for triadimenol in globe artichoke consists of an application rate of 0.01 kg ai/hL with a PHI of 5 days. The residues from trials matching this GAP in ranked order (median underlined) were: < 0.05, 0.08, 0.08, 0.13, 0.14, 0.15, 0.16, 0.24 and 0.55 mg/kg (sum of triadimefon and triadimenol).

The Meeting estimated an STMR value of 0.14 mg/kg and an HR of 0.55 mg/kg (sum of triadimefon and triadimenol) for globe artichokes.

Based on the use of triadimenol the Meeting estimated a maximum residue level of 0.7 mg/kg for the sum of triadimefon and triadimenol in globe artichokes.

The Meeting withdraws its previous recommendation for triadimenol in artichoke, globe of 1 mg/kg.

Cereals, except maize and rice

Triadimefon

Field trials involving triadimefon in barley are available from Germany. The GAP of the Ukraine for the foliar application of triadimefon to barley is 0.13 kg ai/ha with a PHI of 30 days. The residues from trials matching this GAP were < 0.1(9) mg/kg (sum of triadimefon and triadimenol) for barley grain.

Field trials involving triadimefon in oats are available from Germany. The GAP of Belarus, Kazakhstan and Russia for the foliar application of triadimefon to oats is 0.18 kg ai/ha with a PHI of 30 days. The residues from trials matching this GAP were < 0.1(3) mg/kg (sum of triadimefon and triadimenol) for oats grain.

Field trials involving triadimefon in rye are available from Germany. The GAP of Macedonia for the foliar application of triadimefon to rye is 0.25 kg ai/ha with a PHI of 35 days. The residues from trials matching this GAP were < 0.08 and < 0.08 mg/kg (sum of triadimefon and triadimenol) for rye grain.

The GAP of Croatia for the foliar application of triadimefon to rye is 0.1 kg ai/ha with a PHI of 42 days. The residues from trials matching this GAP were: < 0.1(3), 0.15 mg/kg (sum of triadimefon and triadimenol) for rye grain.

Field trials involving triadimefon in wheat are available from Germany. GAP in Croatia for the foliar application of triadimefon to wheat is 0.1 kg ai/ha with a PHI of 42 days. The residues from trials matching this GAP were < 0.1(8) mg/kg (sum of triadimefon and triadimenol) for wheat grain.

Triadimenol

Field trials involving triadimenol in barley are available from Australia, Canada, France, Germany, Italy, Spain, United Kingdom and the United States.

The GAP of Cyprus and Poland for the foliar application of triadimenol to barley is 0.13 kg ai/ha with a PHI of 35 days. The residues from trials matching this GAP were: < 0.05(14), 0.05, 0.06, 0.06, 0.08, 0.09, 0.09 and < 0.1(11) mg/kg (sum of triadimefon and triadimenol) for barley grain.

The GAP for the use of triadimenol as a seed dressing in barley were reported from Australia and New Zealand with application rates of 0.022 kg/100 kg seed. The residue from one trial matching this GAP was < 0.04 mg/kg (sum of triadimefon and triadimenol) for barley grain.

The GAP for the use of triadimenol as seed dressing in barley from Austria, Brazil, Germany, Ireland, Mexico and the United Kingdom is 0.04 kg ai/100 kg/seeds with no specified PHI. The residues from trials matching this GAP in ranked order (median underlined) were: < 0.01(15), 0.02, < 0.05(10) and < 0.1(19) mg/kg (sum of triadimefon and triadimenol) for barley grain.

Field trials involving triadimenol in oats were available from Brazil, Canada, Germany and the United States. The GAP of the United Kingdom for the foliar application of triadimenol to oats is 0.13 kg ai/ha with growth dependent PHI. The residues from trials matching this GAP were: 0.1, 0.11 and 0.12 mg/kg (sum of triadimefon and triadimenol) for oat grain.

The GAP for the use of triadimenol as a seed dressing in oats in Australia is 0.015 kg ai/100 kg seeds with no specified PHI. The residues from trials matching this GAP were < 0.1(4) mg/kg (sum of triadimefon and triadimenol) for oat grain.

GAP in oats for the use of triadimenol as a seed dressing was reported from Brazil, Ireland and the United Kingdom with application rates of 0.04 kg ai/100 kg seed. The residues from trials matching this GAP were: < 0.01(14) and < 0.1(3) mg/kg (sum of triadimefon and triadimenol) for oats grain.

The GAP of Finland for the use of triadimenol as a seed dressing in barley is 0.045 kg ai/100 kg seeds with no specified PHI. The residues from trials matching the GAP were: < 0.01 and < 0.01 mg/kg (sum of triadimefon and triadimenol) for oat grain.

Field trials involving triadimenol in rye were available from Canada, Germany and the United States. The GAP of Poland and the United Kingdom for the foliar application of triadimenol to rye is 0.13 kg ai/ha with a PHI of 35 days. The residues from trials matching this GAP were: < 0.05 and < 0.1(4) mg/kg (sum of triadimefon and triadimenol) for rye grain.

The GAP for Ireland and the United Kingdom, for the use of triadimenol as a seed dressing in rye is 0.038 kg ai/100 kg seed. The residues from trials matching this GAP were: < 0.01(6), 0.02 and < 0.1(4) mg/kg (sum of triadimefon and triadimenol) for rye grain.

Field trials involving triadimenol in wheat are available from Australia, Brazil, Canada, France, Germany, Hungary, Italy, New Zealand, Spain and the United States. The GAP of Australia, Bulgaria, Cyprus, Italy and Poland for the foliar application of triadimenol to wheat is 0.13 kg ai/ha

with PHI of 28 to 35 days. The residues from trials matching this GAP were: < 0.01, < 0.02, 0.03, < 0.05(39), 0.05 and 0.06 mg/kg (sum of triadimefon and triadimenol) for wheat grain.

In France GAP for the foliar application of triadimenol to wheat is 0.075 kg ai/ha with a PHI of 28 days. The residue from one trial matching this GAP was < 0.05 mg/kg (sum of triadimefon and triadimenol) for wheat grain.

The GAP for the use of triadimenol as a seed dressing in wheat were reported from Brazil, Ireland and the United Kingdom with application rates of 0.038 kg ai/100 kg seed. The residues from trials matching this GAP were: < 0.01(20), 0.03 and < 0.05(11) mg/kg (sum of triadimefon and triadimenol) for wheat grain.

The Meeting decided to pool the residue data for triadimefon and triadimenol from all foliar and seed dressing GAPs for cereals. The combined results (n=220) in grain in ranked order (median underlined) were: < 0.01(58), < 0.02, 0.02, 0.02, 0.03, < 0.05(76), 0.05, 0.05, 0.06(3), < 0.08, < 0.08, 0.08, 0.09, 0.09, < 0.1(68), 0.1, 0.11, 0.12 and 0.15 mg/kg (sum of triadimefon and triadimenol).

The Meeting estimated an STMR value of 0.05 mg/kg and a highest residue of 0.15 mg/kg (sum of triadimefon and triadimenol) for cereal grain, except maize and rice.

Based in the uses of both triadimefon and triadimenol the Meeting estimated a maximum residue level of 0.2 mg/kg for the sum of triadimefon and triadimenol in cereals, except maize and rice.

The Meeting withdraws its previous recommendations for the triadimefon in barley of 0.5 mg/kg and in oats, rye and wheat of 0.1 mg/kg. The Meeting also withdraws its previous recommendations for triadimenol in barley of 0.5 mg/kg and in oats, rye and wheat of 0.2 mg/kg.

Coffee beans

Field trials involving triadimenol in coffee were available from Brazil, El Salvador, Guatemala, Mexico and South Africa. The GAP of Brazil and Costa Rica for the foliar application of triadimenol to coffee is 0.25 kg ai/ha with a PHI of 30 days. The residues from trials matching this GAP were: 0.04, 0.04, < 0.05(3), 0.06, 0.07, < 0.1 and 0.4 mg/kg (sum of triadimefon and triadimenol) for coffee beans.

The GAP of Brazil for the broadcast application with incorporation of a granular formulation of triadimenol to coffee is 1.1 kg ai/ha with a PHI of 90 days. The residues from trials matching the GAP were: < 0.01, 0.01, < 0.05(3), 0.06, 0.07, 0.07 and 0.09 mg/kg (sum of triadimefon and triadimenol) for coffee beans.

A further GAP of Brazil, for the broadcast application of a granular formulation of triadimenol to coffee is 1.95 kg ai/ha with a PHI of 90 days. The residues from trials matching this GAP were: < 0.05 and 0.05 mg/kg (sum of triadimefon and triadimenol) for coffee beans.

The Meeting decided to pool the data for coffee beans from trials with foliar and spreading applications. The combined results (n=20) in ranked order (median underlined) were: < 0.01, 0.01, 0.04, 0.04, < 0.05(7), 0.05, 0.06, 0.06, 0.07(3), 0.09, < 0.1 and 0.4 mg/kg (sum of triadimefon and triadimenol) for coffee beans.

The Meeting estimated an STMR value of 0.05 mg/kg (sum of triadimefon and triadimenol) for coffee beans.

Based on the use of triadimenol the Meeting estimated a maximum residue level of 0.5 mg/kg for the sum of triadimefon and triadimenol in coffee beans.

The Meeting withdraws both of its previous recommendations for triadimefon in coffee beans of 0.05(*) mg/kg and for triadimenol in coffee beans of 0.1* mg/kg.

Hops, dry

GAP information for the use of triadimefon and triadimenol on hops was reported from Croatia and Spain. Field trials involving either active substance were not made available to the Meeting.

The Meeting withdraws both of its previous recommendations for triadimefon in hops, dry of 10 mg/kg and for triadimenol in hops, dry of 5 mg/kg.

Sugar beet leaves or tops

Field trials involving the application of triadimenol to sugar beets were available from Germany and the United Kingdom. The GAP of the United Kingdom for sugar beets is 0.13 kg ai/ha with a PHI of 14 days. The residues from trials matching this GAP in ranked order (median underlined) were: 0.08, 0.1, 0.1, 0.14, 0.14, 0.18, 0.19, 0.19 and 0.42 mg/kg (sum of triadimefon and triadimenol) in sugar beet leaves.

The Meeting estimated an STMR value of 0.14 mg/kg and a highest residue of 0.42 mg/kg for the sum of triadimefon and triadimenol in sugar beet leaves (fresh weight).

Fodder beets

GAP information for the use of triadimefon or triadimenol in fodder beets was not submitted.

The Meeting withdraws both of its previous recommendations for triadimefon and triadimenol in fodder beets of 0.05(*) mg/kg.

Cereal forage, except maize forage

Triadimefon

Field trials involving triadimefon in barley were available from Germany. The GAP of the Ukraine for the foliar application of triadimefon to barley is 0.13 kg ai/ha. The residues from trials matching this GAP were: 1.4, 1.7(4), 1.9, 1.9, 2.0 and 2.2 mg/kg (sum of triadimefon and triadimenol) for barley forage.

Field trials involving triadimefon in oats were available from Germany. The GAP of Belarus, Kazakhstan and Russia for the foliar application of triadimefon to oats is 0.18 kg ai/ha. The residues from trials matching this GAP were 0.76, 1.9 and 2.3 mg/kg (sum of triadimefon and triadimenol) for oats forage.

Field trials involving triadimefon in rye were available from Germany. The GAP of Macedonia for the foliar application of triadimefon to rye is 0.25 kg ai/ha. The residues from trials matching this GAP were 5.9 and 10 mg/kg (sum of triadimefon and triadimenol) for rye forage.

The GAP of Croatia for the foliar application of triadimefon to rye is 0.1 kg ai/ha. The residues from trials matching this GAP were: 2.3, 2.5, 5.0 and 5.9 mg/kg (sum of triadimefon and triadimenol) for rye forage.

Field trials involving triadimefon in wheat were available from Germany. The GAP of Croatia for the foliar application of triadimefon to wheat is 0.1 kg ai/ha. The residues from trials matching this GAP were: 1.6, 1.8, 1.8, 2.2, 2.7 and 2.8 mg/kg (sum of triadimefon and triadimenol) for wheat forage.

Triadimenol

Field trials involving triadimenol in barley were available from Australia, Canada, France, Germany, Italy, Spain, United Kingdom and the United States.

The GAP of Cyprus and Poland for the foliar application of triadimenol to barley is 0.13 kg ai/ha. The residues from trials matching the GAP were: 0. 0.28, 1.1, 1.2, 1.6, 1.7, 1.7, 1.8, 1.9(3), 2.0, 2.0, 2.3, 2.3, 2.5, 2.6, 2.8, 2.9, 3.3, 3.4, 3.6, 3.6, 4.4, 4.4, 4.7, 4.8 and 5.0 mg/kg (sum of triadimefon and triadimenol) for barley forage.

The GAP for the use of triadimenol as a seed dressing in barley of Austria, Brazil, Germany, Ireland, Mexico and United Kingdom is 0.04 kg ai/100 kg/seeds with no specified PHI. The residues from trials matching this GAP were: < 0.01(4), 0.02, 0.02, 0.03(3), 0.05, 0.05, 0.06, 0.07, 0.08, < 0.1(13), 0.1, 0.16, 0.2, 0.27 and 1.7 mg/kg (sum of triadimefon and triadimenol) for barley forage.

Field trials involving triadimenol in oats were available from Brazil, Canada, Germany and the United States. The GAP of the United Kingdom for the foliar application of triadimenol to oats is 0.13 kg ai/ha with growth dependent PHI. The residues from trials matching this GAP were 2.4 and 2.5 mg/kg (sum of triadimefon and triadimenol) for oats forage.

The GAP for the use of triadimenol as a seed dressing in oats from Australia is 0.015 kg ai/100 kg seeds with no specified PHI. The residues from trials matching this GAP were < 0.1(4) mg/kg (sum of triadimefon and triadimenol) for oat forage.

GAPs in oats for the use of triadimenol as a seed dressing was reported from Brazil, Ireland and United Kingdom with application rates of 0.04 kg ai/100 kg seed. The residues from trials matching this GAP were: < 0.01, < 0.01, 0.02, 0.03, 0.03, 0.05, 0.08, 0.09, < 0.1(2), 0.1, 0.12, 0.12, 0.15, 0.16, 0.2, 0.27 mg/kg (sum of triadimefon and triadimenol) for oat forage.

The GAP of Finland for the use of triadimenol as a seed dressing in barley is 0.045 kg ai/100 kg seeds with no specified PHI. The residues from trials matching the GAP were 0.2 and 0.23 mg/kg (sum of triadimefon and triadimenol) for oat forage.

Field trials involving triadimenol in rye were available from Canada, Germany and the United States. The GAP of Poland and the United Kingdom for the foliar application of triadimenol to rye is 0.13 kg ai/ha with a PHI of 35 days. The residues from trials matching this GAP were: 1.7, 2.2, 2.7, 4.6 and 6.1 mg/kg (sum of triadimefon and triadimenol) for rye forage.

The GAP of Ireland and the United Kingdom for the use of triadimenol as a seed dressing in rye is 0.038 kg ai/100 kg seed. The residues from trials matching this GAP were: 0.03, 0.05, < 0.1(4), 0.26, 0.28, 0.77, 1.1 and 1.1 mg/kg (sum of triadimefon and triadimenol) for rye forage.

Field trials involving triadimenol in wheat were available from Australia, Brazil, Canada, France, Germany, Hungary, Italy, New Zealand, Spain and the United States.

The GAP of Australia, Bulgaria, Cyprus, Italy and Poland for the foliar application of triadimenol to wheat is 0.13 kg ai/ha with PHI of 28 to 35 days. The residues from trials matching this GAP were: 0.5, 0.61, 0.64, 1.1, 1.4(3), 1.5, 1.7, 1.9(3), 2.0, 2.1, 2.2(3), 2.3, 2.4, 2.5(3), 2.6, 2.6, 2.7, 2.9, 2.9, 3.0, 3.7, 3.9, 4.7 and 5.7 mg/kg (sum of triadimefon and triadimenol) for wheat forage.

In France the GAP for the foliar application of triadimenol to wheat is 0.075 kg ai/ha with a PHI of 28 days. The residue from one trial matching the GAP was 1.0 mg/kg (sum of triadimefon and triadimenol) for wheat forage.

The GAP for the use of triadimenol as a seed dressing in wheat was reported from Brazil, Ireland, and the United Kingdom with an application rate of 0.038 kg ai/100 kg seed (PHI unnecessary). The residues from trials matching this GAP were: < 0.01, < 0.01, 0.04(4), < 0.05(6), 0.09, < 0.1, 0.13, 0.13, 0.15, 0.31, 0.37, 0.38, 0.5, 0.52, 1.1, 1.2 and 1.8 mg/kg (sum of triadimefon and triadimenol) for wheat forage.

The Meeting decided to combine the data for triadimefon and triadimenol from all foliar GAPs for barley, oats, rye and wheat forage. The combined results (n=90) in ranked order (median underlined) were: 0.28, 0.5, 0.61, 0.64, 0.76, 1.1, 1.1, 1.2, 1.4(4), 1.5, 1.6, 1.6, 1.7(8), 1.8(3), 1.9(9), 2.0(4), 2.1, 2.2(6), 2.3(5), 2.4, 2.4, 2.5(6), 2.6(3), 2.7(3), 2.8, 2.8, 2.9(3), 3.0, 3.3, 3.4, 3.6, 3.6, 3.7, 3.9, 4.4, 4.4, 4.6, 4.7, 4.7, 4.8, 5.0, 5.0, 5.7, 5.9, 5.9, 6.1 and 10 mg/kg (sum of triadimefon and triadimenol) for combined barley, oats, rye and wheat forage (fresh based).

The Meeting estimated an STMR value of 2.2 mg/kg and a highest residue of 10 mg/kg for the sum of triadimefon and triadimenol in cereal forage.

Cereal hay

Triadimenol

Field trials involving triadimenol in barley hay were available from the United States. The GAP for the use of triadimenol as a seed dressing in barley for Austria, Brazil, Germany, Ireland, Mexico and the United Kingdom is 0.04 kg ai/100 kg/seeds with no specified PHI. The residues from trials matching this GAP were: 0.02, 0.02, 0.03, 0.04, 0.05 and 0.12 mg/kg (sum of triadimefon and triadimenol) for barley hay.

Field trials involving triadimenol in oats hay were available from the United States. The GAP in oats for the use of triadimenol as seed dressing was reported from Brazil, Ireland and United Kingdom with application rates of 0.04 kg ai/100 kg seed (PHI unnecessary). The residues from trials matching the GAP were: < 0.01, 0.03, 0.05, 0.21, 0.33 and 0.98 mg/kg (sum of triadimefon and triadimenol) for oats hay.

Field trials involving triadimenol in wheat hay were available from the United States. The GAP for the use of triadimenol as a seed dressing in wheat were reported from Brazil, Ireland, and United Kingdom with an application rate of 0.038 kg ai/100 kg seed (PHI unnecessary). The residues from trials matching this GAP were: 0.05, 0.07, 0.07, 0.08, 0.15 and 0.19 mg/kg (sum of triadimefon and triadimenol) for wheat hay.

The Meeting decided to pool the data from barley, oats and wheat hay after seed dressing application of triadimenol. The combined results (n=18) in ranked order (median underlined) were: < 0.01, 0.02, 0.02, 0.03, 0.03, 0.04, 0.05(3), 0.07, 0.07, 0.08, 0.12, 0.15, 0.19, 0.21, 0.33 and 0.98 mg/kg (sum of triadimefon and triadimenol) for cereal hay.

The Meeting estimated an STMR value of 0.06 mg/kg and a highest residue of 0.98 mg/kg for the sum of triadimefon and triadimenol in cereal hay.

Cereal straw, straw and fodder (dry) of cereal grains

Triadimefon

Field trials involving triadimefon in barley were available from Germany. The GAP of the Ukraine for the foliar application of triadimefon to barley is 0.13 kg ai/ha with a PHI of 30 days. The residues from trials matching this GAP were: < 0.1(4), 0.35, 0.42, 0.48, 0.63, 0.7 mg/kg (sum of triadimefon and triadimenol) for barley straw.

Field trials involving triadimefon in oats were available from Germany. The GAP of Belarus, Kazakhstan and Russia for the foliar application of triadimefon to oats is 0.18 kg ai/ha with a PHI of 30 days. The residues from trials matching this GAP were: < 0.1, 0.22 and 0.63 mg/kg (sum of triadimefon and triadimenol) for oats straw.

Field trials involving triadimefon in rye were available from Germany. The GAP of Macedonia for the foliar application of triadimefon to rye is 0.25 kg ai/ha with a PHI of 35 days. The residues from trials matching this GAP were 0.91 and 1.9 mg/kg (sum of triadimefon and triadimenol) for rye straw.

The GAP of Croatia for the foliar application of triadimefon to rye is 0.1 kg ai/ha with a PHI of 42 days. The residues from trials matching this GAP were: 0.23, 1.5, 1.7 and 2.7 mg/kg (sum of triadimefon and triadimenol) for rye straw.

Field trials involving triadimefon in wheat are available from Germany. The GAP of Croatia for the foliar application of triadimefon to wheat is 0.1 kg ai/ha with a PHI 42 days. The residues from trials matching this GAP were: 0.45, 0.53, 0.53, 0.7, 0.83, 0.9, 1.1 and 2.7 mg/kg (sum of triadimefon and triadimenol) for wheat straw.

Triadimenol

Field trials involving triadimenol in barley were available from Australia, Canada, France, Germany, Italy, Spain, the United Kingdom and the United States. The GAP of Cyprus and Poland for the foliar

application of triadimenol to barley is 0.13 kg ai/ha with a PHI of 35 days. The residues from trials matching this GAP were: 0.07, < 0.1, 0.1, 0.13, 0.17, 0.21, 0.24, 0.25, 0.29, 0.31, 0.41, 0.45, 0.48, 0.5, 0.55, 0.61, 0.62, 0.64, 0.67, 0.69, 0.81, 0.84, 0.85, 0.86, 0.92, 0.98, 1.2, 1.3, 1.4 and 4.1 mg/kg (sum of triadimefon and triadimenol) for barley straw.

The GAP for the use of triadimenol as a seed dressing in barley were reported with application rates of 0.022 kg ai/100 kg seed (PHI unnecessary) from Australia and New Zealand. The residue from one trial matching this GAP was < 0.04 mg/kg (sum of triadimefon and triadimenol) for barley straw.

The GAP for the use of triadimenol as a seed dressing in barley for Austria, Brazil, Germany, Ireland, Mexico and the United Kingdom is 0.04 kg ai/100 kg/seeds with no specified PHI. The residues from trials matching this GAP were: < 0.01(14), 0.01, < 0.05(6), 0.05 and < 0.1(20) mg/kg (sum of triadimefon and triadimenol) for barley straw.

Field trials involving triadimenol in oats were available from Brazil, Canada, Germany and the United States. The GAP of the United Kingdom for the foliar application of triadimenol to oats is 0.13 kg ai/ha with growth dependent PHI. The residues from trials matching the GAP were: 1.6 and 2.1 mg/kg (sum of triadimefon and triadimenol) for oat straw.

The GAP in oats for the use of triadimenol as a seed dressing in Australia is 0.015 kg ai/100 kg seeds with no specified PHI. The residues from trials matching this GAP were < 0.1(4) mg/kg (sum of triadimefon and triadimenol) for oat straw.

The GAP in oats for the use of triadimenol as a seed dressing was reported from Brazil, Ireland and United Kingdom with application rates of 0.04 kg ai/100 kg seed (PHI unnecessary). The residues from trials matching this GAP were: < 0.01(9), 0.03(4), 0.05, < 0.1(3) mg/kg (sum of triadimefon and triadimenol) for oat straw.

The GAP of Finland for the use of triadimenol as a seed dressing in barley is 0.045 kg ai/100 kg seeds with no specified PHI. The residues from trials matching this GAP were: < 0.01 and 0.02 mg/kg (sum of triadimefon and triadimenol) for oat grain. Field trials involving triadimenol in rye are available from Canada, Germany and the United States.

The GAP of Poland and the United Kingdom for the foliar application of triadimenol to rye is 0.13 kg ai/ha with a PHI of 35 days. The residues from trials matching this GAP were: 0.36, 1.2, 1.4, 1.9 and 1.9 mg/kg (sum of triadimefon and triadimenol) for rye straw.

The GAP from Ireland and the United Kingdom for the use of triadimenol as a seed dressing in rye were reported with an application rate of 0.038 kg ai/100 kg seed. The residues from trials matching this GAP were: < 0.01(7) and < 0.1(4) mg/kg (sum of triadimefon and triadimenol) for rye straw.

Field trials involving triadimenol in wheat were available from Australia, Brazil, Canada, France, Germany, Hungary, Italy, New Zealand, Spain and the United States. The GAP of Australia, Bulgaria, Cyprus, Italy and Poland for the foliar application of triadimenol to wheat is 0.13 kg ai/ha with a PHI of 28 to 35 days. The residues from trials matching this GAP were: 0.12, 0.12, 0.15, 0.16, 0.27, 0.27, 0.29, 0.31, 0.32, 0.39, 0.46, 0.47, 0.53, 0.56, 0.59, 0.66, 0.68, 0.7, 0.72, 0.75, 0.79, 0.82, 0.82, 0.83, 0.89, 0.91, 0.93, 1.0(3), 1.2, 1.3(3), 1.4, 2.1 and 2.5 mg/kg (sum of triadimefon and triadimenol) for wheat straw.

In France the GAP for the foliar application of triadimenol to wheat is 0.075 kg ai/ha with a PHI of 28 days. The residue from one trial matching the GAP was 0.62 mg/kg (sum of triadimefon and triadimenol) for wheat straw.

The GAP for the use of triadimenol as a seed dressing in wheat were reported from Brazil, Ireland, and the United Kingdom with an application rate of 0.038 kg ai/100 kg seed (PHI unnecessary). The residues from trials matching this GAP were: < 0.01(17), 0.02, 0.03, 0.03, 0.04, < 0.05(8), < 0.1, < 0.1, 0.15 and 0.2 mg/kg (sum of triadimefon and triadimenol) for wheat straw.

The Meeting decided to pool the data for triadimefon and triadimenol from all foliar GAPs for cereal straw. The combined results (fresh, n=101) in ranked order (median underlined) were: 0.07,

< 0.1(6), 0.1, 0.12, 0.12, 0.13, 0.15, 0.16, 0.17, 0.21, 0.22, 0.23, 0.24, 0.25, 0.27, 0.27, 0.29, 0.29, 0.31, 0.31, 0.32, 0.35, 0.36, 0.39, 0.41, 0.42, 0.45, 0.45, 0.46, 0.47, 0.48, 0.48, 0.5, 0.53(3), 0.55, 0.56, 0.59, 0.61, 0.62, 0.62, 0.63, 0.63, 0.64, 0.66, 0.67, 0.68, 0.69, 0.7(3), 0.72, 0.75, 0.79, 0.81, 0.82, 0.82, 0.83, 0.83, 0.84, 0.85, 0.86, 0.89, 0.9, 0.91, 0.91, 0.92, 0.93, 0.98, 1.0(3), 1.1, 1.2(3), 1.3(4), 1.4(3), 1.5, 1.6, 1.7, 1.9(3), 2.1, 2.1, 2.5, 2.7, 2.7 and 4.1 mg/kg (sum of triadimefon and triadimenol).

The Meeting estimated an STMR value of 0.64 mg/kg and a highest residue of 4.1 mg/kg for the sum of triadimefon and triadimenol in cereal straw.

On a dry weight basis (88% DM) the values were: 0.08, < 0.11(6), 0.11, 0.14, 0.14, 0.15, 0.17, 0.18, 0.19, 0.24, 0.25, 0.26, 0.27, 0.28, 0.31, 0.31, 0.33, 0.33, 0.35, 0.35, 0.36, 0.4, 0.41, 0.44, 0.47, 0.48, 0.51, 0.51, 0.52, 0.53, 0.55, 0.55, 0.57, 0.6(3), 0.63, 0.64, 0.67, 0.69, 0.7, 0.7, 0.72, 0.72, 0.73, 0.75, 0.76, 0.77, 0.78, 0.8(3), 0.82, 0.85, 0.9, 0.92, 0.93, 0.93, 0.94, 0.94, 0.95, 0.97, 0.98, 1(4), 1.1(6), 1.3, 1.4(3), 1.5(4), 1.6(3), 1.7, 1.8, 1.9, 2.2(3), 2.4, 2.4, 2.8, 3.1, 3.1 and 4.7 mg/kg (sum of triadimefon and triadimenol).

Based on the uses of both triadimefon and triadimenol in barley, oats, rye and wheat after foliar treatment the Meeting estimated an MRL of 5 mg/kg (sum of triadimefon and triadimenol) for straw and fodder (dry) of cereal grains.

The Meeting withdraws its previous recommendations for the triadimefon in barley, oats, rye and wheat straw and fodder, dry of 2 mg/kg and for triadimenol in barley, oats, rye and wheat straw and fodder, dry of 5 mg/kg.

Fate of residues during processing

Triadimefon and triadimenol are in general stable to hydrolysis during pasteurization, baking and boiling conditions.

Information on the fate of triadimefon and triadimenol during food processing was available for apples, grapes, pineapples, tomatoes and coffee beans.

Calculated processing factors and the mean or best estimate are summarized in the following table (based on the total triadimefon and triadimenol residues).

Raw agricultural commodity (RAC)	Processed commodity	Calculated processing factors	Estimate of the processing factor
Apples	washed	0.83, 1.0	0.92
	juice	0.5, < 0.56, < 0.63, < 0.63, < 0.7, < 0.8, < 0.83	0.63
	sauce	< 0.5, < 0.56, < 0.63, < 0.63, < 0.7, < 0.8, < 0.83	0.63
Grapes	must	0.13, 0.18, < 0.24, < 0.25, 0.29, < 0.35, < 0.41, < 0.42, < 0.47, 0.5, < 0.56, < 0.63, < 0.71(3), < 0.83	0.45
	wine	0.09, 0.1, < 0.25, 0.29, < 0.33, < 0.33, < 0.35, < 0.41, < 0.42, < 0.5, < 0.56, < 0.63, < 0.71(3), < 0.83	0.42
	juice	< 0.25, 0.33, < 0.56, 1.1	0.45
	raisins	0.67, 1.6, 2.3, 3.1, 4.5, 5.7, 5.8	3.1
	wet pomace	1.3, 2.4, 3.5, 16	3
	dry pomace	3.5, 3.9, 7.4, 33	5.7
Pineapples	bran	1.3	1.3
	peel washed	0.4	0.4
Tomatoes	washed	0.94, 1	0.97
	peeled	0.29, 0.37	0.33
	juice	0.56, 0.59, 0.74	0.59
	puree	0.78	0.78
	paste	1.9, 5.2, 5.9	5.2
	preserve	0.58, 0.59	0.585

Raw agricultural commodity (RAC)	Processed commodity	Calculated processing factors	Estimate of the processing factor
	catsup	2.4	2.4
	wet pulp	3.6	3.6
	dry pulp	14	14
Coffee	roasted beans	1.1	1.1
	instant coffee	1.3	1.3

For apples the estimated processing factors are applied to the STMR value of 0.06 mg/kg for pome fruits from the supervised trials. The Meeting estimated STMR-P values for apple juice and apple sauce of 0.04 mg/kg. For apples no processing data for wet pomace is available.

For grapes the estimated processing factors are applied to the STMR value of 0.15 mg/kg from the supervised trials. The Meeting estimated STMR-P values for grape must of 0.07 mg/kg, wine of 0.06 mg/kg, grape juice of 0.07 mg/kg, raisins of 0.47 mg/kg, wet grape pomace of 0.45 mg/kg and dry grape pomace of 0.86 mg/kg. The processing factor for raisins (3.1) was applied to the HR for grapes (3.2 mg/kg) to produce an HR-P value for raisins (9.9 mg/kg).

The Meeting estimated a maximum residue level for the sum of triadimefon and triadimenol, calculated as triadimefon in dried grapes of 10 mg/kg.

For pineapples the estimated processing factors are applied to the STMR value of 1.5 mg/kg for whole pineapple fruits from the supervised trials. The Meeting estimated STMR-P values for pineapple bran of 1.95 mg/kg. For pineapple pulp, juice and syrup the submitted data is not sufficient for a proposal of processing factors.

For tomatoes the estimated processing factors are applied to the STMR value of 0.15 mg/kg from the supervised trials. The Meeting estimated STMR-P values for peeled tomatoes of 0.05 mg/kg, tomato paste of 0.78 mg/kg, tomato puree of 0.12 mg/kg, tomato juice of 0.09 mg/kg, tomato preserve of 0.09 mg/kg, tomato catsup of 0.36 mg/kg, wet tomato pulp of 0.54 mg/kg and dry tomato pulp of 2.1 mg/kg.

Based on the residue data for sweet peppers (< 0.05, < 0.05, 0.11, 0.16, 0.21, 0.21, 0.23, 0.33, 0.33 and 0.38 mg/kg) and the default processing factor for sweet peppers to dried chilli peppers of 10 the Meeting estimated a maximum residue level of 5 mg/kg and an STMR value of 2.1 mg/kg for dried chilli peppers.

For coffee the estimated processing factors are applied to the STMR value of 0.05 mg/kg from the supervised trials. The Meeting estimated STMR-P values for roasted coffee beans of 0.06 mg/kg and instant coffee of 0.07 mg/kg.

Livestock dietary burden

The Meeting estimated the dietary burden of triadimefon and triadimenol in farm animals on the basis of the diets listed in Annex 6 of the 2006 JMPR Report (OECD Feedstuffs Derived from Field Crops). Calculation from highest residue, STMR (some bulk commodities) and STMR-P values provides the levels in feed suitable for estimating MRLs, while calculation from STMR and STMR-P values for feed is suitable for estimating STMR values for animal commodities.

Estimated maximum and mean livestock dietary burdens

Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are provided in Annex 6. The calculations were made according to the animal diets from US-Canada, EU and Australia in the OECD Table (Annex 6 of the 2006 JMPR Report).

	Livestock dietary burden, sum of triadimefon and triadimenol, ppm of dry matter diet		
	US-Canada	EU	Australia

	max	mean	max	mean	max	mean
Beef cattle	12	3.1	9.6	2.1	40 [1]	8.8 [2]
Dairy cattle	18	4.4	9.7	2.1	27 [3]	7.7 [4]
Poultry - broiler	0.1	0.04	0.1	0.04	0.1	0.04
Poultry - layer	0.1	0.04	4.7 [5]	1.0 [6]	0.09	0.03

[1] Highest maximum beef cattle dietary burden suitable for MRL estimates for mammalian meat.

[2] Highest mean beef cattle dietary burden suitable for STMR estimates for mammalian meat.

[3] Highest maximum dairy dietary burden suitable for MRL estimates for milk.

[4] Highest mean dairy cattle dietary burden suitable for STMR estimates for milk.

[5] Highest maximum poultry dietary burden suitable for MRL estimates for poultry meat and eggs.

[6] Highest mean poultry dietary burden suitable for STMR estimates for poultry meat and eggs.

Livestock feeding studies

The Meeting received animal feeding studies on dairy cattle and laying hens. In these studies residues were analysed with two different methods. Only the results from the specific determination of triadimefon and triadimenol are used in this appraisal according to the residue definition for animal matrices. Total triadimefon and triadimenol residues in animal matrices are reported in the evaluation.

Three groups of cows were dosed at levels equivalent to 25 ppm (0.75 mg/kg bw) (1 ×), 75 ppm (2.3 mg/kg bw) (3 ×) and 250 ppm (3.7 mg/kg bw) (10 ×) triadimefon and triadimenol (1:1 mixture) in the diet together with a control group (0 ×). In all matrices except fat (3 × and 10 ×) and milk (10 ×) no residues above the LOQs (0.001 mg/kg for milk, 0.01 mg/kg for other matrices) were detected. In cattle fat from the 3 × group the mean value of triadimefon and triadimenol residues was 0.017 mg/kg (highest value 0.02 mg/kg). In the 10 × group the mean fat residues were 0.02 mg/kg (highest value 0.025 mg/kg). For milk in the 10 × group residues at the LOQ of 0.001 mg/kg were detected.

In the study with laying hens four hens per dose group received levels of 10 ppm (0.71 mg/kg bw), 25 ppm (1.8 mg/kg bw), 75 ppm (5.2 mg/kg bw) and 250 ppm (16.6 mg/kg bw) triadimefon and triadimenol (1:1 mixture) in the diet together with a control group. In liver and muscle no residues above the LOQ of 0.01 mg/kg were detected in all dose groups. Poultry fat contained measurable residues of 0.015 mg/kg in the mean only in the highest dose group (highest value of 0.02 mg/kg). Poultry skin showed one detectable residue of 0.03 mg/kg in the 75 ppm group. In the higher dose group no residues above the LOQ were found in poultry fat. In eggs residues were found in all dose groups: 10 ppm=0.002 mg/kg (highest value 0.003 mg/kg), 25 ppm=0.004 mg/kg (highest value 0.006 mg/kg), 75 ppm=0.008 mg/kg (highest value 0.01 mg/kg) and 250 ppm=0.03 mg/kg (highest value 0.04 mg/kg).

A linear relation between the dose levels and the residue concentrations was observed.

Animal commodity maximum residue levels

The dietary burden for beef and dairy cattle was estimated at a maximum level of 40 and 27 ppm respectively. For poultry the maximum burden was estimated at a level of 4.7 ppm. The mean dietary burdens were estimated at 8.8 and 7.7 ppm for beef and dairy cattle and 1.0 ppm for poultry.

Dietary burden (ppm) Feeding level [ppm]		Milk	Muscle	Liver	Kidney	Fat
		Mean	Highest	Highest	Highest	Highest
MRL, beef cattle	(40)		(< 0.01)	(< 0.01)	(< 0.01)	(0.01)
	[25]					[< 0.01]
	[75]		[< 0.01]	[< 0.01]	[< 0.01]	[0.02]
MRL, dairy cattle	(27)	(< 0.01)				
	[25]					
	[75]	[< 0.001]				
STMR beef cattle	(8.8)		(< 0.01)	(< 0.01)	(< 0.01)	(< 0.01)
	[25]					[< 0.01]

	[75]		[< 0.01]	[< 0.01]	[< 0.01]	[0.02]
STMR	(7.7)	(< 0.01)				
dairy	[25]					
cattle	[75]	[< 0.001]				

Dietary burden (ppm) Feeding level [ppm]		Eggs		Muscle	Liver	Fat
		Highest	Mean	Highest	Highest	Highest
MRL,	(4.7)	(< 0.01)		(< 0.01)	(< 0.01)	(< 0.01)
poultry-	[10]					
layer	[25]	0.003				
	[75]	0.006		[< 0.01]	[< 0.01]	[< 0.01]
STMR	(1.0)		[< 0.01]	(< 0.01)	(< 0.01)	(< 0.01)
poultry-	[10]					
broiler	[25]		0.002			
	[75]		0.004	[< 0.01]	[< 0.01]	[< 0.01]

No residues are expected above the LOQ of 0.01 mg/kg for all cattle animal matrices (except meat in the fat). For eggs detectable residues were found in the livestock feeding studies, but the levels for the sum of triadimefon and triadimenol are about an order of magnitude below the LOQ for the enforcement method.

The Meeting estimated maximum residue levels for the sum of triadimefon and triadimenol of 0.01* mg/kg in edible offal (mammalian), milk, poultry meat, poultry offal and eggs. The Meeting also estimated a maximum residue levels for the sum of triadimefon and triadimenol of 0.02 mg/kg in meat (from mammals except marine mammals) [in the fat].

The HR and STMR values for the sum of triadimefon and triadimenol for meat (from mammals except marine mammals) as muscle was estimated at 0 mg/kg. For meat (from mammals except marine mammals) as fat and eggs HR and STMR values were estimated at 0.01 mg/kg for both. The HR and STMR values for the sum of triadimefon and triadimenol for edible offal (mammalian), milk, poultry meat and poultry offal were estimated at 0 mg/kg.

The Meeting withdraws its previous recommendations for triadimefon in milk, meat (from mammals except marine mammals), poultry meat and eggs of 0.05* mg/kg. The Meeting also withdraws the previous recommendations for triadimenol in milk of 0.01* mg/kg and in meat (from mammals except marine mammals), poultry meat and eggs of 0.05* mg/kg.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes (IEDI) of triadimefon and triadimenol, based on the estimated STMRs were 1–4% of the maximum ADI (0.03 mg/kg bw). The Meeting concluded that the long-term intake of residues of triadimefon and triadimenol from the uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The International Estimated Short Term Intake (IESTI) of triadimefon and triadimenol calculated on the basis of the estimations made by JMPR represented for children 0–60% and for the general population 0–20% of the AR_fD (0.08 mg/kg bw). The IESTI for grapes (excluding wine) for children was 220% of the ARfD.

The Meeting concluded that the short-term intake of residues of triadimefon and triadimenol resulting from the uses that have been considered by the JMPR, except the use on grapes, is unlikely to present a public health concern. The information provided to the JMPR precludes an estimate that the dietary intake would be below the ARfD for consumption of grapes by children. The Meeting noted that no alternative GAP for triadimefon or triadimenol in grapes could be used to identify a lower HR value.

5.23 TRIAZOPHOS (143)

RESIDUE AND ANALYTICAL ASPECTS

Triazophos is an organophosphorus insecticide used to control insect pests on a wide range of crops. It was originally evaluated for residues by the 1983 JMPR and re-evaluated four times in 1986, 1990, 1992 and 1993, with subsequent revisions in 1984 and 1991. It was scheduled for periodic re-evaluation by the 2007 JMPR.

The manufacturer submitted data on physical and chemical properties, metabolism and environmental fate, methods of residue analysis, use patterns, residues resulting from supervised trials on cotton and stability of residues during storage and processing. The government of Thailand provided GAP information and supervised trial data for soya bean (immature seeds).

Animal metabolism

The Meeting received information on the metabolism of triazophos in rats and dogs, but no information on the distribution, excretion or fate of triazophos in livestock and poultry. As both the rat and dog studies were described in detail in the toxicological evaluation of the 2002 JMPR, the studies were not reported here.

Plant metabolism

The Meeting received plant metabolism studies for triazophos on cotton and rice. Both studies included foliar application as well as uptake via water and/or soil.

When [^{14}C]triazophos was applied to leaves of cotton plants, the radioactivity was at first present on the leaf surface but quickly penetrated into the leaf itself, with little translocation into other parts of the plant. The predominant component of the radioactivity was parent triazophos. After field application of ^{14}C-triazophos prior to boll opening, only very low residues of triazophos and its metabolites were present in cotton fibre and seeds. In both trials, the residues consisted of unchanged triazophos, 1-phenyl-3-hydroxy-l, 2, 4-triazole and an unidentified compound. Only traces of the P=O analogue of triazophos (O, O-diethyl-O-l-phenyl-lH-l,2,4-triazol-3-yl phosphate) were detectable on the leaves and stem. In general, triazophos penetrated quickly into deeper layers of the treated leaves but was not translocated in significant amounts into other parts of the plant or roots.

In uptake studies via both soil and a hydroponic medium, parent triazophos was the predominant component of the applied radioactivity, with most of the radioactive residues being present in the plant root, compared to the whole plant, or remaining in the soil or hydroponic medium. Again, most of the extracted radioactivity was composed of parent triazophos, although both the P=O analogue and 1-phenyl-3-hydroxy-l, 2, 4-triazole were also found. The results of field applications showed that only low levels of triazophos and its metabolites are likely to be present in cotton fibre and seeds if the last application takes place prior to boll opening.

Greenhouse grown rice plants were treated with [^{14}C]triazole at the growth stages of either stem elongation or heading. Initially the majority of the applied radioactivity was present on the surface of the rice plants, however by 8 weeks after the application, radioactivity was found in the rice panicles. Little radioactivity was found in rice grain. The major component of the extracted radioactivity was parent triazophos in rice panicles, husks, grain and whole plant. The 1-phenyl-3-hydroxy-l, 2, 4-triazole was also present in whole plant (< 10% of applied radioactivity) and very low levels were in rice grain (0.02% of applied radioactivity). The P=O analogue was also present, but in amounts lower than triazophos or the triazole (< 1% of applied radioactivity).

In addition, uptake studies were conducted in rice, with application of ^{14}C-triazophos to water or soil and water. As with the cotton study a large proportion of the applied radioactivity remained in the soil or soil and water medium, with little radioactivity present in either the whole plant or the

panicle. Again parent triazophos was the major component of the radioactivity, although the 1-phenyl-3-hydroxy-l, 2, 4-triazole and the P=O analogue were also detected.

In conclusion, the results from the field study show that very little of the applied radioactivity is present in rice grain following multiple applications under field conditions.

Uptake from soil by leek plants

The Meeting received information on the uptake of triazophos from soil by leek plants.

Plots of loamy soil and sandy soil were treated with [^{14}C]triazophos at application rates equivalent to 0.48 and 0.96 kg ai/ha. Leek plants were present in the treated plots. At 90 days after application, samples of soil, taken at various depths, and leek plants were collected for determination of radioactivity. No detectable radioactivity was found in the leek plants. In the soil samples up to 2.2% of the applied radioactivity was found (0–10 cm depth), with lower concentrations (< 0.2% of applied radioactivity) present at 10–20 cm and 20–30 cm depths. The radioactivity was predominantly composed of parent triazophos and 1-phenyl-3-hydroxy-l, 2, 4-triazole.

Methods of analysis

The Meeting received information on methods capable of determining residues of triazophos in plant materials and animal commodities, using GC with N or P selective detectors. The limits of quantitation were typically 0.02 mg/kg for plant commodities and 0.01 for animal commodities. Reported recoveries were within acceptable limits of 70–110%.

Stability of residues in stored analytical samples

Studies were provided to the Meeting demonstrating the stability of residues in stored samples of cotton fibre, cotton seed, oranges, carrots and soil. No significant decrease of triazophos was observed in analytical samples of cotton fibre, cotton seed, oranges and carrots stored at ≤ -18 °C for up to 24 months.

Residue definition in Plants

The results of the plant metabolism studies on cotton and rice, including foliar application and uptake from soil and water, indicate that parent triazophos is the major component of the recovered radioactivity, with the P=O analogue (O, O-diethyl-O-l-phenyl-lH-l, 2, 4-triazol-3-yl phosphate) and 1-phenyl-3-hydroxy-l, 2, 4-triazole also being present.

Analytical methods for plant matrices determine triazophos only.

On the basis of the metabolism in plants and the analytical methodology submitted, the Meeting confirmed the previous residue definition for the purposes of compliance monitoring and for estimation of dietary intake.

Definition of residue (for compliance with the MRL and for estimation of dietary intake): triazophos.

Results of supervised trials on crops

Cotton

Data were received from ten field trials for triazophos on cotton; nine trials were conducted in nine regions of India and a single trial was conducted in Brazil. In 2005 in India, 5 sprays were applied at 0.87 kg ai/ha (or 0.435 kg ai/hL) and in Brazil in 2001, 3 sprays were applied at 0.80 kg ai/ha (i.e., 0.27 kg ai/hL) or 1.60 kg ai/ha (i.e., 0.53 kg ai/hL). The GAP in India is 0.63 to 0.84 kg ai/ha with a 21 day PHI and 1–5 applications. In Brazil, the GAP is 0.3 to 0.8 kg ai/ha with a 28 day PHI and 1–3 applications.

The Meeting was informed that in India, as cotton plants do not mature simultaneously, harvest usually occurs over three separate picks, with the majority of cotton collected from first two

with an average interval of 10 days between these picks. The raw cotton from, the different picks, is generally pooled prior to sale. Following sale the raw cotton is ginned where the separation of lint and seed occurs. As a consequence the Meeting considered the supervised trials reported from India as representing local practice for the use of triazophos in cotton. In trials from India the cotton samples from two picks (at 21–23 days and 31–33 days after the last application) were pooled and processed by ginning to separate the lint and seeds. Cotton seed oil was then extracted from cotton seeds using n-hexane in soxhlet extractor, the solvent was removed by rotary evaporation with the resultant oil used for analysis.

Residues of triazophos measured in nine trials conducted according to the GAP in India were 0.020, 0.021 (2), 0.023, 0.028, 0.042, 0.054, 0.059 and 0.060 mg/kg in cotton seed and 0.042, 0.044, 0.085, 0.088, 0.13, 0.17, 0.26, 0.31 and 0.78 mg/kg in cotton seed oil.

From one trial matching GAP in Brazil the residue of triazophos in cotton seed was 0.03 mg/kg; residues in cotton seed oil were not determined. Residues from the trial conducted at double rate reached a maximum of 0.2 mg/kg in cotton seed.

Based on the 10 trials with GAP in India and Brazil, residues were 0.020, 0.021 (2), 0.023, 0.028, 0.03, 0.042, 0.054, 0.059 and 0.060 mg/kg in cotton seed and 0.042, 0.044, 0.085, 0.088, 0.13, 0.17, 0.26, 0.31 and 0.78 mg/kg in cotton seed oil.

The Meeting estimated an STMR of 0.029 mg/kg for triazophos in cotton seed and 0.13 mg/kg in cotton seed oil, and an HR of 0.060 mg/kg for triazophos in cotton seed and 0.78 mg/kg in cotton seed oil. The Meeting recommended a maximum residue level of 0.2 mg/kg in cotton seed and 1 mg/kg in cotton seed oil (crude) for triazophos.

The Meeting also recommended the withdrawal of the current MRL of 0.1 mg/kg for triazophos in cotton seed.

Soya bean

In six field trials conducted in Thailand during 1992 to 2006, 2 to 4 sprays of triazophos were applied at 0.1 kg ai/hL. The GAP in Thailand is 0.1 kg ai/hL with a 14 day PHI. Residues of triazophos in whole pod including immature seeds at 14–17 days after the last application were 0.05, 0.17, 0.31, 0.43, 0.52, and 0.60 mg/kg.

The Meeting recommended a maximum residue level of 1 mg/kg for triazophos in soya beans (immature seeds with the pod). The Meeting also estimated an STMR of 0.37 mg/kg and an HR of 0.60 mg/kg.

The Meeting recommended withdrawal of the previous recommendation of 0.05 mg/kg for triazophos in soya bean (dry).

Other commodities

No data on GAP and residues for triazophos was provided on broad bean (shelled), Brussels sprouts, cabbage (head), carrot, cauliflower, cereal grains, coffee beans, common bean, onion (bulb), pea, pome fruit, potato, strawberry and sugar beet. The Meeting recommended withdrawal of the previous recommendations made for these commodities.

Fate of residues during processing

Information regarding the magnitude of triazophos residues in different processed commodities of cotton was provided to the Meeting.

In three field trials conducted in the USA in cotton, residues were found in the processed non oily matrices and in the processed oil. No processing factors could be determined as residue concentrations in unprocessed cotton seed were not reported.

Residues in animal commodities

The Meeting received a feeding study on lactating Holstein cows. The dosing regime involved a 2-day pre-conditioning phase, one week prior to the dosing period, at a dose level of 100 mg triazophos per cow. During the following period of 7 days, one cow was dosed with 50 mg triazophos (2.38 ppm in the feed) and the second cow with 100 mg (4.76 ppm in the feed), the third cow received untreated feed. Neither the pre-conditioning at 100 mg per cow and day nor the dosing of 50 and 100 mg per cow and day resulted in any residues above the LOQ of 0.05 mg/kg for milk and 0.01 mg/kg for muscle, fat, kidney and liver. The Meeting noted that because of the lack of an appropriate livestock metabolism study, a residue definition for animal products could not be determined and therefore the Meeting could not make use of the results of the feeding study.

The Meeting agreed to withdraw the previous recommendations for triazophos of 0.01 mg/kg in cattle meat and cattle milk.

DIETARY RISK ASSESSMENT

Long-term intake

The evaluation of triazophos has resulted in recommendations for MRLs and STMR values for raw and processed commodities. Consumption data were available for 2 food commodities and were used in the dietary intake calculations. The results are shown in Annex 3.

The IEDIs for the 13 GEMS/Food regional diets, based on estimated STMRs were in the range 0–20% of the maximum ADI of 0.001 mg/kg bw (Annex 3). The Meeting concluded that the long-term intake of residues of triazophos from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The IESTI for triazophos was calculated for the food commodities for which maximum residue levels and HRs were estimated and for which consumption data were available. The results are shown in Annex 4.

The IESTI calculated for cotton seed oil for the general population and children were 2% and 5% of the ARfD (0.001 mg/kg bw), respectively. The IESTI calculated for soya bean (immature seeds with the pod) for the general population and children were 140% and 230% of the ARfD, respectively (Annex 4). The Meeting concluded that the short-term intake of residues of triazophos from the consumption of cotton seed oil is unlikely to present a public health concern. The information provided to the JMPR precludes an estimate that the dietary intake would be below the ARfD for consumption for soya bean (immature seeds with pod) by the general population and children.

The Meeting noted that the pod is not normally consumed and that no residue data relating to residues in the edible portion of soya bean pods or alternative GAP were submitted for soya bean (immature seeds with pod).

5.24 ZOXAMIDE (227)

TOXICOLOGY

Zoxamide is the ISO approved name for (*RS*)-3,5-dichloro-*N*-(3-chloro-1-ethyl-1-methyl-2-oxopropyl)-4-methylbenzamide (CAS; CAS No. 156052-68-5). Zoxamide is a chlorinated benzamide fungicide acting against late blight (*Phytophthora infestans)* and powdery mildew (*Plasmopara viticola)*. The mechanism of fungicidal action involves disruption of microtubule formation by binding to β-tubulin.

Zoxamide has not been evaluated previously by the JMPR and was reviewed at the present Meeting at the request of the CCPR.

All the pivotal studies met the basic requirements of the relevant OECD or national test guideline and contained certificates of compliance with GLP.

Biochemical aspects

In rats given zoxamide, approximately 60% of a dose of 10 mg/kg bw was absorbed, with peak plasma concentrations of radioactivity occurring at 8 h after dosing. Zoxamide was extensively distributed among organs and tissues with highest concentrations reported in the liver. Excretion was primarily in the faeces, via the bile. The overall elimination half-life was 13–14 h. At 1000 mg/kg bw, there was some evidence of saturation of absorption, with C_{max} and AUC values being approximately 40–50 times those at 10 mg/kg bw, but with a similar elimination half-life. Females excreted approximately twice as much radiolabel in the urine as males. Very little radioactivity remained in tissues (< 0.2% of the administered dose) or carcass (< 2% of the administered dose) at 5 days after dosing. Pre-treatment of animals with diets containing zoxamide for 2 weeks or with five daily gavage doses of radiolabelled zoxamide did not significantly alter the absorption or distribution of radiolabel compared with that in untreated animals.

The metabolism of zoxamide was extensive, involving a variety of pathways including hydrolysis, glutathione-mediated reactions, and reductive dehalogenation, secondary oxidation on both the aromatic methyl and the aliphatic side-chain, limited deamidation; and terminal glucuronic acid and amino-acid conjugation. Thirty-two separate metabolites were identified; no single metabolite accounted for more than 10% of the administered dose. After repeated doses, there was an indication of an increase in glutathione-mediated metabolism.

Toxicological data

Zoxamide was of low acute toxicity when administered orally (LD_{50} > 5000 mg/kg bw), dermally (LD_{50} > 2000 mg/kg bw) or after a 4-h inhalation exposure (LC_{50} > 5.3 mg/L). Zoxamide is not a skin irritant, but is a slight, transient eye irritant. Zoxamide produced delayed contact hypersensitivity in guinea-pigs in the maximization and Buehler tests.

In repeat-dose studies, the main effects of zoxamide were reduced body-weight gain and liver hypertrophy. The reductions in body-weight gain were not consistent across studies. Investigative work performed as part of the study of reproductive toxicity indicated there might be palatability problems with diet containing zoxamide. However, food consumption was not reduced consistently in studies in which reduced body-weight gain was reported. Liver hypertrophy was not associated with any histopathological or clinical chemistry changes that indicated damage to liver cells. Therefore, in line with the guidance developed by the 2006 JMPR, increased liver weight and hepatocyte hypertrophy were considered to be adaptive rather than adverse effects of exposure to zoxamide.

In a 90-day study of toxicity in mice, the NOAEL was 2500 ppm (equal to 574 mg/kg bw per day) on the basis of reduced body-weight gains in females at 7000 ppm (equal to 1606 mg/kg bw per day). Increases in relative liver weights (by approximately 10%) were not associated with any pathological or clinical chemistry changes and are not considered to be adverse. In a 90-day study of toxicity and neurotoxicity in rats, the NOAEL was 20 000 ppm (equal to 1509 mg/kg bw per day), the highest dose tested.

In a 28-day study of toxicity in dogs, the NOAEL was 30 000 ppm, equal to 1045 mg/kg bw per day, the highest dose tested. Soft stools were present at an increased incidence at doses of 5000 ppm, equal to 175 mg/kg bw per day, and above, but as this finding was not seen consistently in other studies in dogs given similar doses and the same formulated diet, this finding is not considered to be an adverse effect of treatment. In the 90-day study of toxicity in dogs, the NOAEL was 7500 ppm, equal to 281 mg/kg bw per day, on the basis of reductions in body-weight gain, serum albumin concentrations and erythrocyte counts in both sexes at 30 000 ppm, equal to 1055 mg/kg bw per day. Increases in liver weights (by approximately 25%) in females at 7500 ppm were not associated with any histopathological or clinical chemistry changes and were not considered to be adverse. In the 1-year study of toxicity in dogs, reduced body-weight gain (45%) was present from the beginning of the

study in females at 7500 ppm, equal to 255 mg/kg bw per day, and a deficit in body-weight gain (20%) was still present at the end of the study. Males receiving zoxamide at 7500 ppm also had reduced body-weight gain during the early stages of the study, but these animals had terminal body weights that were higher than those of the controls. Although food consumption was reduced transiently, there was no clear link between body weights of individual animals and food consumption. At the highest dose of 30 000 ppm, there were marked effects on body weight and food consumption, with females taking up to 7 weeks to regain their pre-test body weight. Reduced concentrations of serum albumin, and increases in liver and thyroid weights and serum alkaline phosphatase activities were also seen in both sexes at 30 000 ppm. The NOAEL in the 1-year study was 1500 ppm, equal to 48 mg/kg bw per day.

In the 90-day and 1-year studies in dogs, cases of canine juvenile polyarteritis syndrome (CJPS) were seen in the groups receiving zoxamide, but not in the controls. CJPS is reported to be specific to beagle dogs, occurring spontaneously but with unknown aetiology. A genetic link has been postulated, which might explain the occurrence in the 90-day and 1-year studies, which were started at the same time and used animals from the same supplier. Therefore, CJPS was not considered to be related to exposure to zoxamide.

In a 28-day study of dermal toxicity in rats, zoxamide produced significant local effects at doses of ≥ 107 mg/kg bw per day. Findings of systemic toxicity were most likely to be secondary to the local effects and the NOAEL for systemic effects was 714 mg/kg bw per day.

Negative results were obtained in assays for gene mutation in vitro and in assays for micronucleus formation in bone marrow of rats and mice in vivo. Zoxamide was found to induce polyploidy in an assay for chromosomal aberration in Chinese hamster ovary cells in vitro. These findings are consistent with the mechanism of fungicidal action of zoxamide, involving binding to the β-subunit of tubulin. Zoxamide also inhibits microtubule assembly in mouse lymphoma cells (IC_{50}, 23.5 μmol/L). The induction of polyploidy after inhibition of tubulin polymerization and disruption of microtubule formation has been investigated for other compounds and is considered to be a threshold-mediated effect. The assay for micronucleus formation in rats included kinetochore staining and produced negative results for micronuclei and chromosomal damage. A supplementary kinetic study in mice demonstrated that there was exposure of the bone marrow after administration of zoxamide.

The Meeting concluded that zoxamide was unlikely to pose a genotoxic risk to humans at levels typical of dietary exposures.

In long-term studies of toxicity in mice and rats, zoxamide exhibited no general toxicity and was not carcinogenic in either species. Increased liver weights (approximately 20%) in female rats killed after a 1-year exposure to zoxamide at a dietary concentration of ≥ 5000 ppm were not considered to be adverse as there were no associated histopathological or clinical chemistry findings at any time during the study. An apparent increase in thyroid C-cell lesions in male rats at the highest dose was not statistically significant, did not exhibit a dose–response relationship, was not reproduced in females and was within the range for historical controls. The NOAEL in mice was 7000 ppm, equal to 1021 mg/kg bw per day, and the NOAEL in rats was 20 000 ppm, equal to 1058 mg/kg bw per day, both values being based on the absence of treatment-related toxicity at the highest doses tested.

In view of the absence of carcinogenic potential in rodents and the lack of genotoxicity in vivo, the Meeting concluded that zoxamide was unlikely to pose a carcinogenic risk to humans.

The reproductive toxicity of zoxamide has been investigated in a two-generation study in rats and studies of developmental toxicity in rats and rabbits. In the study of reproductive toxicity in rats, the NOAEL for effects on fertility, parental toxicity and pup development was 20 000 ppm, equal to 1474 mg/kg bw per day. Reductions in pup body-weight gain and spleen weights and reduced extramedullary haematopoiesis in the spleen were seen in F_{1a} F_{1b} and F_{2a} offspring, but these effects appeared to be related to palatability as they were not evident in the F_{2b} generation, when pups and dams received equivalent exposures of zoxamide by gavage, rather than from the diet, from postnatal days 14 to 21. Increased relative liver weight was noted at doses of ≥ 5000 ppm in males and females, and in absolute liver weight only in males at 20 000 ppm. The changes in liver weight were not

associated with any histopathological or clinical chemistry change and were not considered to be adverse.

There was no evidence of toxicity in the studies of prenatal developmental toxicity in rats or rabbits. The NOAEL in both studies was 1000 mg/kg bw per day on the basis of absence of toxicity to dams or foetuses at the highest dose tested. Zoxamide was not teratogenic in rats or rabbits.

Zoxamide was not neurotoxic in a study of acute neurotoxicity at doses of up to 2000 mg/kg bw. No adverse effects were seen during neurological and behavioural examinations performed during routine repeat-dose studies with zoxamide.

Studies on two plant metabolites of zoxamide, [RH-141,452 (3,5-dichloro-4-hydroxymethyl benzoic acid) RH-141,455 (3,5-dichloro-1,4-benzene-dicarboxylic acid)] formed to a limited extent in rats, showed them to be rapidly absorbed and rapidly excreted, essentially unchanged; to have low acute oral toxicities to mice (LD_{50}s, > 5000 mg/kg bw), and to be negative in assays for gene mutation with strains of *Salmonella typhimurium.*

There are two reports of mild adverse effects following exposure to a diluted formulation containing zoxamide and mancozeb. In one case there was a report of skin irritation, in the other "flu-like" symptoms were reported. It is considered to be unlikely that these effects are related directly to exposure to zoxamide.

Toxicological evaluation

An ADI of 0–0.5 mg/kg bw was established for zoxamide based on the NOAEL of 48 mg/kg bw per day in the 1-year study in dogs, on the basis of reduced body-weight gain in females at 255 mg/kg bw per day.

An ARfD was considered to be unnecessary for zoxamide as it is of low acute toxicity did not produce developmental effects and did not produce any other significant effects following acute exposures.

A toxicological monograph was produced.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Mouse	Two-year studies of toxicity and carcinogenicity[a]	Toxicity	7000 ppm, equal to 1021 mg/kg bw per day[c]	—
		Carcinogenicity	7000 ppm, equal to 1021 mg/kg bw per day[c]	—
Rat	Two-year studies of toxicity and carcinogenicity [a]	Toxicity	20 000 ppm, equal to 1058 mg/kg bw per day[c]	—
		Carcinogenicity	20 000 ppm, equal to 1058 mg/kg bw per day[c]	—
	Multigeneration study of reproductive toxicity[a]	Reproductive toxicity	30 000 ppm, equal to 1474 mg/kg bw per day[c]	—
		Parental toxicity	30 000 ppm, equal to 1474 mg/kg bw per day[c]	—

		Offspring toxicity	30 000 ppm, equal to 1474 mg/kg bw per day[c]	—
	Developmental toxicity[b]	Maternal toxicity	1000 mg/kg bw per day[c]	—
		Embryo/fetotoxicity	1000 mg/kg bw per day[c]	—
	Acute neurotoxicity[b]		2000 mg/kg bw per day[c]	—
Rabbit	Developmental toxicity[a]	Maternal toxicity	1000 mg/kg bw per day[c]	—
		Embryo/fetotoxicity	1000 mg/kg bw per day[c]	—
Dog	One-year study of toxicity[a]	Reduced body-weight gain	1500 ppm, equal to 48 mg/kg bw per day	7500 ppm, equal to 255 mg/kg bw per day

[a] Dietary administration.
[b] Gavage administration.
[c] Highest dose tested.

Estimate of acceptable daily intake for humans

0–0.5 mg/kg bw

Estimate of acute reference dose

Unnecessary

Studies that would be useful for the continued evaluation of the compound

Results from epidemiological, occupational health and other such observational studies of human exposure

Critical end-points for setting guidance values for exposure to zoxamide

Absorption, distribution, excretion and metabolism in mammals	
Rate and extent of oral absorption	Moderate (C_{max}, 8h); approximately 60% absorbed at 10 mg/kg bw
Dermal absorption	Approximately 1% from concentrate; 6% from dilution
Distribution	Extensive. Highest levels in liver.
Potential for accumulation	Low
Rate and extent of excretion	> 85% in 48 h. Urine (approximately 10–20%); bile (approximately 45%); faeces (approximately 50–80%).
Metabolism in animals	Extensive. Primarily via hydrolysis, dehalogenation, oxidation and conjugation.
Toxicologically significant compounds in animals, plants and the environment	Zoxamide.
Acute toxicity	
Rat, LD_{50}, oral	> 5000 mg/kg bw
Rat, LD_{50}, dermal	> 2000 mg/kg bw
Rat, LC_{50}, inhalation	> 5.3 mg/L
Rabbit, skin irritation	Not irritating
Rabbit, eye irritation	Slight transient irritant

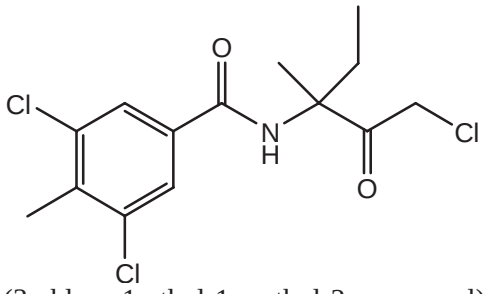
Guinea-pig, skin sensitization (test method used)	A skin sensitizer (Buehler; Magnusson & Kligman)
Short-term studies of toxicity	
Target/critical effect	Body-weight gain
Lowest relevant oral NOAEL	1500 ppm (48 mg/kg bw per day) in a 1-year study in dogs
Lowest relevant dermal NOAEL	< 107 mg/kg bw for local effects; 714 mg/kg bw per day for systemic effects.
Lowest relevant inhalation NOAEC	No data (not required)
Genotoxicity	
	Not genotoxic in vivo
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	None.
Lowest relevant NOAEL	7000 ppm (1021mg/kg bw per day) in mice (highest dose tested)
Carcinogenicity	Not carcinogenic
Reproductive toxicity	
Reproduction target/critical effect	None
Lowest relevant reproductive NOAEL	20 000 ppm (1047 mg/kg bw per day) in rats (highest dose tested)
Developmental target/critical effect	None
Lowest relevant developmental NOAEL	1000 mg/kg bw per day in rats and rabbits (highest dose tested)
Neurotoxicity/delayed neurotoxicity	
	No indications of neurotoxicity in studies of acute toxicity or repeat-doses
Acute neurotoxicity	NOAEL was 2000 mg/kg bw in rats (highest dose tested)
Other toxicological studies	
	RH-141,452 Rapid excretion essentially unmetabolized. Oral LD_{50} in mice > 5000 mg/kg bw Negative in an Ames test. RH-141,455 Rapid excretion essentially unmetabolized. Oral LD_{50} in mice > 5000 mg/kg bw Negative in an Ames test
Medical data	
	Two reports (one case of irritation & one of flu-like symptoms) following exposure to a diluted formulation of mancozeb/zoxamide. Unlikely to be directly related to zoxamide.

Summary

	Value	**Study**	**Safety factor**
ADI	0–0.5 mg/kg bw	Dog, 1-year study	100
ARfD	Unnecessary	—	—

RESIDUE AND ANALYTICAL ASPECTS

Zoxamide, a benzamide fungicide, was identified as a priority new compound at the 38th Session of the CCPR (ALINORM 06/29/24) for evaluation by the 2007 JMPR. The Meeting received information on physical and chemical properties, animal and plant metabolism, environmental fate, analytical methods, storage stability, use patterns, supervised trials and processing.



(*RS*)-3,5-dichloro-*N*-(3-chloro-1-ethyl-1-methyl-2-oxopropyl)-4-methylbenzamide

In this appraisal, the following abbreviated names were used for metabolites.

RH-127450	3,5-dichloro-*N*-(1-ethyl-1-methyl-2-oxopropyl)-4-methylbenzamide
RH-129151	2-(3,5-dichloro-4-methylphenyl)-4-ethyl-4-methyl-4H-1,3-oxazin-5(6H)-one
RH-139432	3,5-dichloro-4-methylbenzamide
RH-141288	3,5-dichloro-*N*-(3-hydroxy-1-ethyl-1-methyl--2-oxopropyl)-4-methylbenzamide
RH-1452	3,5-dichloro-4-hydroxymethylbenzoic acid
RH-1455	3,5-dichloro-1,4-benzene-dicarboxylic acid
RH-149736	3,5-dichloro-4-hydroxymethylbenzamide
RH-149737	4-carboxy-3,5-dichlorobenzamide
RH-150721	(3-amino-3-methyl-2-oxo)pentyl-(3,5-dichloro-4-methyl)benzoate
RH-163353	3,5-dichloro-*N*-(2-carboxy-1-ethyl-1-methyl-2-oxoethyl)-4-methylbenzamide
RH-24549	3,5-dichloro-4-methylbenzoic acid

Animal metabolism

The Meeting received information on the fate of orally-dosed zoxamide in a lactating goat.

When [U-^{14}C-phenyl]zoxamide was administered orally at a dose equivalent to a dietary concentration of 60.7 ppm to a lactating goat once a day for 7 consecutive days, 95% of the recovered radioactivity (77.5% of the administered dose) was found in urine (37.1%) and faeces (36.1%). None of individual tissues or cumulative milk sample on day 7 contained more than 3% of the administered dose. On day 4 the radioactive residues in milk was the highest at 0.24 mg/kg in parent equivalents.

Unextracted radioactivity was less than 10% of total radioactive residues (TRR) (< 0.05 mg/kg) in all samples except liver (12%).

No parent compound was found in any of tissues or milk sample. A number of metabolites were detected in milk and tissues. In fat, RH-127450 was found at 0.13 mg/kg in parent equivalent. However, as the dose administered in the study was about 14 times the highest concentration found in

any commodity after treatment of the respective crop in accordance with GAP, significant residue concentrations are unlikely to occur in milk or any tissues in practice.

Zoxamide was extensively metabolized and readily eliminated following oral administration to a lactating goat. Once administered orally, zoxamide underwent dechlorination, then oxidation of either position 4 of the benzene ring or the end of the side-chain and further hydrolysis.

The metabolism of zoxamide in the lactating goat was qualitatively similar to that described in the toxicology section (see page 282).

Plant metabolism

The Meeting received information on the fate of zoxamide after foliar application of [U-^{14}C-phenyl]zoxamide to grapes, cucumber, tomato and potato.

When grape vines were sprayed at a rate of 1.9 kg ai/ha three times at 30 day intervals, grapes harvested 1 day after the last application contained 0.74 mg/kg of radioactive residues. The parent compound was the major residue at 0.43 mg/kg (58% of TRR). RH-129151, RH-139432, RH-141288, RH-149736, RH-149737 and RH-150721 were identified but all were less than 0.021 mg/kg in parent equivalents (≤ 2.8% of TRR).

Cucumber plants were sprayed three times at the rate of 1.3 kg ai/ha at a 7 day intervals and foliage and fruit samples were harvested 1 day after the last application. While an average radioactive residue in foliage was 108 mg/kg in parent equivalent, that in fruits was 1.5 mg/kg, which indicates that translocation of zoxamide, was not significant one day after the final application. Extraction of foliage and fruit samples with acetonitrile-water mixture solubilised 100% of the total radioactivity and there were no volatile or unextracted residues. Zoxamide accounted for 87% of TRR in fruits and 89% in foliage indicating that the parent is predominant. Minor metabolites were identified in fruits and foliage. Among them, RH-150721 and RH-157450 were present at the highest concentrations but still less than 0.1 mg/kg (< 5% of TRR).

Tomato plants received three foliar applications at 0.86 mg/kg with 18 day intervals and tomato fruits were collected 1 day after the last application. The TRR was 0.29 mg/kg in green tomato and 0.50 mg/kg in red tomato. The parent was the major component of residues amounting to 0.14 mg/kg (48% of TRR) in green tomato and 0.22 mg/kg (44% of TRR) in red tomato. Minor amounts of metabolites were identified but none exceeded 3% of TRR. RH-1452 and RH-141288 were identified in two different fractions but their actual concentrations were not determined.

Three foliar applications were made at the rate of 0.9 kg ai/ha on potato plants with the first application at 39 days after planting, and the second and third made at intervals of 21 and 17 days respectively. Mature potato tubers were harvested 14 days after the last application. The TRR was 0.18 mg/kg parent equivalents. Unlike other plants tested, the parent compound was not found in the harvested commodity, i.e., the potato tuber. The metabolites RH-1455 and RH-1452 were found at 0.069 and 0.037 mg/kg accounting for 39% and 21% of the TRR, respectively.

The nature of minor metabolites suggests that zoxamide, when applied to plants, underwent dechlorination and hydrolysis or oxidation. Zoxamide was the major residue in grape, cucumber and tomato when harvested one day after the last application. However, the parent compound was not found in potato sampled 14 days after the last application.

Environmental fate in soil

The Meeting reviewed information on aerobic soil metabolism and rotational crop study as zoxamide was intended for protection of potatoes.

Aerobic soil metabolism studies were conducted using [U-^{14}C-phenyl]zoxamide applied to various soils which were then incubated under aerobic conditions at 20 or 25 °C. Under aerobic conditions, zoxamide applied to soil was rapidly degraded. After 120–122 days, only small amounts (0.6–10%) of applied zoxamide remained as the parent. Carbon dioxide was steadily evolved from all soils and accounted for 34–58% of the dose applied after 120–122 days. RH-127450, RH-129151,

RH-24549, RH-139432 and RH-163353 were formed and then degraded during the study periods. Unextracted radioactivity, 0.4-3.3% of the applied dose (3.3% in silt loam dosed at 1.5 mg/kg; for other soils tested 0.4–0.8%) on day 0, increased steadily to reach 24–38% of the applied dose on day 120–122. Several other degradates were observed at very low concentrations. These results indicate that none of zoxamide or its identified metabolites are persistent in soil.

Residues in succeeding crops

In an outdoor confined rotation study, mustard, radish, turnip, sorghum and soya bean were planted at 30, 137, 210, 365 days following the last of four applications of [^{14}C-phenyl]zoxamide. Zoxamide was applied to bare soil between mid April and early June (18 day intervals) at a rate of 0.5 kg ai/ha. Crops were harvested at an intermediate stage and when mature.

TRRs were very low for all samples at all plant back intervals. In general, the amount of extractable residues was low in all the crop samples. Between 7% and 40% of the TRR was recovered in the polar MeOH/H_2O fractions for all the crops grown on treated soil. About 2 to 36% of the TRR was found in the organic extracts ($CHCl_3$, CH_3CN and hexane) of all the crops. The concentrations in these samples did not exceed 0.023 mg/kg. The values of extracts for all the crop samples showed a significant fraction of unextracted residues: generally 49% or greater.

Concentrations of RH-1452 and one other metabolite were generally below 0.01 mg/kg. The second metabolite was not fully identified. Other metabolites were detected at lower concentrations in some crops.

Zoxamide residues are not expected to occur in succeeding crops.

Methods of analysis

Analytical methods for determination of residues of zoxamide were developed for a wide range of matrices including cucurbits, grapes, tomato, potato and their processed commodities and byproducts.

In most of the methods for determination of zoxamide only, zoxamide was extracted with organic solvent or a mixture of organic solvent and aqueous solution specific to the matrix; cleaned up with liquid-liquid partition followed by solid phase extraction using carbon, alumina, Florisil and silica singly or in combination; and analysed by gas chromatography using electron capture detection (GC/ECD) for quantitation and mass selective detection (GC/MSD) for confirmation. For detection, ELCD or NPD may also be used. These methods were validated in independent laboratories. Most of the methods were suitable as enforcement methods with the limit of quantification at 0.01 mg/kg. One method for potato and its products has an LOQ of 0.02 mg/kg.

The existing multi-residue enforcement methods, one of FDA screen methods and DFG S19 were also tested to be suitable for analysing zoxamide.

The methods for potato and its processed commodities determine zoxamide and two metabolites, RH-1452 and RH-1455. While zoxamide is extracted in the organic phase in liquid-liquid partition, these metabolites were extracted in the aqueous phase. After methylation of these metabolites using diazomethane, and further clean-up, they were analysed using GC/ECD or GC/MSD. The LOQ was 0.02 mg/kg.

Stability of residues in stored analytical samples

Stability of zoxamide (0.1–2 mg/kg) in homogenized samples of grapes (433 days), cucumbers (868 days), tomatoes (810 days), and potatoes (708 days); grape juice (858 days); dried grapes (789 days); wine (8 months); tomato juice (832 days); tomato paste (237 days); and tomato puree (228 days) stored in deep freezer at a temperature below -10 ˚C was investigated.

No decrease of zoxamide was observed in all samples of cucumbers, tomatoes and its processed products and potatoes during the test periods.

In the case of grapes and its products, in particular grape juice, relatively large fluctuations were observed in the percentage of remaining zoxamide during the test period. However, the Meeting

concluded that zoxamide was sufficiently stable for 14 months in grapes, 28 months in grape juice, 26 months in dried grapes and 8 months in wine.

RH-1452 and RH-1455 were shown to be stable for 29 months of storage while frozen.

Definition of the residue

In grapes, zoxamide represented 58% of the TRR with no metabolite exceeding 5% of the TRR. Also in cucumber and tomato, zoxamide is the major residue component: 87% of TRR in cucumber, 48% of TRR in green tomatoes and 44% of TRR in red tomatoes. No metabolite was found to be more than 10% of the TRR in all cucumber and tomato samples. Most metabolite residues were present at less than 5% of the total residues. These indicate that the residue of concern in grapes, cucurbit and tomato be defined as parent although samples analysed were taken only one day after the last application.

In potato, however, no parent zoxamide was detected. RH-1452 and RH-1455, comprising 21% and 39% of the total residue, respectively, were the major components of the residue. Another 16% of the residue was identified as glucose and/or other sugars. No other metabolites were present at or higher than 10% of TRR. In supervised field trials in Northern and Southern Europe, the United States, Canada and Mexico, samples were analysed for zoxamide, RH-1452 and RH-1455. In all trials, residues of parent were below the LOQ and concentrations of the metabolites were also below the LOQ in all but two trials where zoxamide was found at 0.02 mg/kg.

Methods of analysis are available for determination of zoxamide in grapes, cucurbits, tomatoes and potatoes and their processed products. A method is available also for determination of RH-1452 and RH-1455 in potatoes.

The current Meeting concluded that only zoxamide is toxicologically significant.

In the lactating goat study, the main components of residues were RH-127450 in milk and fat, glucuronic acid conjugates of 4-hydroxymethyl-RH-141288 in liver, with the highest concentration of 0.13 mg/kg parent equivalents of RH-12740 in liver. However, as the administered dose was 14 times higher than the highest residue concentration found in the reported trials, no residue was expected to be found in animals given feed with incurred residues of zoxamide. No method of analysis is currently available for these metabolites. For these reasons, the Meeting concluded that it was not in a position to recommend a residue definition for animal commodities.

In the lactating goat study, the concentration of radioactive residues expressed in parent equivalent in fat was about 4 times that in muscle but about one half of that in kidney or liver. Therefore, the Meeting considered residues not fat-soluble.

In countries where there are MRLs for zoxamide, the residue definition was mostly “zoxamide” except in the USA where it is zoxamide including its metabolites RH-1452 and RH-1455 for potato and its products.

The Meeting recommended the following residue definition for zoxamide in plant commodities.

For plants: Definition of the residue (for compliance with the MRL and for estimation of dietary intake): zoxamide

Results of supervised residue trials on crops

The Meeting received supervised trial data for zoxamide uses on grapes, cucurbits, tomato and potato.

Grapes

Numerous residue trials were conducted on grapes in Brazil, Canada, Germany, France, Greece, Italy, Republic of Korea, Spain and the USA.

The trials conducted in Germany used six applications rather than four as on the label. The Meeting decided to use the results of these trials for MRL estimation as the last applications contribute most to the residue concentration at harvest. In 12 German trials in accordance with German GAP

(maximum rate of 0.24 kg ai/ha in 800-1600 L/ha, 4 applications, with a PHI of 56 days) (except application number), zoxamide residues in rank order were: 0.34, 0.38, 0.39, 0.41, 0.41, 0.45, 0.49, 0.55, 0.59, 0.60, 0.66 and 0.72 mg/kg.

The trials conducted in France used ten applications rather than three on the label. The Meeting decided to use the results of these trials for MRL estimation as it is the last applications that contribute the most to the residue concentration at the harvest. In 21 Northern French trials in accordance with French GAP (0.12 kg ai/ha, 3 applications, PHI 28 days)(except application number), zoxamide residues in rank order were: 0.09, 0.17, 0.19, 0.19, 0.33, 0.35, 0.45, 0.47, 0.48, 0.50, 0.50, 0.51, 0.55, 0.56, 0.67, 0.77, 0.77, 0.81, 0.88, 1.31, 1.55 mg/kg. In 15 Southern French trials conducted in accordance with French GAP, zoxamide residues in rank order were: 0.21, 0.21, 0.33, 0.42, 0.42, 0.46, 0.49, 0.54, 0.58, 0.61, 0.63, 1.07, 1.11, 1.53 and 2.84 mg/kg. Since the residue populations in the Northern and Southern France are similar and there is a uniform GAP for the whole of France, the Meeting considered it appropriate to combine the results from 36 trials in France: 0.09, 0.17, 0.19, 0.19, 0.21, 0.21, 0.33, 0.33, 0.35, 0.42, 0.42, 0.45, 0.46, 0.47, 0.48, 0.49, 0.50, 0.50, 0.51, 0.54, 0.55, 0.56, 0.58, 0.61, 0.63, 0.67, 0.77, 0.77, 0.81, 0.88, 1.07, 1.11, 1.31, 1.53, 1.55 and 2.84 mg/kg.

In 15 Italian trials conducted in accordance with Italian GAP (maximum rate of 0.17 kg ai/ha, 0.017 kg ai/hL, 5 applications, PHI 28 days), zoxamide residues in rank order were: 0.24, 0.28, 0.29, 0.30, 0.33, 0.48, 0.48, 0.54, 0.59, 0.65, 0.66, 0.81, 0.82, 1.37 and 1.56 mg/kg.

In six Spanish trials conducted in accordance with Italian GAP, zoxamide residues in rank order were: 0.36, 0.53, 1.17, 1.21, 1.42 and 1.92 mg/kg.

In four Greek trials conducted in accordance with Italian GAP, zoxamide residues in rank order were: 0.27, 0.32, 0.34 and 0.64 mg/kg.

Combined residues from Italian, Spanish and Greek trials in accordance with Italian GAP in rank order were: 0.24, 0.27, 0.28, 0.29, 0.30, 0.32, 0.33, 0.34, 0.36, 0.48, 0.48, 0.53, 0.54, 0.59, 0.64, 0.65, 0.66, 0.81, 0.82, 1.17, 1.21, 1.37, 1.42, 1.56 and 1.92 mg/kg.

Six trials were conducted in Canada but none was in accordance with Canadian GAP (0.19 kg ai/ha, 6 applications, PHI 66 days). However, four trials were in accordance with US GAP (maximum rate of 0.22 kg ai/ha, 8 applications, PHI 14 days). Residues in rank order were: 1.12, 1.46, 1.52 and 1.69 mg/kg.

Among numerous US trials, 17 trials were conducted in accordance with US GAP. Zoxamide residues in rank order were: 0.22, 0.31, 0.34, 0.34, 0.42, 0.46, 0.49, 0.52, 0.61, 0.66, 0.83, 0.91, 1.08, 1.18, 1.61, 1.65 and 4.34 mg/kg.

Combined residues from the US and Canadian trials conducted in accordance with US GAP (ranked order, median underlined) were: 0.22, 0.31, 0.34, 0.34, 0.42, 0.46, 0.49, 0.52, 0.61, 0.66, <u>0.83,</u> 0.91, 1.08, 1.12, 1.18, 1.46, 1.52, 1.61, 1.65, 1.69 and 4.34 mg/kg.

In seven Brazilian trials conducted in accordance with Brazilian GAP (maximum rate of 0.13 kg ai/ha, 600–1000 L/ha, PHI 7 days), zoxamide residues in rank order were: 0.07, 0.08, 0.14, 0.14, 0.15, 0.16 and 0.36 mg/kg.

Three trials conducted in the Republic of Korea seemed to be in accordance with Korean GAP (0.01 kg ai/ha, three applications, PHI 7 days). The residues were: 0.05, 0.06 and 0.08 mg/kg.

Among results of these trials, residues from US trials would lead to the highest maximum residue level. Based on the results from US and Canadian trials, the Meeting estimated a maximum residue level and an STMR for zoxamide in grapes of 5 and 0.83 mg/kg respectively.

Fruiting Vegetables, cucurbits

Protected supervised trials were conducted on cucumber in France and Spain and field trials in the Republic of Korea and the USA. Supervised trials were also conducted in the USA for cantaloupe and squash.

Six supervised indoor trials on cucumber in France were in accordance with Polish GAP (maximum rate of 0.15 kg ai/ha, 700–800 L/ha, 3 applications, PHI 4 days) although five applications were made. Residues from these trials in rank order were: 0.01, 0.03, 0.04, 0.06, 0.06 and 0.48 mg/kg. In three Spanish trials conducted in accordance with Polish GAP, zoxamide residues in rank order were: 0.25, 0.44 and 0.45 mg/kg. Combined residues in rank order (median underlined) were: 0.01, 0.03, 0.04, 0.06, 0.06, 0.25, 0.44, 0.45 and 0.48 mg/kg.

Seven outdoor trials were conducted in the USA but only one trial was in accordance with the current US GAP for cucurbits (maximum rate of 0.19 kg ai/ha, 8 applications, PHI 5 days). The residues were: 0.04 mg/kg.

Four trials were conducted in the Republic of Korea on cucumber but none were in accordance with Korean GAP.

Seven trials on cantaloupe and six on summer squash were conducted in the USA but only one each was in accordance with the current US GAP. The residue level in one cantaloupe trial was 0.04 mg/kg and that in one squash trial was 0.09 mg/kg.

On the basis of indoor trials in Europe, the Meeting estimated a maximum residue level and an STMR for zoxamide in cucumber at 1 and 0.06 mg/kg respectively.

Tomato

Protected supervised trials were conducted on tomato in Greece and Spain; and field trials in Brazil, Italy, Spain and the USA.

In 10 Spanish indoor trials conducted in accordance with Italian GAP (maximum rate of 0.17 kg ai/ha, 0.017 kg ai/hL, 5 applications, PHI 3 days), zoxamide residues in rank order were: 0.07, 0.08, 0.09, 0.09, 0.10, 0.12, 0.12, 0.15, 0.24 and 0.29 mg/kg.

In two French indoor trials conducted in accordance with Italian GAP, zoxamide residues in rank order were: 0.28 and 0.31 mg/kg.

In three Greek indoor trials conducted in accordance with Italian GAP, zoxamide residues in rank order were: 0.15, 0.30 and 0.30 mg/kg.

Combined residues from the indoor trials in Spain, France and Greece in accordance with Italian GAP were: 0.07, 0.08, 0.09, 0.09, 0.10, 0.12, 0.12, 0.15, 0.15, 0.24, 0.28, 0.29, 0.30, 0.30 and 0.31 mg/kg.

In 12 Italian outdoor trials conducted in accordance with Italian GAP, zoxamide residues in rank order were: 0.12, 0.13, 0.14, 0.15, 0.16, 0.18, 0.18, 0.20, 0.22, 0.24, 0.24 and 0.30 mg/kg. In five Spanish outdoor trials conducted in accordance with Italian GAP, zoxamide residues in rank order were: 0.03, 0.04, 0.04, 0.05 and 0.05 mg/kg. Combined residues were: 0.03, 0.04, 0.04, 0.05, 0.05, 0.12, 0.13, 0.14, 0.15, 0.16, 0.18, 0.18, 0.20, 0.22, 0.24, 0.24 and 0.30 mg/kg.

Eighteen US outdoor trials were considered to have been conducted in accordance with US GAP (maximum rate of 0.19 kg ai/ha, 8 applications, PHI 5 days) although application number was mostly 10 up to 13 despite the label specification of 8 applications; however the Meeting concluded that the last applications contribute the most to residue concentrations at harvest. Zoxamide residues in ranked order (median underlined) were: 0.07, 0.10, 0.11, 0.12, 0.13, 0.16, 0.18, 0.18, 0.19, 0.20, 0.21, 0.21, 0.22, 0.23, 0.32, 0.38, 0.40 and 1.0 mg/kg.

In five Brazilian outdoor trials conducted in accordance with Brazilian GAP (maximum rate of 0.13 kg ai/ha, applied in 800 L/ha, with a PHI of 7 days), zoxamide residues in rank order were: 0.01, 0.02, 0.02, 0.03 and 0.14 mg/kg.

Among results from the above trials, those from US trials would lead to the highest maximum residue level. Based on the US data, the Meeting estimated a maximum residue level and an STMR for zoxamide in tomato of 2 and 0.195 mg/kg respectively.

Potato

Supervised trials were conducted on potato in Argentina, Brazil, Canada, France, Germany, Greece, Italy, Republic of Korea, Mexico, the Netherlands, Spain, the UK and the USA.

In six trials in Northern France, seven in Germany, one in the Netherlands and 11 from the UK conducted in accordance with GAP in Ireland, the Netherlands and the UK (maximum rate of 0.15 kg ai/ha, 200–600 L/ha, 10 applications, PHI 7 days), zoxamide residues were all < 0.02 mg/kg (25).

In six trials in Southern France, four in Greece, seven in Italy and six in Spain conducted in accordance with Italian GAP (maximum rate of 0.17 kg ai/ha (0.017 kg ai/hL), 5 applications, PHI 7 days), zoxamide residues were all < 0.02 mg/kg (23).

Twelve Canadian trials were considered to have been conducted in accordance with Canadian GAP (0.19 kg ai/ha, 6 applications, PHI 3 days) although 10 applications were made; however the Meeting concluded that the later applications contribute the most to residue concentrations at harvest. The residues were all < 0.02 mg/kg (12). A total of 27 USA trials were considered to be in compliance with US GAP (0.19 kg ai/ha, 6 applications, PHI 3 days) although 10 applications were made. The residues were all below the LOQ (0.02 mg/kg) (4) or LOD (0.006 mg/kg) (22) and hence < 0.02 mg/kg (27). Even with double rate applications, residues were below the LOQ.

Eight trials were conducted in Mexico but samples were taken 13 or 14 days after the last application instead of the PHI of 7 days as specified on the label.

In two Argentine trials, conducted in accordance with Argentine GAP (0.15 kg ai/ha, 400–1000 L/ha, PHI 7 days), zoxamide residues were < 0.05 mg/kg (2).

In six Brazilian trials, conducted in accordance with Brazilian GAP (maximum rate of 0.13 kg ai/ha, 650 L/ha, PHI 7 days), zoxamide residues (ranked order, median underlined) were: < 0.<u>01</u> (4) (two were below the LOD) and 0.02 mg/kg (2).

Six trials were conducted in the Republic of Korea but none were in compliance with Korean GAP.

On the basis of the Brazilian trials and the fact that, other than two Brazilian trials, residues from trials done in accordance with respective GAP were all below the LOQ, the Meeting estimated a maximum residue level and an STMR at 0.02 and 0.02 mg/kg.

Fate of residues during processing

The Meeting received information on processing of grapes to dried grapes, juice, wine and pomace, tomatoes to puree and paste, and potatoes into flakes, chips and peel.

Processing factors were calculated for grapes (dried grapes, juice, wine and pomace), tomato (puree and paste) and potato (peel) and are shown in the Table below. Processing factors could not be calculated for potato flakes or chips because the residue concentrations were below the LOQ in both potatoes and processed products.

Mean processing factors and STMR-P for food and feed.

Commodity	Processing factor	Median or best estimate	STMR-P mg/kg
Grapes			0.83
Unclarified juice	0.10, 0.16	0.13	0.11
Dried grapes	2.2, 3.5	2.9	2.4
Wine	< 0.01, < 0.01, < 0.01, < 0.01, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.03, < 0.03, < 0.04	< 0.02	0.02
Pomace, wet	0.01, 0.02, 0.05, 0.05, 0.13, 0.79, 1.1, 1.5, 3.1	1.3 [1]	1.1
Tomato			0.195
Puree	0.43	0.43	0.08
Paste	0.97	0.97	0.19
Potato			0.02
Peel	> 3.0	3.0	0.06

[1] As the spread of processing factors of wet pomace calculated from trial results is very large, the Meeting decided to take a conservative approach and use four values at the higher end to provide the best estimate of the processing factor.

Dried grapes are expected to contain higher residues than grapes. Multiplying the highest residue concentration found in the supervised trials (4.34 mg/kg) by the processing factor of 2.9, resulted in an estimate of 12.6 mg/kg, the Meeting estimated a maximum residue level at 15 mg/kg.

Residues in animal commodities

Potato wet peel and wet grape pomace may be fed to dairy cattle and beef cattle but not as major feed ingredients. The calculated maximum and mean livestock animal burden was 0.03–1.50 ppm.

In the metabolism study, in which zoxamide equivalent to 60.7 ppm in the diet was orally administered to a lactating goat for 7 consecutive days, no parent compound was found in any tissue or milk. A number of metabolites were present in tissues and milk but mostly below 0.1 mg/kg parent equivalents. Given the low estimated animal burden, about one fortieth of the administered level, no zoxamide or its metabolite is expected to be present at detectable levels in tissues or milk.

The Meeting agreed that no maximum residue level was necessary for commodities derived from mammals.

The livestock dietary burden was also calculated for layers and broilers with potato wet peel and wet grape pomace and were 0–0.73 ppm. No information was available on the fate of zoxamide in poultry. In addition, no method of analysis was submitted for zoxamide or metabolites in commodities derived from poultry.

The Meeting agreed that no maximum residue level could be estimated for commodities of poultry origin.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Dietary Intakes (IEDIs) of zoxamide were calculated for the 13 GEMS/Food cluster diets using STMRs/STMR-Ps estimated by the current Meeting (Annex 3). The ADI is 0–0.5 mg/kg bw and the calculated IEDIs were all 0% of the maximum ADI. The Meeting concluded that the long-term intakes of residues of zoxamide, resulting from the uses considered by the current JMPR, are unlikely to present a public health concern.

Short-term intake

The 2007 JMPR decided that an ARfD is unnecessary. The Meeting therefore concluded that the short-term intake of residues of zoxamide is unlikely to present a public health concern.

6. RECOMMENDATIONS

6.1 Short-term dietary intake assessment

- With regard to the assessment of short-term dietary intake, including the use of HR versus MRL in the IESTI equation, the Meeting reiterated its recommendation from 2006 that FAO and WHO should host a consultation to address the issues identified in the reports of the present Meeting and of the Meeting of the previous year, with the participation of relevant stakeholders.
- The Meeting recommended investigation of the practicalities of using the MRL in IESTI calculations, because allowance would be needed for residues in edible portions, for the risk-assessment residue definition and in situations where no residues are detectable in the edible portion. Furthermore, the issue of whether it is appropriate to use the IESTI equations for evaluating the safety of individual consignments should be further investigated. The discussion should include how to improve communication between JMPR and risk managers and the public on the output of the risk assessment conducted by the Meeting.
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6.2 Toxicological relevance of triazole fungicides and their common metabolites

- The Meeting recommended that a full evaluation of the metabolites of triazole fungicides should be performed and that work be undertaken to identify which triazole fungicides should be considered together in a cumulative risk assessment.

6. FUTURE WORK

The items listed below should be considered by the Meeting in 2009 and 2010. The compounds listed include those recommended as priorities by the CCPR at its 39th and earlier sessions and compounds scheduled for re-evaluation within the CCPR periodic review programme.

Updated calls for data are available at least ten months before each JMPR meeting from the web pages of the Joint Secretariat:

http://www.fao.org/ag/AGP/AGPP/Pesticid/

http://www.who.int/ipcs/food/en/

2009 JMPR

Toxicological evaluations		**Residue evaluations**	
New compounds			
Fluopicolide		Fluopicolide	
Spirodiclofen		Spirodiclofen	
Pyroxsulam		Pyroxsulam	
Flubendiamide		Flubendiamide	
Periodic re-evaluations			
Bifenthrin (178)	2010R	Benalaxyl (155)	2005T
Cadusafos (174)	2010R	Bioresmethrin (093)	2008T
Chlorothalonil (081)	2010R	Buprofezin (173)	2008T
Chlorpyrifos-methyl (090)		Chlorpyrifos-methyl (090)	
Cycloxydim (179)	2010R	Haloxyfop (194)	
		Hexythiazox (176)	2008T
		Procymidone (136)	2007T
Evaluations			
		Acephate (95) – alternative GAP (mandarin, flower head brassicas)	
		Fenbuconazole (197) - re-evaluation of the pome fruits CXL; additional CXLs for almonds, blueberries, citrus, cranberries, plums and prunes	
		Methoxyfenozide (209) – additional MRLs for beans, blueberry, citrus, cucurbits, papaya, pea,	

peanut, root crops,
strawberry, sweet potato
Phorate (112) - acute
intake for potatoes
Prochloraz (142) – acute
intake for mushroom
Spices – additional MRLs

2010 JMPR

Toxicological evaluations		**Residue evaluations**	
New Compounds			
Dicamba		Dicamba	
Meptyldinocap		Meptyldinocap	
Periodic re-evaluations			
Aldicarb (117)	2011R	Amitraz (111)	1998T
Dicofol (026)	2011R	Azinphos methyl (002)	2007T
Dithianon (028)	2011R	Bifenthrin (178)	2009T
Fenbutatin oxide (109)	2011R	Cadusafos (174)	2009T
		Chlorothalonil (081)	2009T
		Cycloxydim (179)	2009T

ANNEX 1: ACCEPTABLE DAILY INTAKES, SHORT-TERM DIETARY INTAKES, ACUTE REFERENCE DOSES, RECOMMENDED MAXIMUM RESIDUE LIMITS AND SUPERVISED TRIALS MEDIAN RESIDUE VALUES RECORDED BY THE 2007 MEETING

The following extracts of the results of the annual Joint FAO/WHO Meeting on Pesticide Residues (JMPR) are provided to make them accessible to interested parties at an early date.

The Meeting evaluated 31 pesticides, of which 6 were new compounds, and 10 were re-evaluated within the Periodic Re-evaluation Programme of the Codex Committee on Pesticide Residues (CCPR). The Meeting established acceptable daily intakes (ADIs) and acute reference doses (ARfDs).

The Meeting estimated maximum residue levels, which it recommended for use as maximum residue limits (MRLs) by the CCPR. It also estimated supervised trials median residue (STMR) and highest residue (HR) levels as a basis for estimation of the dietary intake of residues of the pesticides reviewed. Application of HR levels is explained in the report of the 1999 Meeting (section 2.4). The allocations and estimates are shown in the table.

Pesticides for which the estimated dietary intakes might, on the basis of the available information, exceed their ADIs are marked with footnotes, as explained in detail in the report of the 1999 Meeting (section 2.2). Footnotes are also applied to specific commodities when the available information indicated that the ARfD of a pesticide might be exceeded when the commodity was consumed. It should be noted that these distinctions apply only to new compounds and those re-evaluated within the CCPR Periodic Re-evaluation Programme.

The table includes the Codex reference numbers of the compounds and the Codex classification numbers (CCNs) of the commodities, to facilitate reference to the Codex maximum limits for pesticide residues (*Codex Alimentarius*, Vol. 2B) and other documents and working documents of the Codex Alimentarius Commission. Both compounds and commodities are listed in alphabetical order.

Apart from the abbreviations indicated above, the following qualifications are used in the Table.

* (following name of pesticide)	New compound
** (following name of pesticide)	Compound reviewed within CCPR Periodic Re-evaluation Programme
* (following recommended MRL)	At or about the limit of quantification
HR-P	Highest residue in a processed commodity, in mg/kg, calculated by multiplying the HR in the raw commodity by the processing factor
Po	The recommendation accommodates post-harvest treatment of the commodity.
PoP (following recommendation for processed foods (classes D and E in the Codex classification)	The recommendation accommodates post-harvest treatment of the primary food commodity.
STMR-P	An STMR for a processed commodity calculated by applying the concentration or reduction factor for the process to the STMR calculated for the raw agricultural commodity.
W (in place of a recommended MRL)	The previous recommendation is withdrawn, or withdrawal of the recommended MRL or existing Codex or draft MRL is recommended.

Recommended maximum residue levels, STMR and HR values and allocated ADI and ARfD values

Pesticide (Codex reference number)	**CCN**	**Commodity**	**Recommended MRL mg/kg**		**STMR or STMR-P mg/kg**	**HR or HR-P mg/kg**
			New	Previous		
Aminopyralid (220)*	GC 0640	Barley	0.1	–	*0.01*	
ADI: 0–0.9 mg/kg bw	MO 0105	Edible offal (Mammalian) (1)	0.05	–	*0.01*	
ARfD: unnecessary	PE 0112	Eggs	0.01*	–	*0.01*	
	MO 0098	Kidney of cattle, goats, pigs and sheep	1	–	*0.1*	
	GC 0647	Oats	0.1	–	*0.01*	
	MM 0095	Meat (from mammals other than marine mammals)	0.1	–	*0.01*	
	ML 0106	Milks	0.02	–	*0.01*	
	PM 0110	Poultry meat	0.01*	–	*0.01*	
	PO 0111	Poultry, Edible offal of	0.01*	–	*0.01*	
	GC 0653	Triticale	0.1	–	*0.01*	
	GC 0654	Wheat	0.1	–	*0.01*	
	CM 0654	Wheat bran, unprocessed	0.3	–	*0.024*	
	AS 0081	Straw and fodder (dry) of cereal grains	0.3	–	*0.07*	
	AS 0162	Hay or fodder (dry) of grasses	3	–	*1*	
	AS -	Grass hay	70	–	*21*	
Definition of the residue for compliance with the MRL and for estimation of dietary intake: *aminopyralid and its conjugates that can be hydrolysed, expressed as aminopyralid.*						
(1) Except kidney						
Atrazine						
Group						
ADI*: 0-0.02 mg/kg bw						
Group						
ARfD*: 0.1 mg/kg bw						
Hydroxyatrazine:						
ADI: 0–0.04 mg/kg bw						
ARfD: unnecessary						
*for atrazine, deethyl-atrazine (DEA); deisopropyl-atrazine (DIA) and diaminochlorotriazine (DACT)						
Azinphos methyl (002)						
ADI: 0–0.03 mg/kg bw						
ARfD: 0.1 mg/kg bw						
Beta cyfluthrin (228) *	See Cyfluthrin					
Bifenazate (219)	MM 0095	Meat (from mammals other than marine mammals)	0.05 (fat)	-	0.01 Muscle 0.01 fat	
ADI: 0–0.01 mg/kg bw						
ARfD: unnecessary						
Definition of the residue for compliance with the MRL and for estimation of dietary intake: Sum of bifenazate and bifenazatediazene (diazenecarboxylic acid, 2-(4-methoxy-[1,1'-biphenyl-3-yl] 1-methylethyl ester), expressed as bifenazate. *The residue is fat soluble.*						
Note: Bifenazate is a fat-soluble compound. Previously, the milk MRL would have been marked with an F to indicate a procedure for calculating "MRLs" for processed dairy products. Currently, bifenazate MRLs for milk and milk fat are available to support "MRLs" for processed dairy products.						

Pesticide (Codex reference number)	CCN	Commodity	Recommended MRL mg/kg New	Recommended MRL mg/kg Previous	STMR or STMR-P mg/kg	HR or HR-P mg/kg
Captan (007) ADI: 0–0.1 mg/kg bw ARfD: 0.3 mg/kg bw (for women of child-bearing age)						
Carbaryl (008)	VO 0444	Chilli peppers	0.5	-	0.09	0.25
ADI: 0–0.008 mg/kg bw	HS 0444	Chilli peppers, dried	2	50	0.63	
ARfD: 0.2 mg/kg bw	FB 0265	Cranberry	5	-	1.33	2.95
Definition of the residue for compliance with the MRL and for estimation of dietary intake: carbaryl						
Clofentezine (156) **	AM 0660	Almond hulls	5		1.01	
ADI: 0–0.02 mg/kg bw	MM 0812	Cattle meat	W (1)	0.05*		
ARfD: unnecessary	ML 0812	Cattle milk	W (1)	0.01*		
	MO 0812	Cattle, Edible offal of	W (1)	0.1		
	FC 0001	Citrus fruits	0.5	0.5	0.10 (flesh 0.02)	
	JF 0004	Orange juice			0.014	
	VC 0424	Cucumber	0.5	1	0.125	
	FB 0021	Currants, Black, Red, White	0.2	0.05	0.04	
	MO 0105	Edible offal (mammalian)	0.05 *		0.05 *	
	PE 0112	Eggs	0.05 * (2)	0.05 *	0	
	FB 0269	Grapes	2	1	0.25	
	JF 0269	Grape juice			0	
		Wine			0.011	
	DF 0269	Dried grapes (= currants, Raisins and Sultanas)	2		0.28	
	MM 0095	Meat (from mammals other than marine mammals)	0.05 *		0	
	VC 0046	Melons, expect Watermelon	0.1		0	
	ML 0106	Milks	0.05 *		0	
	FP 0009	Pome fruit	0.5	0.5	0.05	
	JF 0226	Apple juice			0.0055	
	PM 0110	Poultry meat	0.05 * (2)	0.05*	0	
	PO 0111	Poultry, edible offal	0.05 * (2)	0.05*	0	
	FS 0012	Stone fruits	0.5	0.2	0.11	
	FB 0275	Strawberry	2	2	0.72	
	VO 0448	Tomato	0.5		0.09	
	TN 0085	Tree nuts	0.5		0.05	
Definition of the residue for compliance with MRLs and estimation of dietary intake for plant commodities: clofentezine						
Definition of the residue for compliance with MRLs for animal commodities: sum of clofentezine, and all metabolites containing the 2-chlorobenzoyl moiety, expressed as clofentezine						
The residue is fat soluble.						
(1) Replaced by a group MRL		(2) Residues are not expected as dietary burden in poultry is zero.				
Cyfluthrin (157) **	FP 0226	Apple	0.1	0.5	0.02	0.06
Group	VB 0400	Broccoli	2		0.20	1.5(1)
ADI: 0–0.04 mg/kg bw						
Group	VB 0041	Cabbages, Head	4		0.245	2.1(1)
ARfD: 0.04 mg/kg bw						
	VB 0404	Cauliflower	2		0.24	0.91
	HS 0444	Peppers Chilli (dry)	1		0.42	0.84
	FC 0001	Citrus fruits	0.3		0.06	0.2
	AB 0001	Citrus pulp (dry)	2		0.318	

Pesticide (Codex reference number)	CCN	Commodity	Recommended MRL mg/kg		STMR or STMR-P mg/kg	HR or HR-P mg/kg
			New	Previous		
	SO 0691	Cotton seed	0.7	0.05	0.1	
	OC 0691	Cotton seed oil, crude	1		0.19	
	VO 0440	Egg plant	0.2		0.05	0.12
	PE 0112	Eggs	0.01*		0	0
	MO 0099	Liver of cattle, goats, pigs and sheep	0.05		< 0.01	0.021
	MO 0098	Kidney of cattle, goats, pigs and sheep	0.05		< 0.01	0.027
	GC 0645	Maize	W	0.05		
	ML 0106	Milks	0.04		0.0022	
	MM 0095	Meat (from mammals other than marine mammals)	1 fat		0.0378 fat < 0.01 muscle	0.37 fat < 0.01 muscle
	ML 0812	Cattle milk	W	0.01 F		
	FP 0230	Pear	0.07		0.02	0.06
	VO 0051	Peppers	0.2		0.06	0.12
	VO 0445	Peppers sweet	W	0.2		
	VR 0589	Potato	0.01 *		0	0
	PM 0110	Poultry meat	0.01 *(fat)		0	0
	PO 0111	Poultry, edible offal of	0.01 *		0	0
	SO 0495	Rape seed	0.07	0.05	0.05	
	VO 0448	Tomato	0.2	0.5	0.07	0.10

Definition of the residue for compliance with MRLs and estimation of dietary intake: cyfluthrin (sum of isomers)

(1) The information provided to the JMPR precludes an estimate that the dietary intake would be below the ARfD.

lambda Cyhalothrin (146)
Group
ADI*: 0–0.02 mg/kg bw
Group
ARfD*: 0.02 mg/kg bw
*for cyhalothrin and lambda-cyhalothrin

Cyromazine (169) **	VS 0620	Artichoke, globe	3		1.0	1.3
ADI: 0–0.06 mg/kg bw	VD 0071	Beans (dry)	3		1.0	
ARfD: 0.1 mg/kg bw	VB 0400	Broccoli	1		0.15	0.51
	VB 0041	Cabbages, head	10		0.26	6.1(3)
	VX 0624	Celery	4		0.58	2.3
	VC 0424	Cucumber	2	0.2	0.48	1.3
	M 0105	Edible offal (Mammalian)	0.3		0.01	0.19
	PE 0112	Eggs	0.3	0.2* (1)	0.07	0.16
	VO 0050	Fruiting vegetables, other than cucurbits (2)	1		0.16	0.58
	VL 0482	Lettuce, head	4		0.34	2
	VL 0483	Lettuce, leafy	4		0.34	2
	VP 0534	Lima beans, young pods and or immature beans.	1		0.23	0.58
	FI 0345	Mango	0.5		0.125	0.25
	MM 0095	Meat (from mammals other than marine mammals)	0.3		0.01	0.20
	MF0100	Mammalian fat			0	0
	VC 0046	Melons, except Watermelon	0.5	0.2	0.04	0.19
	ML 0106	Milks	0.01	0.01*(1)	0.005	
	VO 0450	Mushroom	7	5	2.2	4.2
	VL 0485	Mustard greens	10		2.7	7.4
	VA 0385	Onion, bulb	0.1		0.05	0.07
	VO 0051	Peppers	W	1		
	PO 0111	Poultry, edible offal	0.2		0.065	0.08

Pesticide (Codex reference number)	CCN	Commodity	Recommended MRL mg/kg		STMR or STMR-P mg/kg	HR or HR-P mg/kg
			New	Previous		
	PM 0110	Poultry meat	0.1	0.05*(1)	0.05	0.05
	PF0111	Poultry fat			0	0
	MM 0822	Sheep meat	W	0.05*(1)		
	VL 0502	Spinach	10		2.0	6.1(3)
	VA 0389	Spring onion	3		0.345	1.7
	VC 0431	Summer squash	2		0.16	1
	VO 0448	Tomato	W	0.5		
	JF 0448	Tomato juice			0.12	
		Tomato, washed			0.11	
		Tomato, canned			0.09	
		Ketchup			0.13	
		Tomato, puree			0.19	
		Tomato, paste			0.34	

Definition of residues for compliance with MRL and for estimation of dietary intake for plants and animal commodities: cyromazine.

(1) MRL accommodates external animal treatment (2) Except mushrooms and sweet corn-on-the-cob

(3) The information provided to the JMPR precludes an estimate that the dietary intake would be below the ARfD.

Difenoconazole (224) *	VS 0621	Asparagus	0.03		0.02	0.02
ADI: 0–0.01 mg/kg bw	FI 0327	Banana	0.1		0.02	0.02
ARfD:0.3 mg/kg bw	VB 0400	Broccoli	0.5		0.065	0.41
	VB 0402	Brussels sprouts	0.2		0.065	0.14
	VB 0041	Cabbages, head	0.2		0.035	0.19
	VR 0577	Carrots	0.2		0.05	0.13
	VB 0404	Cauliflowers	0.2		0.02	0.10
	VR 0578	Celeriac	0.5		0.12	0.22
	VS 0624	Celery	3		0.14	2.0
	FS 0013	Cherries	0.2		0.04	0.10
	DF 0269	Dried grapes (= currants, Raisins and Sultanas) (1)	(1)		0.036	0.084
	MO 0105	Edible offal (Mammalian)	0.2		0.043	0.11
	PE 0112	Eggs	0.01*		0.0020	0.0054
	VA 0381	Garlic	0.02*		0	0
	FB 0269	Grapes	0.1		0.03	0.07
	VA 0384	Leek	0.3		0.08	0.21
	VL 0482	Lettuce, Head	2		0.41	1.0
	VL 0483	Lettuce, Leaf	2		0.41	1.0
	FI 0345	Mango	0.07		0.03	0.04
	MM 0095	Meat (from mammals other than marine mammals)	0.05 (fat)		0.01 muscle 0.012 fat	0.019 muscle 0.028 fat
	ML 0106	Milks	0.005*		0.001	
	FS 0245	Nectarine	0.5		0.15	0.26
	FT 0305	Olives	2		0.465	1.2
	FI 0350	Papaya	0.2		0.01	0.02
	FS 0247	Peach	0.5		0.15	0.26
	FS 0014	Plums (including prunes)	0.2		0.04	0.10
	FP 0009	Pome fruits	0.5		0.11	0.28
	VR 0589	Potato	0.02		0.01	0.01
	PM 0110	Poultry meat	0.01* (fat)		0.0002 muscle 0.0002 fat	0.00054 muscle 0.00054 fat
	PO 0111	Poultry, Edible offal of	0.01*		0.0002	0.00054
	SO 0495	Rape seed	0.05		0.02	
	VD 0541	Soya bean (dry)	0.02*		0.02	
	VR 0596	Sugar beet	0.2		0.02	

Pesticide (Codex reference number)	CCN	Commodity	Recommended MRL mg/kg New	Recommended MRL mg/kg Previous	STMR or STMR-P mg/kg	HR or HR-P mg/kg
	SO 0702	Sunflower seed	0.02		0.01	
	VO 0448	Tomato	0.5		0.10	0.36
	GC 0654	Wheat	0.02*		0	
	AS 0654	Wheat straw and fodder, Dry	3		0.685	1.2
	JF 0226	Apple juice			0.0022	
		Apple puree			0.015	
		Carrot, canned			0.002	
		Carrot, juice			0.0028	
	JF 0269	Grape juice			0.015	
	OR 0305	Olive oil, refined			0.65	
	OC 0305	Olive oil, virgin			0.70	
	JF 0448	Tomato juice			0.022	
		Tomato puree			0.066	
		Tomato, canned			0.0065	
		Wine			0.0054	

Definition of the residue for compliance with MRLs and estimation of dietary intake for plant commodities: difenoconazole

Definition of the residue for compliance with MRLs for animal commodities: sum of difenoconazole and 1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-(1,2,4-triazol)-1-yl-ethano), expressed as difenoconazole.

The residue is fat soluble.

(1) The estimated maximum residue level is the same as for grapes, so no separate MRL recommendation is necessary.

Dimethomorph (225) *	VB 0400	Broccoli	1		0.19	0.52
ADI: 0–0.1 mg/kg bw	VB 0041	Cabbages, Head	2		0.4	1.4
ARfD: 0.6 mg/kg bw	VL 0470	Corn salad	10		3.4	7.1
	DF 0269	Dried grapes	5		0.7	
	MO 0105	Edible offal (Mammalian)	0.01 *		0	0
	PE 0112	Eggs	0.01 *		0	0
	VC 0045	Fruiting vegetables, Cucurbits	0.5		edible peel 0.15 inedible peel 0.02	edible peel 0.24 inedible peel 0.05
	VO 0050	Fruiting vegetables, other than cucurbits (1)	1		0.22	0.56
	FB 0269	Grapes	2		0.39	1.7
	DH 1100	Hops, dry	80		26	
	VB 0405	Kohlrabi	0.02		0.02	0.02
	VL 0482	Lettuce, Head	10		3.6	7.2
	MM 0095	Meat (from mammals except marine mammals)	0.01*		0	0
	ML 0106	Milks	0.01 *		0	
	FI 0353	Pineapple	0.01 *		0	0
	VR 0589	Potato	0.05		0.02	0.05
	PM 0110	Poultry meat	0.01 *		0	0
	PO 0111	Poultry, Edible offal of	0.01 *		0	0
	FB 0275	Strawberry	0.05		0.01	0.02
	JF 0448	Tomato juice			0.055	
	HS 0444	Peppers, chilli dried	5		1.54	
		Tomato paste			0.264	
		Wine			0.11	
		Beer			0.052	

Definition of the residue for compliance with MRLs and estimation of dietary intake: dimethomorph (sum of isomers)

(1) Except fungi, edible; mushrooms; sweet corn (corn-on-the-cob); sweet corn (kernels)

Fenitrothion (037)	GC 0080	Cereal grains (1)	6 (Po)	10 (Po)	4.25	5.6
ADI: 0–0.006 mg/kg bw	MO 0105	Edible offal (mammalian)	0.05*	0.05*	Liver 0	Liver 0

Pesticide (Codex reference number)	CCN	Commodity	Recommended MRL mg/kg		STMR or STMR-P mg/kg	HR or HR-P mg/kg
			New	Previous		
					kidney 0	kidney 0
ARfD: 0.04 mg/kg bw	PE 0112	Eggs	0.05*	0.05*	0	0
	MM 0095	Meat (from mammals other than marine mammals)	0.05*	0.05*	Muscle 0 Fat 0	Muscle 0 Fat 0
	ML 0106	Milks	0.01*	0.01	0	
	PM 0110	Poultry meat	0.05*	-	Muscle 0 Fat 0	Muscle 0 Fat 0
	CM 1206	Rice bran, unprocessed	40 PoP	60	30.6	40.3
	CM 0649	Rice, Husked			2.72	
	CM 1205	Rice, polished			0.638	
		Cooked husked rice			0.468	
		Cooked polished rice			0.17	
		Washed polished rice			0.196	
		Cooked washed polished rice			0.085	
		Wheat flour			1	
		White bread			0.425	
		Wholemeal bread			1.615	
		Barley malt			0.85	
	VD 0541	Soya beans, dry	0.01	W	0.01	
	CM 0654	Wheat bran (unprocessed)	25 PoP	30 PoP	16.79	22.12[(2)]

Definition of the residue for compliance with MRLs and estimation of dietary intake: fenitrothion

(1) Except maize.

(2) The intake of 110% was for unprocessed wheat bran. Since this is not the edible commodity and further processing is likely to reduce the level of residues, the Meeting assumed that the intake from processed wheat bran would be below the ARfD.

Fenpyroximate (193) ADI: 0–0.01 mg/kg bw ARfD: 0.02 mg/kg bw	FP 0226	Apples	0.3[(1)]		0.09	

Definition of the residue for compliance with MRLs and estimation of dietary intake: Fenpyroximate

The residue is fat soluble.

(1) The maximum residue level was recommended by the 1999 JMPR. The 2007 JMPR calculated the IESTI and concluded that the short-term intake of residues is unlikely to present a public health concern.

Flusilazole (165) **	JF 0226	Apple juice			0.008	
ADI: 0–0.007 mg/kg bw	AB 0226	Apple pomace, dry	2		0.48	
ARfD: 0.02 mg/kg bw	FS 0240	Apricot	0.2	0.5	0.05	0.10
	FI 0327	Banana	0.03	0.1	0.01	0.01
	GC 0640	Barley	W	0.1		
	AS 0640	Barley straw and fodder, dry	W	2		
	MF 0812	Cattle fat	W	0.01*		
	MM 0812	Cattle meat	W	0.01*		
	ML 0812	Cattle milk	W	0.01*		
	MO 0812	Cattle, Edible offal of	W	0.02*		
	GC 0080	Cereal grains[(1)]	0.2		0.04	0.08
	PE 0840	Chicken eggs	W	0.01*		
	PM 0840	Chicken meat	W	0.01*		
	PO 0840	Chicken, Edible offal of	W	0.01*		
	DF 0269	Dried grapes (= currants, raisins, sultanas)	0.3	1	0.054	
	MO 0105	Edible offal (Mammalian)	2		0.65	1.68
	PE 0112	Eggs	0.1		0.02	0.07
	JF 0269	Grape juice			0.012	
	AB 0269	Grape pomace, dry	2		0.33	
	FB 0269	Grapes	0.2	0.5	0.03	0.11

Pesticide (Codex reference number)	CCN	Commodity	Recommended MRL mg/kg		STMR or STMR-P mg/kg	HR or HR-P mg/kg
			New	Previous		
	MM 0095	Meat (from mammals other than marine mammals)	1(fat)		0.285	0.73
	ML 0106	Milks	0.05		0.01	0.03
	FS 0245	Nectarine	0.2	0.5	0.06	0.10
	FS 0247	Peach	0.2	0.5	0.06	0.10
	FP 0009	Pome fruits	0.3	0.2	0.04	0.13
	PM 0110	Poultry meat	0.2		0.05	0.13
	PO 0111	Poultry, Edible offal of	0.2		0.02	0.09
	SO 0495	Rape seed	0.1	0.05	0.01	0.04
	GC 0650	Rye	W	0.1		
	AS 0650	Rye straw and fodder, dry	W	2		
	VD 0541	Soya bean (dry)	0.05		0.02	0.03
	AB 0541	Soya bean hulls	0.05		0.022	
	AS 0081	Straw and fodder(dry) of cereal grains (1)	5		1.6	2.5
	OR 0541	Soya bean oil, refined	0.1		0.044	
	VR 0596	Sugar beet	0.05	0.01*	0.01	0.03
	SO 0702	Sunflower seeds	0.1		0.01	0.04
	VO 0447	Sweet corn (corn-on-the-cob)	0.01*		0.01	0.01
	GC 0654	Wheat	W	0.1		
	AS 0654	Wheat straw and fodder dry	W	2		
	CM 0654	Wheat bran			0.012	
	CF 1211	Wheat flour, low-grade			0.036	
		Wine			0.003	

Definition of the residue for compliance with MRLs and estimation of dietary intake for plant commodities: flusilazole

Definition of the residue for compliance with MRLs and estimation of dietary intake for animal commodities: flusilazole plus [bis(4-fluorophenyl)methyl]silanol.

Flusilazole is fat-soluble.

(1) Except rice

Folpet (041)
ADI: 0–0.1 mg/kg bw
ARfD: 0.2 mg/kg bw (for women of child-bearing age)

Indoxacarb (216) ADI: 0–0.01 mg/kg bw ARfD: 0.1 mg/kg bw	VB 0041	Cabbages, head	3 (1)	2.0		

Definition of the residue for compliance with MRLs and estimation of dietary intake for plant commodities: sum of indoxacarb

Definition of the residue for compliance with MRLs and estimation of dietary intake for animal commodities: sum of indoxacarb, its R enantiomer and methyl 7-chloro-2,5-dihydro-2-[[[4- (trifluoromethoxy)phenyl]amino]carbonyl]indeno[1,2-e][1,3,4]oxadiazine-4a(3H)- carboxylate, expressed as indoxacarb.

The residue is fat soluble.

(1) From 2005 JMPR

Phosmet (103) ADI: 0–0.01 mg/kg bw ARfD: 0.2 mg/kg bw	FS 0240	Apricot	10	10	1.6	6.8
	FB 0020	Blueberries	15	15	4.0	9.9
	FC 0001	Citrus fruits	3	3	0.21	0.52
	FS 0245	Nectarine	10	10	1.6	6.8
	FP 0230	Pome fruit	3	10	0.38	1.8

Definition of the residue for compliance with MRLs and estimation of dietary intake: phosmet

Pesticide (Codex reference number)	CCN	Commodity	Recommended MRL mg/kg		STMR or STMR-P mg/kg	HR or HR-P mg/kg
			New	Previous		
Procymidone (136) **						
ADI: 0–0.1 mg/kg bw						
ARfD: 0.1 mg/kg bw						
Profenofos (171) **						
ADI: 0–0.03 mg/kg bw						
ARfD: 1 mg/kg bw						
Propiconazole (160) **	TN 0660	Almonds	W	0.05		
ADI: 0–0.07 mg/kg bw	FI 0327	Banana	0.1	0.1	0.06	0.087
ARfD: 0.3 mg/kg bw	GC 0640	Barley	0.2	0.05	0.0675	
	AS 0640	Barley straw and fodder, dry	2		2.6	9.7
	SB 0716	Coffee beans	0.02	0.1	0.06	
	FB 0265	Cranberry	0.3	0.3	0.174	0.39
	MO 0105	Edible offal (mammalian)	0.01*	0.05	0.6	0.8
	PE 0112	Eggs	0.01*	0.05*	0.05	0.05
	FB 0269	Grapes	W	0.5		
	GC 0645	Maize	0.05		0.05	
	FI 0345	Mango	W	0.05		
	MM 0095	Meat (from mammals other than marine mammals)	0.01* (fat)	0.05*	muscle 0.05 fat 0.05	muscle 0.05 fat 0.05
	ML 0106	Milks	0.01*	0.01*	0.01	
	GC 0647	Oats	W	0.05*		
	SO 0697	Peanut	W	0.05		
	SO 0703	Peanut, whole	W	0.1		
	TN 0672	Pecan	0.02*	0.05	0.02	0.02
	GC 0656	Popcorn	0.05		0.05	
	FI 0353	Pineapple	0.02*		0.02	0.02
	PM 0110	Poultry meat	0.01* (fat)	0.05*	muscle 0.05 fat 0.05	muscle 0.05 fat 0.05
	SO 0495	Rape seed	0.02	0.05	0.06	
	GC 0650	Rye	0.02	0.05*	0.06	
	AS 0650	Rye straw and fodder, dry	2		2.6	9.7
	VD 0541	Soya bean (dry)	0.07		0.03	
	AL 0541	Soya bean fodder	5		2.025	9.6
	AL 1265	Soya bean forage (green)	2		1.875	3.45
	FS 0012	Stone fruits	W	1		
	VR 0596	Sugar beet	0.02	0.05	0.06	
	GS 0659	Sugar cane	0.02*	0.05	0	
	VO 0447	Sweet corn (corn-on-the-cob)	0.05		0.05	
	GC 0653	Triticale	0.02		0.06	
	AS 0653	Triticale straw and fodder, dry	2		2.6	9.7
	GC 0654	Wheat	0.02	0.05*	0.06	
	AS 0654	Wheat straw and fodder, dry	2		2.6	9.7
Definition of the residue for compliance with MRLs for plant and animal commodities: propiconazole						
Definition of residue for estimation of dietary intake for plant and animal commodities: propiconazole plus all metabolite convertible to 2,4-dichloro-benzoic acid, expressed as propiconazole.						
The residue is fat soluble.						
Pyrimethanil (226) *	TN 0660	Almond	0.2		0.05	
ADI: 0–0.2 mg/kg bw	AM 0660	Almond hulls	12		2.6	
ARfD: unnecessary	JF 0226	Apple juice	-		0.32	

Pesticide (Codex reference number)	**CCN**	**Commodity**	**Recommended MRL mg/kg**		**STMR or STMR-P mg/kg**	**HR or HR-P mg/kg**
			New	Previous		
	AB 0226	Apple pomace (dry)	40		7.2 (2.9 wet)	
	FS 0240	Apricot	3		1.2	
	FI 0327	Banana	0.1		0.05	
	VR 0577	Carrot	1		0.14	
	FS 0013	Cherries	4 (Po)		1.3	
	FC 0001	Citrus fruits	7 (Po)		2.8	
	JF 0001	Citrus juice	-		0.028	
		Citrus oil			56	
	VP 0526	Common bean (pods and/or immature seeds)	3		0.22	
	DF 0269	Dried grapes (= currants, raisins, and sultanas)	5		1.1	
	MO 0105	Edible offal (mammalian)	0.1		0.065	
	VD 0561	Field pea (dry)	0.5		0.09	
	FB 0269	Grapes	4		0.71	
	JF 0269	Grape juice			0.50	
	VL 0482	Lettuce, head	3		0.85	
	MF0100	Mammalian fats (except milk fat)			0	
	MM 0095	Meat (from mammals other than marine mammals)	0.05 *		0	
	ML 0106	Milks	0.01		0.01	
	FS 0245	Nectarine	4		1.3	
	VA 0385	Onion, bulb	0.2		0.062	
	VA 0389	Onion, spring	3		0.38	
	AL 0072	Pea hay	3		0.20	
	FS 0247	Peach	4		1.3	
	FS 0014	Plums (including Prunes)	2		0.59	
	FP 0009	Pome fruits	7 (Po)		0.70	
	VR 0589	Potato	0.05 *		0.05	
	DF 0014	Prunes			0.48	
	FB 0275	Strawberry	3		1.2	
	VO 0448	Tomato	0.7		0.32	
		Apple puree			0.26	
		Carrot, frozen/canned			0.073	
		Carrot juice			0.028	
		Carrot puree			0.063	
		Common beans, frozen/ canned			0.11	
		Tomato puree			0.10	
		Tomato paste			0.35	
		Wine			0.34	

Definition of the residue for compliance with MRLs and estimation of dietary intake for plant commodities: pyrimethanil

Definition of the residue for compliance with MRLs for milk: the sum of pyrimethanil and 2-anilino-4,6-dimethylpyrimidin-5-ol, expressed as pyrimethanil, and for livestock tissues (excluding poultry) is the sum of pyrimethanil and 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine, expressed as pyrimethanil.

Quinoxyfen (222)	MM 0095	Meat (from mammals other than marine mammals)	0.2 (fat)	0.02 fat	0.011 fat 0.002 muscle	

ADI: 0–0.2 mg/kg bw
ARfD: unnecessary

Definition of the residue for compliance with MRLs and estimation of dietary intake: quinoxyfen.

The residue is fat soluble.

Pesticide (Codex reference number)	CCN	Commodity	Recommended MRL mg/kg		STMR or STMR-P mg/kg	HR or HR-P mg/kg
			New	Previous		
Thiabendazole (065) ADI: 0-01 mg/kg bw ARfD: 0.3 mg/kg/bw for women of child-bearing age ARfD: 1 mg/kg/bw for the general population	FC 0001	Citrus fruits	7 (Po)	5 Po	0.045	0.84
Definition of the residue for compliance with MRLs and estimation of dietary intake for plant commodities: thiabendazole *Definition of the residue for compliance with MRLs for animal commodities:* sum of thiabendazole and 5-hydroxythiabendazole; and for estimation of dietary intake for animal commodities: sum of thiabendazole, 5-hydroxythiabendazole and its sulfate conjugate.						
Triadimefon(133) ** ADI: 0–0.03 mg/kg bw ARfD: 0.08 mg/kg bw	FP 0226	Apples	0.3(3)	-	0.06	0.18
	JF 0226	Apple juice			0.04	
		Apple sauce			0.04	
	VS 0620	Artichoke, globe	0.7(3)	1(3)	0.14	0.55
	FI 0327	Bananas	1(3)	0.2(3)	0.04	0.3
	GC 0640	Barley	W	0.5(1)		
	AS 0640	Barley straw and fodder, dry	W	2(2) 5(3)		
	GC 0080	Cereal grain (4)	0.2(1)		0.05	0.15
	VD 0524	Chick-pea	W	0.05*(1)		
	HS 0444	Chilli peppers, dried	5(1)		2.1	
	SB 0716	Coffee beans	0.5(3)	0.05*(2) 0.1*(3)	0.05	0.4
		Coffee beans, roasted			0.06	
	FB 0021	Currants, black, red, white	0.7(3)	0.2(2) 0.5(3)	0.23	0.39
	DF 0269	Dried grapes	10(1)		0.47	9.9
	MO 0105	Edible offal (mammalian)	0.01*(1)		0	0
	PE 0112	Eggs	0.01*(1)	0.05*(1)	0.01	0.01
	AM 1051	Fodder Beets	W	0.05*[1]		
	VO 0050	Fruiting vegetables other than cucurbits (5)	1(1)		0.15	0.15
	VC 0045	Fruiting vegetables, cucurbits	0.2(1)	0.1(2) 2(3)	0.05	0.05
	FB 0269	Grapes	5(1)	0.5(2) 2(3)	0.15(7)	3.2
	JF 0269	Grape juice			0.07	0.07
	DH 1100	Hops	W	10[2] 5[3]		
	FI 0345	Mango	W	0.05*(1)		
	MM 0095	Meat (from mammals other than marine mammals) [in the fat]	0.02(1)	0.05*(1)	0.01	0.01
	ML 0106	Milks	0.01*(1)	0.05*(2) 0.01*(3)	0	0
	GC 0647	Oats	W	0.1[2] 0.2[3]		
	AS 0647	Oats straw and fodder, dry	W	2[2] 5[3]		
	VA 0389	Onion, spring	W	0.05*(1)		
	VA 0387	Onion, welsh	W	0.05*(1)		
	VP 0063	Peas	W	0.05*(2) 0.1(3)		
	VO 0445	Peppers, sweet	W	0.1(1)		
	FI 0353	Pineapples	5(3) (Po)	2(2) 1(3)	0.11	0.16
	FP 0009	Pome fruit	W	0.5(1)	0.06	0.18

Pesticide (Codex reference number)	CCN	Commodity	Recommended MRL mg/kg		STMR or STMR-P mg/kg	HR or HR-P mg/kg
			New	Previous		
	PM 0110	Poultry meat	0.01*(1)	0.05*(1)	0	0
	PO 0111	Poultry, Edible offal of	0.01*(1)		0	0
	FB 0272	Raspberries, red and black	W	1(2) 0.5(3)		
	GC 0650	Rye	W	0.1(2) 0.2(3)		
	AS 0650	Rye straw and fodder, dry	W	2(2) 5(3)		
	AS 0081	Straw and fodder (dry) of cereal grains (6)	5(1)		0.64 (fresh matter)	4.1 (fresh matter)
	FB 0275	Strawberries	0.7(3)	0.1(1)	0.265	0.41
	AV 0596	Sugar beet leafs or tops (dry)	2(3)		0.35	1.1
	AV 0596	Sugar beet leaves or tops	2(3)		0.14 (fresh matter)	0.42 (fresh matter)
	VR 0596	Sugar beets	0.05*(3)	0.1*(1)	0.05	0.05
	VO 0448	Tomato	W	0.2(2) 0.5(3)		
	JF 0448	Tomato juice			0.09	
		Tomato paste			0.78	
		Tomato puree			0.12	
	GC 0654	Wheat	W	0.1[2] 0.2[3]		
	AS 0654	Wheat straw and fodder, dry	W	2[2] 5[3]		
		Wine			0.06	

Definition of the residue for compliance with MRLs and estimation of dietary intake: sum of triadimefon and triadimenol. *The residue is fat soluble.*

(1) Based on triadimefon and triadimenol uses. (2) Based on triadimefon use only (3) Based on triadimenol use only
(4) Except maize and rice (5) Except fungi and sweet corn (6) Except maize
(7) The information provided to the JMPR precludes an estimate that the dietary intake would be below the ARfD.

Triadimenol (168) **	See triadimefon (133)					
Triazophos (143) **	VP 0523	Broad bean, shelled (succulent) (=immature seeds)	W	0.02*		
ADI: 0–0.001 mg/kg bw	VB 0402	Brussels sprouts	W	0.1		
ARfD: 0.001 mg/kg bw	VB 0041	Cabbages, Head	W	0.1		
	VR 0577	Carrot	W	0.5		
	MM 0812	Cattle meat	W	0.01*		
	ML 0812	Cattle milk	W	0.01*		
	VB 0404	Cauliflower	W	0.1		
	GC 0080	Cereal grains	W	0.05*		
	SB 0716	Coffee beans	W	0.05*		
	VP 0526	Common bean (pods and / or immature seeds)	W	0.2		
	SO 0691	Cotton seed	0.2	0.1	0.029	
	OC 0691	Cotton seed oil, crude	1		0.13	
	VA 0385	Onion, Bulb	W	0.05*		
	VP 0063	Peas (pods and succulent = immature seeds)	W	0.1		
	FP 0009	Pome fruits	W	0.2		
	VR 0589	Potato	W	0.05*		
	VD 0541	Soya bean (dry)	W	0.05*		
	VP 0541	Soya bean (immature	1		0.37	0.60(2)

Pesticide (Codex reference number)	CCN	Commodity	Recommended MRL mg/kg		STMR or STMR-P mg/kg	HR or HR-P mg/kg
			New	Previous		
		seeds)[1]				
	FB 0275	Strawberry	W	0.05*		
	VR 0596	Sugar beet	W	0.05*		
Definition of the residue for compliance with MRLs and estimation of dietary intake: triazophos						
(1) With the pod (2) The information provided to the JMPR precludes an estimate that the dietary intake would be below the ARfD.						
Zoxamide (227) *	VC 0424	Cucumber	1		0.06	
ADI: 0–0.5 mg/kg bw	DF 0269	Dried grapes	15		2.4	
ARfD: unnecessary	FB 0269	Grapes	5		0.83	
	JF 0269	Grape juice [1]			0.11	
		Wine			0.02	
	VR 0589	Potato	0.02		0.02	
	VO 0448	Tomato	2		0.195	
		Tomato puree			0.08	
		Tomato paste			0.19	
Definition of the residue for compliance with MRLs and estimation of dietary intake for plant commodities: zoxamide						
(1) Unclarified						

ANNEX 2: INDEX OF REPORTS AND EVALUATIONS OF PESTICIDES BY THE JMPR

Numbers in parentheses after the names of pesticides are Codex classification numbers. The abbreviations used are:

T, evaluation of toxicology

R, evaluation of residue and analytical aspects

E, evaluation of effects on the environment

Abamectin (177)	1992 (T,R), 1994 (T,R), 1995 (T), 1997 (T,R), 2000 (R)
Acephate (095)	1976 (T, R), 1979 (R), 1981 (R), 1982 (T), 1984 (T,R), 1987 (T), 1988 (T), 1990 (T,R), 1991 (corr. to 1990 R evaluation), 1994 (R), 1996 (R), 2002 (T), 2003 (R), 2004 (corr. to 2003 report), 2005 (T), 2006 (R)
Acrylonitrile	1965 (T, R)
Aldicarb (117)	1979 (T, R), 1982 (T, R), 1985 (R), 1988 (R), 1990 (R), 1991 (corr. to 1990 evaluation), 1992 (T), 1993 (R), 1994 (R), 1996 (R), 2001 (R), 2002 (R), 2006 (R)
Aldrin (001)	1965 (T), 1966 (T,R), 1967 (R), 1974 (R), 1975 (R), 1977 (T), 1990 (R), 1992 (R)
Allethrin	1965 (T,R)
Aminocarb (134)	1978 (T,R), 1979 (T,R)
Aminomethylphosphonic acid (AMPA, 198)	1997 (T,R)
Aminopyralid (220)	2006 (T, R), 2007 (T, R)
Amitraz (122)	1980 (T,R), 1983 (R), 1984 (T,R), 1985 (R), 1986 (R), 1989 (R), 1990 (T,R), 1991 (R & corr. to 1990 R evaluation), 1998 (T)
Amitrole (079)	1974 (T,R), 1977 (T), 1993 (T,R), 1997 (T), 1998 (R)
Anilazine (163)	1989 (T,R), 1992 (R)
Atrazine	2007 (T)
Azinphos-ethyl (068)	1973 (T,R), 1983 (R)
Azinphos-methyl (002)	1965 (T), 1968 (T,R), 1972 (R), 1973 (T), 1974 (R), 1991 (T,R), 1992 (corr. to 1991 report), 1993 (R), 1995 (R), 2007 (T)
Azocyclotin (129)	1979 (R), 1981 (T), 1982 (R),1983 (R), 1985 (R), 1989 (T,R), 1991 (R), 1994 (T), 2005 (T,R)
Benalaxyl (155)	1986 (R), 1987 (T), 1988 (R), 1992 (R), 1993 (R), 2005 (T)
Bendiocarb (137)	1982 (T,R), 1984 (T,R), 1989 (R), 1990 (R)
Benomyl (069)	1973 (T,R), 1975 (T,R), 1978 (T,R), 1983 (T,R), 1988 (R), 1990 (R), 1994 (R), 1995 (T,E), 1998 (R)
Bentazone (172)	1991 (T,R), 1992 (corr. to 1991 report, Annex I), 1994 (R), 1995 (R), 1998 (T,R), 1999 (corr. to 1998 report), 2004(T)
BHC (technical-grade)	1965 (T), 1968 (T,R), 1973 (T,R) (see also Lindane)
Bifenazate (219)	2006 (T, R)

Bifenthrin (178)	1992 (T,R), 1995 (R), 1996 (R), 1997 (R)
Binapacryl (003)	1969 (T,R), 1974 (R), 1982 (T), 1984 (R), 1985 (T,R)
Bioresmethrin (093)	1975 (R), 1976 (T,R), 1991 (T,R)
Biphenyl	See Diphenyl
Bitertanol (144)	1983 (T), 1984 (R), 1986 (R), 1987 (T), 1988 (R), 1989 (R), 1991 (R), 1998 (T), 1999 (R), 2002 (R)
Boscalid (221)	2006 (T, R)
Bromide ion (047)	1968 (R), 1969 (T,R), 1971 (R), 1979 (R), 1981 (R), 1983 (R), 1988 (T,R), 1989 (R), 1992 (R)
Bromomethane (052)	1965 (T,R), 1966 (T,R), 1967 (R), 1968 (T,R), 1971 (R), 1979 (R), 1985 (R), 1992 (R)
Bromophos (004)	1972 (T,R), 1975 (R), 1977 (T,R), 1982 (R), 1984 (R), 1985 (R)
Bromophos-ethyl (005)	1972 (T,R), 1975 (T,R), 1977 (R)
Bromopropylate (070)	1973 (T,R), 1993 (T,R)
Butocarboxim (139)	1983 (R), 1984 (T), 1985 (T), 1986 (R)
Buprofezin (173)	1991 (T,R), 1995 (R), 1996 (corr. to 1995 report.), 1999 (R)
sec-Butylamine (089)	1975 (T,R), 1977 (R), 1978 (T,R), 1979 (R), 1980 (R), 1981 (T), 1984 (T,R: withdrawal of temporary ADI, but no evaluation)
Cadusafos (174)	1991 (T,R), 1992 (R), 1992 (R)
Campheclor (071)	1968 (T,R), 1973 (T,R)
Captafol (006)	1969 (T,R), 1973 (T,R), 1974 (R), 1976 (R), 1977 (T,R), 1982 (T), 1985 (T,R), 1986 (corr. to 1985 report), 1990 (R), 1999 (acute Rf D)
Captan (007)	1965 (T), 1969 (T,R), 1973 (T), 1974 (R), 1977 (T,R), 1978 (T,R), 1980 (R), 1982 (T), 1984 (T,R), 1986 (R), 1987 (R and corr. to 1986 R evaluation), 1990 (T,R), 1991 (corr. to 1990 R evaluation), 1994 (R), 1995 (T), 1997 (R), 2000 (R), 2004 (T), 2007 (T)
Carbaryl (008)	1965 (T), 1966 (T,R), 1967 (T,R), 1968 (R), 1969 (T,R), 1970 (R), 1973 (T,R), 1975 (R), 1976 (R), 1977 (R), 1979 (R), 1984 (R), 1996 (T), 2001 (T), 2002 (R), 2007 (R)
Carbendazim (072)	1973 (T,R), 1976 (R), 1977 (T), 1978 (R), 1983 (T,R), 1985 (T,R), 1987 (R), 1988 (R), 1990 (R), 1994 (R), 1995 (T,E), 1998 (T,R), 2003 (R), 2005 (T)
Carbofuran (096)	1976 (T,R), 1979 (T,R), 1980 (T), 1982 (T), 1991 (R), 1993 (R), 1996 (T), 1997 (R), 1999 (corr. to 1997 report), 2002 (T, R), 2003 (R) (See also carbosulfan), 2004 (R)
Carbon disulfide (009)	1965 (T,R), 1967 (R), 1968 (R), 1971 (R), 1985 (R)
Carbon tetrachloride (010)	1965 (T,R), 1967 (R), 1968 (T,R), 1971 (R), 1979 (R), 1985 (R)
Carbophenothion (011)	1972 (T,R), 1976 (T,R), 1977 (T,R), 1979 (T,R),

	1980 (T,R), 1983 (R)
Carbosulfan (145)	1984 (T,R), 1986 (T), 1991 (R), 1992 (corr. to 1991 report), 1993 (R), 1997 (R), 1999 (R), 2002 (R), 2003 (T, R), 2004 (R, corr. to 2003 report)
Cartap (097)	1976 (T,R), 1978 (T,R), 1995 (T,R)
Chinomethionat (080)	1968 (T,R) (as oxythioquinox), 1974 (T,R), 1977 (T,R), 1981 (T,R), 1983 (R), 1984 (T,R), 1987 (T)
Chlorbenside	1965 (T)
Chlordane (012)	1965 (T), 1967 (T,R), 1969 (R), 1970 (T,R), 1972 (R), 1974 (R), 1977 (T,R), 1982 (T), 1984 (T,R), 1986 (T)
Chlordimeform (013)	1971 (T,R), 1975 (T,R), 1977 (T), 1978 (T,R), 1979(T), 1980(T), 1985(T), 1986 (R), 1987 (T)
Chlorfenson	1965 (T)
Chlorfenvinphos (014)	1971 (T,R), 1984 (R), 1994 (T), 1996 (R)
Chlormequat (015)	1970 (T,R), 1972 (T,R), 1976 (R), 1985 (R), 1994 (T,R), 1997 (T), 1999 (acute Rf D), 2000 (R)
Chlorobenzilate (016)	1965 (T), 1968 (T,R), 1972 (R), 1975 (R), 1977 (R), 1980 (T)
Chloropicrin	1965 (T,R)
Chloropropylate	1968 (T,R), 1972 (R)
Chlorothalonil (081)	1974 (T,R), 1977 (T,R), 1978 (R), 1979 (T,R), 1981 (T,R), 1983 (T,R), 1984 (corr. to 1983 report and T evaluation), 1985 (T,R), 1987 (T), 1988 (R), 1990 (T,R), 1991 (corr. to 1990 evaluation), 1992 (T), 1993 (R), 1997 (R)
Chlorpropham (201)	1965 (T), 2000 (T), 2001 (R), 2005 (T)
Chlorpyrifos (017)	1972 (T,R), 1974 (R), 1975 (R), 1977 (T,R), 1981 (R), 1982 (T,R), 1983 (R), 1989 (R), 1995 (R), 1999 (T), 2000 (R), 2004 (R), 2006 (R)
Chlorpyrifos-methyl (090)	1975 (T,R), 1976 (R, Annex I only), 1979 (R), 1990, (R), 1991 (T,R), 1992 (T and corr. to 1991 report), 1993 (R), 1994 (R), 2001 (T)
Chlorthion	1965 (T)
Clethodim (187)	1994 (T,R), 1997 (R), 1999 (R), 2002 (R)
Clofentezine (156)	1986 (T,R), 1987 (R), 1989 (R), 1990 (R), 1992 (R), 2005 (T), 2007 (R)
Coumaphos (018)	1968 (T,R), 1972 (R), 1975 (R), 1978 (R), 1980 (T,R), 1983 (R), 1987 (T), 1990 (T,R)
Crufomate (019)	1968 (T,R), 1972 (R)
Cyanophenfos (091)	1975 (T,R), 1978 (T: ADI extended, but no evaluation), 1980, (T), 1982 (R), 1983 (T)
Cycloxydim (179)	1992 (T,R), 1993 (R)
Cyfluthrin (157)/ beta-Cyfluthrin (228)	1986 (R), 1987 (T and corr. to 1986 report), 1989 (R), 1990 (R), 1992 (R), 2006 (T), 2007 (R)
Cyhalothrin (146)/ lambda-Cyhalothrin	1984 (T,R), 1986 (R), 1988 (R), 2007 (T)

Cyhexatin (067)	1970 (T,R), 1973 (T,R), 1974 (R), 1975 (R)*, 1977 (T), 1978 (T,R), 1980 (T), 1981 (T), 1982 (R), 1983 (R), 1985 (R), 1988 (T), 1989 (T), 1991 (T,R), 1992 (R), 1994 (T), 2005 (T,R)
Cypermethrin (118)	1979 (T,R), 1981 (T,R), 1982 (R), 1983 (R), 1984 (R), 1985 (R), 1986 (R), 1987 (corr. to 1986 evaluation), 1988 (R), 1990 (R), 2006 (T)
Cyprodinil (207)	2003 (T,R), 2004 (corr. to 2003 report)
Cyromazine (169)	1990 (T,R), 1991 (corr. to 1990 R evaluation), 1992 (R), 2006 (T), 2007 (R)
2,4-D (020)	1970 (T,R), 1971 (T,R), 1974 (T,R), 1975 (T,R), 1980 (R), 1985, (R), 1986 (R), 1987 (corr. to 1986 report, Annex I), 1996 (T), 1997 (E), 1998 (R), 2001 (R)
Daminozide (104)	1977 (T,R), 1983 (T), 1989 (T,R), 1991 (T)
DDT (021)	1965 (T), 1966 (T,R), 1967 (T,R),1968 (T,R), 1969 (T,R), 1978 (R), 1979 (T), 1980 (T), 1983 (T), 1984 (T), 1993 (R), 1994 (R), 1996 (R)
Deltamethrin (135)	1980 (T,R), 1981 (T,R), 1982 (T,R), 1984 (R), 1985 (R), 1986 (R), 1987 (R), 1988 (R), 1990 (R), 1992 (R), 2000 (T), 2002 (R)
Demeton (092)	1965 (T), 1967 (R), 1975 (R), 1982 (T)
Demeton-S-methyl (073)	1973 (T,R), 1979 (R), 1982 (T), 1984 (T,R), 1989 (T,R), 1992 (R), 1998 (R)
Demeton-S-methylsulphon (164)	1973 (T,R), 1982 (T), 1984 (T,R), 1989 (T,R), 1992 (R)
Dialifos (098)	1976 (T,R), 1982 (T), 1985 (R)
Diazinon (022)	1965 (T), 1966 (T), 1967 (R), 1968 (T,R), 1970 (T,R), 1975 (R), 1979 (R), 1993 (T,R), 1994 (R), 1996 (R), 1999 (R), 2001 (T) , 2006 (T, R)
1,2-Dibromoethane (023)	1965 (T,R), 1966 (T,R), 1967 (R), 1968 (R), 1971 (R), 1979 (R), 1985 (R)
Dichlorfluanid (082)	1969 (T,R), 1974 (T,R), 1977 (T,R), 1979 (T,R), 1981 (R),1982 (R), 1983 (T,R), 1985 (R)
1,2-Dichloroethane (024)	1965 (T,R), 1967 (R), 1971 (R), 1979 (R), 1985 (R)
Dichlorvos (025)	1965 (T,R), 1966 (T,R), 1967 (T,R), 1969 (R), 1970 (T,R), 1974 (R), 1977 (T), 1993 (T,R)
Dicloran (083)	1974 (T,R), 1977 (T,R), 1998 (T,R), 2003 (R)
Dicofol (026)	1968 (T,R), 1970 (R), 1974 (R), 1992 (T,R), 1994 (R)
Dieldrin (001)	1965 (T), 1966 (T,R), 1967 (T,R), 1968 (R), 1969 (R), 1970, (T,R), 1974 (R), 1975 (R), 1977 (T), 1990 (R), 1992 (R)
Difenoconazole (224)	2007 (T, R)
Diflubenzuron (130)	1981 (T,R), 1983 (R), 1984 (T,R), 1985 (T,R), 1988 (R), 2001 (T), 2002 (R)
Dimethenamid- P (214)	2005 (T,R)
Dimethipin (151)	1985 (T,R), 1987 (T,R), 1988 (T,R), 1999 (T),

	2001 (R), 2004 (T)
Dimethoate (027)	1965 (T), 1966 (T), 1967 (T,R), 1970 (R), 1973 (R in evaluation of formothion), 1977 (R), 1978 (R), 1983 (R) 1984 (T,R) 1986 (R), 1987 (T,R), 1988 (R), 1990 (R), 1991 (corr. to 1990 evaluation), 1994 (R), 1996 (T), 1998 (R), 2003 (T,R), 2004 (corr. to 2003 report), 2006 (R)
Dimethomorph	2007 (T, R)
Dimethrin	1965 (T)
Dinocap (087)	1969 (T,R), 1974 (T,R), 1989 (T,R), 1992 (R), 1998 (R), 1999 (R), 2000 (T), 2001 (R)
Dioxathion (028)	1968 (T,R), 1972 (R)
Diphenyl (029)	1966 (T,R), 1967 (T)
Diphenylamine (030)	1969 (T,R), 1976 (T,R), 1979 (R), 1982 (T), 1984 (T,R), 1998 (T), 2001 (R), 2003 (R)
Diquat (031)	1970 (T,R), 1972 (T,R), 1976 (R), 1977 (T,R), 1978 (R), 1994 (R)
Disulfoton (074)	1973 (T,R), 1975 (T,R), 1979 (R), 1981 (R), 1984 (R), 1991 (T,R), 1992 (corr. to 1991 report, Annex I), 1994 (R), 1996 (T), 1998 (R), 2006 (R)
Dithianon (180)	1992 (T,R), 1995 (R), 1996 (corr. to 1995 report)
Dithiocarbamates (105)	1965 (T), 1967 (T,R), 1970 (T,R), 1983 (R propineb, thiram), 1984 (R propineb), 1985 (R), 1987 (T thiram), 1988 (R thiram), 1990 (R), 1991 (corr. to 1990 evaluation), 1992 (T thiram), 1993 (T,R), 1995 (R), 1996 (T,R ferbam, ziram;, R thiram), 2004 (R)
4,6-Dinitro-*ortho*-cresol (DNOC)	1965 (T)
Dodine (084)	1974 (T,R), 1976 (T,R), 1977 (R), 2000 (T), 2003(R) 2004 (corr. to 2003 report)
Edifenphos (099)	1976 (T,R), 1979 (T,R), 1981 (T,R)
Endosulfan (032)	1965 (T), 1967 (T,R), 1968 (T,R), 1971 (R), 1974 (R), 1975 (R), 1982 (T), 1985 (T,R), 1989 (T,R), 1993 (R), 1998 (T), 2006 (R)
Endrin (033)	1965 (T), 1970 (T,R), 1974 (R), 1975 (R), 1990 (R), 1992 (R)
Esfenvalerate (204)	2002 (T, R)
Ethephon (106)	1977 (T,R), 1978 (T,R), 1983 (R), 1985 (R), 1993 (T), 1994 (R), 1995 (T), 1997 (T), 2002 (T)
Ethiofencarb (107)	1977 (T,R), 1978 (R), 1981 (R), 1982 (T,R), 1983 (R)
Ethion (034)	1968 (T,R), 1969 (R), 1970 (R), 1972 (T,R), 1975 (R), 1982 (T), 1983 (R), 1985 (T), 1986 (T), 1989 (T), 1990 (T), 1994 (R)
Ethoprophos (149)	1983 (T), 1984 (R), 1987 (T), 1999 (T), 2004 (R)
Ethoxyquin (035)	1969 (T,R), 1998 (T), 1999 (R). 2005 (T)
Ethylene dibromide	See 1,2-Dibromoethane
Ethylene dichloride	See 1,2-Dichloroethane
Ethylene oxide	1965 (T,R), 1968 (T,R), 1971 (R)

Ethylenethiourea (ETU) (108)	1974 (R), 1977 (T,R), 1986 (T,R), 1987 (R), 1988 (T,R), 1990 (R), 1993 (T,R)
Etofenprox (184)	1993 (T,R)
Etrimfos (123)	1980 (T,R), 1982 (T,R[1]), 1986 (T,R), 1987 (R), 1988 (R), 1989 (R), 1990 (R)
Famoxadone (208)	2003 (T,R)
Fenamiphos (085)	1974 (T,R), 1977 (R), 1978 (R), 1980 (R), 1985 (T), 1987 (T), 1997 (T), 1999 (R), 2002 (T), 2006 (R)
Fenarimol (192)	1995 (T, R, E), 1996 (R and corr. to 1995 report)
Fenbuconazole (197)	1997 (T,R)
Fenbutatin oxide (109)	1977 (T,R), 1979 (R), 1992 (T), 1993 (R)
Fenchlorfos (036)	1968 (T,R), 1972 (R), 1983 (R)
Fenhexamid (215)	2005 (T,R)
Fenitrothion (037)	1969 (T,R), 1974 (T,R), 1976 (R), 1977 (T,R), 1979(R), 1982, (T) 1983 (R), 1984 (T,R), 1986 (T,R), 1987 (R and corr. to 1986 R evaluation), 1988 (T), 1989 (R), 2000 (T), 2003 (R), 2004 (R, corr. to 2003 report), 2007 (T, R)
Fenpropathrin (185)	1993 (T,R), 2006 (R)
Fenpropimorph (188)	1994 (T), 1995 (R), 1999 (R), 2001 (T), 2004 (T)
Fenpyroximate (193)	1995 (T,R), 1996 (corr. to 1995 report.), 1999 (R), 2004 (T), 2007 (T)
Fensulfothion (038)	1972 (T,R), 1982 (T), 1983 (R)
Fenthion (039)	1971 (T,R), 1975 (T,R), 1977 (R), 1978 (T,R), 1979 (T), 1980 (T), 1983 (R), 1989 (R), 1995 (T,R,E), 1996 (corr. to 1995 report), 1997 (T), 2000 (R)
Fentin compounds (040)	1965 (T), 1970 (T,R), 1972 (R), 1986 (R), 1991 (T,R), 1993 (R), 1994 (R)
Fenvalerate (119)	1979 (T,R), 1981 (T,R), 1982 (T), 1984 (T,R), 1985 (R), 1986 (T,R), 1987 (R and corr. to 1986 report), 1988 (R), 1990 (R), 1991 (corr. to 1990 R evaluation)
Ferbam	See Dithiocarbamates, 1965 (T), 1967 (T,R), 1996 (T,R)
Fipronil (202)	1997 (T), 2000 (T), 2001 (R)
Fipronil-desulfinyl	1997 (T)
Flucythrinate (152)	1985 (T, R), 1987 (R), 1988 (R), 1989 (R), 1990 (R), 1993 (R)
Fludioxonil (211)	2004 (T,R), 2006 (R)
Flumethrin (195)	1996 (T,R)
Flusilazole (165)	1989 (T, R), 1990 (R), 1991 (R), 1993 (R), 1995 (T), 2007 (T, R)
Flutolanil (205)	2002 (T, R)
Folpet (041)	1969 (T,R), 1973 (T), 1974 (R), 1982 (T), 1984 (T,R), 1986 (T), 1987 (R), 1990 (T,R), 1991 (corr. to 1990 R evaluation), 1993 (T,R), 1994 (R),

	1995 (T), 1997 (R), 1998 (R), 1999(R) , 2002 (T), 2004 (T), 2007 (T)
Formothion (042)	1969 (T,R), 1972 (R), 1973 (T,R), 1978 (R), 1998 (R)
Glufosinate-ammonium (175)	1991 (T,R), 1992 (corr. to 1991 report, Annex I), 1994 (R), 1998 (R), 1999 (T,R)
Glyphosate (158)	1986 (T,R), 1987 (R and corr. to 1986 report), 1988 (R), 1994 (R), 1997 (T,R), 2004 (T), 2005 (R)
Guazatine (114)	1978 (T.R), 1980 (R), 1997 (T,R)
Haloxyfop (194)	1995 (T,R), 1996 (R and corr. to 1995 report), 2001 (R), 2006 (T)
Heptachlor (043)	1965 (T), 1966 (T,R), 1967 (R), 1968 (R), 1969 (R), 1970 (T,R), 1974 (R), 1975 (R), 1977 (R), 1987 (R), 1991 (T,R), 1992 (corr. to 1991 report, Annex I), 1993 (R), 1994 (R)
Hexachlorobenzene (044)	1969 (T,R), 1973 (T,R), 1974 (T,R), 1978(T), 1985 (R)
Hexaconazole (170)	1990 (T,R), 1991 (R and corr. to 1990 R evaluation), 1993 (R)
Hexythiazox (176)	1991 (T,R), 1994 (R), 1998 (R)
Hydrogen cyanide (045)	1965 (T,R)
Hydrogen phosphide (046)	1965 (T,R), 1966 (T,R), 1967 (R), 1969 (R), 1971 (R)
Imazalil (110)	1977 (T,R), 1980 (T,R), 1984 (T,R), 1985 (T,R), 1986 (T), 1988 (R), 1989 (R), 1991 (T), 1994 (R), 2000 (T), 2001 (T), 2005 (T)
Imidacloprid (206)	2001 (T), 2002 (R), 2006 (R)
Indoxacarb (216)	2005 (T,R), 2007 (R)
Iprodione (111)	1977 (T,R), 1980 (R), 1992 (T), 1994 (R), 1995 (T), 2001 (R)
Isofenphos (131)	1981 (T,R), 1982 (T,R), 1984 (R), 1985 (R), 1986 (T,R), 1988 (R), 1992 (R)
Kresoxim-methyl (199)	1998 (T,R), 2001 (R)
Lead arsenate	1965 (T), 1968 (T,R)
Leptophos (088)	1974 (T,R), 1975 (T,R), 1978 (T,R)
Lindane (048)	1965 (T), 1966 (T,R), 1967 (R), 1968 (R), 1969 (R), 1970 (T,R, published as Annex VI to 1971 evaluations), 1973 (T,R), 1974 (R), 1975 (R), 1977 (T,R), 1978 (R), 1979 (R), 1989 (T,R), 1997 (T), 2002 (T), 2003 (R), 2004 (corr. to 2003 report)
Malathion (049)	1965 (T), 1966 (T,R), 1967 (corr. to 1966 R evaluation), 1968 (R), 1969 (R), 1970 (R), 1973 (R), 1975 (R), 1977 (R), 1984 (R), 1997 (T), 1999 (R), 2000 (R), 2003 (T), 2004 (R), 2005 (R)
Maleic hydrazide (102)	1976 (T,R), 1977 (T,R), 1980 (T), 1984 (T,R), 1996 (T), 1998 (R)
Mancozeb (050)	1967 (T,R), 1970 (T,R), 1974 (R), 1977 (R), 1980 (T,R), 1993 (T,R)
Maneb	See Dithiocarbamates, 1965 (T), 1967 (T,R),

	1987 (T), 1993 (T,R)
Mecarbam (124)	1980 (T,R), 1983 (T,R), 1985 (T,R), 1986 (T,R), 1987 (R)
Metalaxyl (138)	1982 (T,R), 1984 (R), 1985 (R), 1986 (R), 1987 (R), 1989 (R), 1990 (R), 1992 (R), 1995 (R)
Metalaxyl –M (212)	2002 (T), 2004 (R)
Methacrifos (125)	1980 (T,R), 1982 (T), 1986 (T), 1988 (T), 1990 (T,R), 1992 (R)
Methamidophos (100)	1976 (T,R), 1979 (R), 1981 (R), 1982 (T,R), 1984 (R), 1985 (T), 1989 (R), 1990 (T,R), 1994 (R), 1996 (R), 1997 (R), 2002 (T), 2003 (R), 2004 (R, corr. to 2003 report)
Methidathion (051)	1972 (T,R), 1975 (T,R), 1979 (R), 1992 (T,R), 1994 (R), 1997 (T)
Methiocarb (132)	1981 (T,R), 1983 (T,R), 1984 (T), 1985 (T), 1986 (R), 1987 (T,R), 1988 (R), 1998 (T), 1999 (R), 2005 (R)
Methomyl (094)	1975 (R), 1976 (R), 1977 (R), 1978 (R), 1986 (T,R), 1987 (R), 1988 (R), 1989 (T,R), 1990 (R), 1991 (R), 2001 (T,R), 2004 (R)
Methoprene (147)	1984 (T,R), 1986 (R), 1987 (T and corr. to 1986 report), 1988 (R), 1989 (R), 2001 (T), 2005 (R)
Methoxychlor	1965 (T), 1977 (T)
Methoxyfenozide (209)	2003 (T, R), 2004 (corr. to 2003 report), 2006 (R)
Methyl bromide (052)	See Bromomethane
Metiram (186)	1993 (T), 1995 (R)
Mevinphos (053)	1965 (T), 1972 (T,R), 1996 (T), 1997 (E,R), 2000 (R)
MGK 264	1967 (T,R)
Monocrotophos (054)	1972 (T,R), 1975 (T,R), 1991 (T,R), 1993 (T), 1994 (R)
Myclobutanil (181)	1992 (T,R), 1997 (R), 1998 (R)
Nabam	See Dithiocarbamates, 1965 (T), 1976 (T,R)
Nitrofen (140)	1983 (T,R)
Novaluron (217)	2005 (T,R)
Omethoate (055)	1971 (T,R), 1975 (T,R), 1978 (T,R), 1979 (T), 1981 (T,R), 1984 (R), 1985 (T), 1986 (R), 1987 (R), 1988 (R), 1990 (R), 1998 (R)
Organomercury compounds	1965 (T), 1966 (T,R), 1967 (T,R)
Oxamyl (126)	1980 (T,R), 1983 (R), 1984 (T), 1985 (T,R), 1986 (R), 2002 (T,R)
Oxydemeton-methyl (166)	1965 (T, as demeton-*S*-methyl sulfoxide), 1967 (T), 1968 (R), 1973 (T,R), 1982 (T), 1984 (T,R), 1989 (T,R), 1992 (R), 1998 (R), 1999 (corr. to 1992 report), 2002 (T), 2004 (R)
Oxythioquinox	See Chinomethionat
Paclobutrazol (161)	1988 (T,R), 1989 (R)
Paraquat (057)	1970 (T,R), 1972 (T,R), 1976 (T,R), 1978 (R),

	1981 (R), 1982 (T), 1985 (T), 1986 (T), 2003 (T), 2004 (R)
Parathion (058)	1965 (T), 1967 (T,R), 1969 (R), 1970 (R), 1984 (R), 1991 (R), 1995 (T,R), 1997 (R), 2000 (R)
Parathion-methyl (059)	1965 (T), 1968 (T,R), 1972 (R), 1975 (T,R), 1978 (T,R), 1979 (T), 1980 (T), 1982 (T), 1984 (T,R), 1991 (R), 1992 (R), 1994 (R), 1995 (T), 2000 (R), 2003 (R)
Penconazole (182)	1992 (T,R), 1995 (R)
Permethrin (120)	1979 (T,R), 1980 (R), 1981 (T,R), 1982 (R), 1983 (R), 1984 (R), 1985 (R), 1986 (T,R), 1987 (T), 1988 (R), 1989 (R), 1991 (R), 1992 (corr. to 1991 report), 1999 (T)
2-Phenylphenol (056)	1969 (T,R), 1975 (R), 1983 (T), 1985 (T,R), 1989 (T), 1990 (T,R), 1999 (T,R), 2002 (R)
Phenothrin (127)	1979 (R), 1980 (T,R), 1982 (T), 1984 (T), 1987 (R), 1988 (T,R)
Phenthoate (128)	1980 (T,R), 1981 (R), 1984 (T)
Phorate (112)	1977 (T,R), 1982 (T), 1983 (T), 1984 (R), 1985 (T), 1990 (R), 1991 (R), 1992 (R), 1993 (T), 1994 (T), 1996 (T), 2004 (T), 2005 (R)
Phosalone (060)	1972 (T,R), 1975 (R), 1976 (R), 1993 (T), 1994 (R), 1997 (T), 1999 (R), 2001 (T)
Phosmet (103)	1976 (R), 1977 (corr. to 1976 R evaluation), 1978 (T,R), 1979 (T,R), 1981 (R), 1984 (R), 1985 (R), 1986 (R), 1987 (R and corr. to 1986 R evaluation), 1988 (R), 1994 (T), 1997 (R), 1998 (T), 2002 (R), 2003 (R), 2007 (R)
Phosphine	See Hydrogen phosphide
Phosphamidon (061)	1965 (T), 1966 (T), 1968 (T,R), 1969 (R), 1972 (R), 1974 (R), 1982 (T), 1985 (T), 1986 (T)
Phoxim (141)	1982 (T), 1983 (R), 1984 (T,R), 1986 (R), 1987 (R), 1988 (R)
Piperonyl butoxide (062)	1965 (T,R), 1966 (T,R), 1967 (R), 1969 (R), 1972(T,R), 1992 (T,R), 1995 (T), 2001 (R), 2002 (R)
Pirimicarb (101)	1976 (T,R), 1978 (T,R), 1979 (R), 1981 (T,R), 1982 (T), 1985 (R), 2004 (T), 2006 (R)
Pirimiphos-methyl (086)	1974 (T,R), 1976 (T,R), 1977 (R), 1979 (R), 1983 (R), 1985 (R), 1992 (T), 1994 (R), 2003 (R), 2004 (R, corr. to 2003 report), 2006 (T)
Prochloraz (142)	1983 (T,R), 1985 (R), 1987 (R), 1988 (R), 1989 (R), 1990 (R), 1991 (corr. to 1990 report, Annex I, and R evaluation), 1992 (R), 2001 (T), 2004 (R)
Procymidone(136)	1981 (R), 1982 (T), 1989 (T,R), 1990 (R), 1991 (corr. to 1990 Annex I), 1993 (R), 1998 (R), 2007 (T)
Profenofos (171)	1990 (T,R), 1992 (R), 1994 (R), 1995 (R), 2007 (T)
Propamocarb (148)	1984 (T,R), 1986 (T,R), 1987 (R), 2005 (T), 2006 (R)
Propargite (113)	1977 (T,R), 1978 (R), 1979 (R), 1980 (T,R),

	1982 (T,R), 1999 (T), 2002 (R), 2006 (R)
Propham (183)	1965 (T), 1992 (T,R)
Propiconazole (160)	1987 (T,R), 1991 (R), 1994 (R), 2004 (T), 2006 (R), 2007 (R)
Propineb (105)	1977 (T,R), 1980 (T), 1983 (T), 1984 (R), 1985 (T,R), 1993 (T,R), 2004 (R)
Propoxur (075)	1973 (T,R), 1977 (R), 1981 (R), 1983 (R), 1989 (T), 1991 (R), 1996 (R)
Propylenethiourea (PTU, 150)	1993 (T,R), 1994 (R), 1999 (T)
Pyraclostrobin (210)	2003 (T), 2004 (R), 2006 (R)
Pyrazophos (153)	1985 (T,R), 1987 (R), 1992 (T,R), 1993 (R)
Pyrethrins (063)	1965 (T), 1966 (T,R), 1967 (R), 1968 (R), 1969 (R), 1970 (T), 1972 (T,R), 1974 (R), 1999 (T), 2000 (R), 2003 (T,R), 2005 (R)
Pyrimethanil (226)	2007 (T, R)
Pyriproxyfen (200)	1999 (R,T), 2000 (R), 2001 (T)
Quinoxyfen (222)	2006 (T, R)
Quintozene (064)	1969 (T,R) 1973 (T,R), 1974 (R), 1975 (T,R), 1976 (Annex I, corr. to 1975 R evaluation), 1977 (T,R), 1995 (T,R), 1998 (R)
Spinosad (203)	2001 (T,R, 2004 (R)
Sulfuryl fluoride (218)	2005 (T,R)
2,4,5-T (121)	1970 (T,R), 1979 (T,R), 1981 (T)
Tebuconazole (189)	1994 (T,R), 1996 (corr. to Annex II of 1995 report), 1997 (R)
Tebufenozide (196)	1996 (T,R), 1997 (R), 1999 (R), 2001 (T,R), 2003(T)
Tecnazine (115)	1974 (T,R), 1978 (T,R), 1981 (R), 1983 (T), 1987 (R), 1989 (R), 1994 (T,R)
Teflubenzuron (190)	1994 (T), 1996 (R)
Temephos	2006 (T)
Terbufos (167)	1989 (T,R), 1990 (T,R), 2003 (T), 2005 (R)
Thiabendazole (065)	1970 (T,R), 1971 (R), 1972 (R), 1975 (R), 1977 (T,R), 1979 (R), 1981 (R), 1997 (R), 2000 (R), 2006 (T, R)
Thiacloprid (223)	2006 (T, R)
Thiodicarb (154)	1985 (T,R), 1986 (T), 1987 (R), 1988 (R), 2000 (T), 2001 (R)
Thiometon (076)	1969 (T,R), 1973 (T,R), 1976 (R), 1979 (T,R), 1988 (R)
Thiophanate-methyl (077)	1973 (T,R), 1975 (T,R), 1977 (T), 1978 (R), 1988 (R), 2002 (R), 1990 (R), 1994 (R), 1995 (T,E), 1998 (T,R), 2006 (T)
Thiram (105)	See Dithiocarbamates, 1965 (T), 1967 (T,R), 1970 (T,R), 1974 (T), 1977 (T), 1983 (R), 1984 (R), 1985 (T,R), 1987 (T), 1988 (R), 1989 (R), 1992 (T), 1996 (R)
Tolclofos-methyl (191)	1994 (T,R) 1996 (corr. to Annex II of 1995 report)

Tolylfluanid (162)	1988 (T,R), 1990 (R), 1991 (corr. to 1990 report), 2002 (T,R), 2003 (R)
Toxaphene	See Camphechlor
Triadimefon (133)	1979 (R), 1981 (T,R), 1983 (T,R), 1984 (R), 1985 (T,R), 1986 (R), 1987 (R and corr. to 1986 R evaluation), 1988 (R), 1989 (R), 1992 (R), 1995 (R), 2004 (T), 2007 (R)
Triadimenol (168)	1989 (T, R), 1992 (R), 1995 (R), 2004 (T), 2007 (R)
Triazolylalanine	1989 (T, R)
Triazophos (143)	1982 (T), 1983 (R), 1984 (corr. to 1983 report, Annex I), 1986 (T, R), 1990 (R), 1991 (T and corr. to 1990 R evaluation), 1992 (R), 1993 (T,R), 2002 (T), 2007 (R)
Trichlorfon (066)	1971 (T,R), 1975 (T,R), 1978 (T,R), 1987 (R)
Trichloronat	1971 (T,R)
Trichloroethylene	1968 (R)
Tricyclohexyltin hydroxide	See Cyhexatin
Trifloxystrobin (213)	2004 (T, R)
Triforine (116)	1977 (T), 1978 (T, R), 1997 (T)
Triphenyltin compounds	See Fentin compounds
Vamidothion (078)	1973 (T, R), 1982 (T), 1985 (T,R), 1987 (R), 1988 (T), 1990 (R), 1992 (R)
Vinclozolin (159)	1986 (T, R), 1987 (R and corr. to 1986 report and R evaluation), 1988 (T,R), 1989 (R), 1990 (R), 1992 (R), 1995 (T)
Zineb (105)	See Dithiocarbamates, 1965 (T), 1967 (T, R), 1993 (T)
Ziram (105)	See Dithiocarbamates, 1965 (T), 1967 (T, R), 1996 (T, R)
Zoxamide (227)	2007 (T, R)

ANNEX 3: INTERNATIONAL ESTIMATED DAILY INTAKES OF PESTICIDE RESIDUES

13 Clusters:	A	B	C	D	E	F	G	H	I	J	K	L	M
Regional diet:	Africa	Africa/Europe/Middle East	Africa/Middle East	Europe/Middle East	Europe	Europe	Far East	Latin America	Africa	Africa	Latin America	Far East	Europe/La–tin America

AMINOPYRALID (220) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0001 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
GC 0640	Barley (incl pot, incl pearled, incl flour & grits, incl beer)	0.01	40,6	0,4	16,8	0,2	93,9	0,9	13,2	0,1	48,6	0,5	36,1	0,4
MO 1280	Cattle kidney	0,1	0,4	0,0	4,4	0,4	0,0	0,0	0,9	0,1	0,0	0,0	0,6	0,1
MO 1281	Cattle liver	0.01	0,4	0,0	4,4	0,0	1,7	0,0	0,9	0,0	1,0	0,0	0,6	0,0
PE 0112	Eggs	0.01	2,5	0,0	29,7	0,3	25,1	0,3	24,5	0,2	37,8	0,4	27,4	0,3
MM 0095	Meat from mammals other than marine mammals	0.01	27,7	0,3	116,5	1,2	38,5	0,4	55,1	0,6	90,2	0,9	131,3	1,3
ML 0106	Milks (excl processed products)	0.01	68,8	0,7	190,6	1,9	79,4	0,8	302,6	3,0	179,6	1,8	237,9	2,4
GC 0647	Oats (incl rolled)	0.01	1,4	0,0	0,6	0,0	0,2	0,0	4,2	0,0	5,7	0,1	8,9	0,1
PM 0110	Poultry meat	0.01	7,1	0,1	58,5	0,6	31,9	0,3	24,0	0,2	61,0	0,6	27,3	0,3
PO 0111	Poultry, edible offal of	0.01	0,4	0,0	0,4	0,0	1,7	0,0	0,1	0,0	0,6	0,0	0,2	0,0
MO 1288	Sheep kidney	0,1	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
MO 1289	Sheep liver	0.01	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
GC 0653	Triticale (incl flour)	0.01	0,0	0,0	115,8	1,2	0,0	0,0	0,0	0,0	0,3	0,0	0,0	0,0
GC 0654	Wheat (incl bulgur wholemeal, incl flour)	0.01	88,4	0,9	396,3	4,0	426,5	4,3	390,2	3,9	236,3	2,4	216,0	2,2
CM 0654	Wheat bran, unprocessed	0.024	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
	Total intake (µg/person)=			2,4		9,7		7,0		8,2		6,6		6,9
	Bodyweight per region (kg bw) =			60		60		60		60		60		60
	ADI (µg/person)=			54000		54000		54000		54000		54000		54000

AMINOPYRALID (220) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0001 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
	%ADI=			0,0%		0,0%		0,0%		0,0%		0,0%		0,0%
	Rounded %ADI=			0%		0%		0%		0%		0%		0%

AMINOPYRALID (220) International Estimated Daily Intake (IEDI) ADI = 0 - 0.9000 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person													
			G		H		I		J		K		L		M	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
GC 0640	Barley (incl pot, incl pearled, incl flour & grits, incl beer)	0.01	5.9	0.1	20.5	0.2	5.9	0.1	2.5	0.0	20.2	0.2	16.8	0.2	43.8	0.4
MO 1280	Cattle kidney	0.1	0.0	0.0	0.9	0.1	0.4	0.0	0.2	0.0	0.7	0.1	0.0	0.0	0.0	0.0
MO 1281	Cattle liver	0.01	0.0	0.0	0.9	0.0	0.4	0.0	0.2	0.0	0.7	0.0	0.0	0.0	0.4	0.0
PE 0112	Eggs	0.01	22.1	0.2	71.5	0.7	16.6	0.2	5.1	0.1	17.6	0.2	35.2	0.4	57.4	0.6
MM 0095	Meat from mammals other than marine mammals	0.01	54.8	0.5	89.4	0.9	30.6	0.3	28.6	0.3	82.1	0.8	61.1	0.6	158.3	1.6
ML 0106	Milks (excl processed products)	0.01	66.0	0.7	121.1	1.2	81.6	0.8	102.4	1.0	207.7	2.1	57.0	0.6	287.9	2.9
GC 0647	Oats (incl rolled)	0.01	0.2	0.0	2.0	0.0	0.8	0.0	0.0	0.0	3.5	0.0	0.7	0.0	7.6	0.1
PM 0110	Poultry meat	0.01	17.6	0.2	131.3	1.3	25.1	0.3	4.7	0.0	145.9	1.5	27.7	0.3	115.1	1.2
PO 0111	Poultry, edible offal of	0.01	0.4	0.0	1.0	0.0	1.9	0.0	0.0	0.0	0.7	0.0	1.0	0.0	0.3	0.0
MO 1288	Sheep kidney	0.1	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
MO 1289	Sheep liver	0.01	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
GC 0653	Triticale (incl flour)	0.01	1.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
GC 0654	Wheat (incl bulgur wholemeal, incl flour)	0.01	172.9	1.7	79.0	0.8	68.1	0.7	41.9	0.4	114.1	1.1	103.4	1.0	234.2	2.3
CM 0654	Wheat bran, unprocessed	0.024	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
	Total intake (µg/person)=			3.4		5.3		2.4		1.9		6.0		3.0		9.1
	Bodyweight per region (kg bw) =			55		60		60		60		60		55		60
	ADI (µg/person)=			49500		54000		54000		54000		54000		49500		54000
	%ADI=			0.0%		0.0%		0.0%		0.0%		0.0%		0.0%		0.0%
	Rounded %ADI=			0%		0%		0%		0%		0%		0%		0%

Annex 3

CARBARYL (008) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0080 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
FB 0265	Cranberries	1.4	0.1	0.1	0.0	0.0	0.0	0.0	0.3	0.4	0.0	0.0	0.6	0.8
VO 0444	Peppers, chilli	0.63	0.7	0.4	14.9	9.4	4.1	2.6	3.2	2.0	3.1	2.0	2.0	1.3
	Total intake (µg/person)=			0.6		9.4		2.6		2.4		2.0		2.1
	Bodyweight per region (kg bw) =			60		60		60		60		60		60
	ADI (µg/person)=			480		480		480		480		480		480
	%ADI=			0.1%		2.0%		0.5%		0.5%		0.4%		0.4%
	Rounded %ADI=			0%		2%		1%		1%		0%		0%

CARBARYL (008) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0080 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person													
			G		H		I		J		K		L		M	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
FB 0265	Cranberries	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.5	3.5
VO 0444	Peppers, chilli	0.63	8.7	5.5	13.0	8.2	4.2	2.6	4.7	3.0	1.7	1.1	2.6	1.6	4.4	2.8
	Total intake (µg/person)=			5.5		8.2		2.6		3.0		1.1		1.6		6.3
	Bodyweight per region (kg bw) =			55		60		60		60		60		55		60
	ADI (µg/person)=			440		480		480		480		480		440		480
	%ADI=			1.2%		1.7%		0.6%		0.6%		0.2%		0.4%		1.3%
	Rounded %ADI=			1%		2%		1%		1%		0%		0%		1%

CLOFENTEZINE (156) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0200 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day Intake = daily intake: µg/person A diet	A intake	B diet	B intake	C diet	C intake	D diet	D intake	E diet	E intake	F diet	F intake
FC 0001	Citrus fruit (incl lemon juice, incl mandarin juice, excl orange juice, incl grapefruit juice, incl NES juice)	0.02	15.7	0.3	96.7	1.9	55.3	1.1	25.3	0.5	23.4	0.5	16.2	0.3
JF 0004	Orange juice	0.014	0.0	0.0	2.1	0.0	4.4	0.1	1.4	0.0	16.2	0.2	22.6	0.3
TN 0085	Tree nuts	0.05	4.2	0.2	21.5	1.1	3.9	0.2	3.0	0.2	5.5	0.3	10.2	0.5
FP 0009	Pome fruit (excl apple juice)	0.05	0.5	0.0	79.9	4.0	21.8	1.1	43.6	2.2	51.5	2.6	35.1	1.8
JF 0226	Apple juice	0.0055	0.0	0.0	2.8	0.0	0.1	0.0	1.1	0.0	6.8	0.0	7.4	0.0
FS 0012	Stone fruit (incl dried plums, incl dried apricots)	0.11	0.7	0.1	44.7	4.9	14.1	1.6	26.9	3.0	27.7	3.0	10.0	1.1
FB 0021	Currants, red, black, white	0.04	0.0	0.0	0.0	0.0	0.0	0.0	2.2	0.1	3.1	0.1	2.0	0.1
FB 0269	Grape (excl dried, excl juice, excl wine)	0.25	1.9	0.5	9.2	2.3	23.8	6.0	9.8	2.5	0.0	0.0	0.0	0.0
DF 0269	Grape, dried (= currants, raisins and sultanas)	0.28	0.0	0.0	2.9	0.8	0.4	0.1	0.4	0.1	2.3	0.6	1.7	0.5
JF 0269	Grape juice	0	0.0	0.0	0.1	0.0	0.1	0.0	0.1	0.0	1.4	0.0	1.0	0.0
-	Wine	0.011	1.3	0.0	76.8	0.8	1.1	0.0	15.4	0.2	68.8	0.8	25.6	0.3
FB 0275	Strawberry	0.72	0.0	0.0	5.0	3.6	2.0	1.4	1.7	1.2	5.2	3.7	4.1	3.0
VC 0046	Melons, except watermelon	0	3.6	0.0	26.7	0.0	22.6	0.0	11.5	0.0	5.6	0.0	2.0	0.0
VC 0424	Cucumber	0.125	0.3	0.0	12.7	1.6	5.9	0.7	11.5	1.4	6.1	0.8	7.1	0.9
VO 0448	Tomato (incl juice, incl paste, incl peeled)	0.09	11.8	1.1	185.0	16.7	118.0	10.6	60.7	5.5	31.6	2.8	40.9	3.7
MM 0095	Meat from mammals other than marine mammals	0	27.7	0.0	116.5	0.0	38.5	0.0	55.1	0.0	90.2	0.0	131.3	0.0
MO 0105	Edible offal (mammalian)	0.05	3.9	0.2	14.4	0.7	5.2	0.3	11.8	0.6	11.7	0.6	7.6	0.4
PM 0110	Poultry meat	0	7.1	0.0	58.5	0.0	31.9	0.0	24.0	0.0	61.0	0.0	27.3	0.0
PO 0111	Poultry, edible offal of	0	0.4	0.0	0.4	0.0	1.7	0.0	0.1	0.0	0.6	0.0	0.2	0.0
ML 0106	Milks (excl processed products)	0	68.8	0.0	190.6	0.0	79.4	0.0	302.6	0.0	179.6	0.0	237.9	0.0
PE 0112	Eggs	0	2.5	0.0	29.7	0.0	25.1	0.0	24.5	0.0	37.8	0.0	27.4	0.0
	Total intake (µg/person)=			2.4		38.5		23.1		17.4		16.1		12.8
	Bodyweight per region (kg bw) =			60		60		60		60		60		60
	ADI (µg/person)=			1200		1200		1200		1200		1200		1200
	%ADI=			0.2%		3.2%		1.9%		1.4%		1.3%		1.1%
	Rounded %ADI=			0%		3%		2%		1%		1%		1%

Annex 3

CLOFENTEZINE (156) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0200 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day Intake = daily intake: µg/person													
			G		H		I		J		K		L		M	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
FC 0001	Citrus fruit (incl lemon juice, incl mandarin juice, excl orange juice, incl grapefruit juice, incl NES juice)	0.02	16.9	0.3	155.0	3.1	8.6	0.2	42.5	0.9	220.5	4.4	28.9	0.6	30.1	0.6
JF 0004	Orange juice	0.014	0.2	0.0	1.0	0.0	3.5	0.0	0.0	0.0	1.3	0.0	6.4	0.1	56.8	0.8
TN 0085	Tree nuts	0.05	16.3	0.8	15.7	0.8	9.7	0.5	1.9	0.1	19.1	1.0	29.0	1.5	5.6	0.3
FP 0009	Pome fruit (excl apple juice)	0.05	20.8	1.0	11.6	0.6	3.3	0.2	0.1	0.0	10.7	0.5	23.6	1.2	36.9	1.8
JF 0226	Apple juice	0.0055	0.1	0.0	0.5	0.0	0.1	0.0	0.0	0.0	0.7	0.0	0.9	0.0	5.7	0.0
FS 0012	Stone fruit (incl dried plums, incl dried apricots)	0.11	7.0	0.8	4.9	0.5	1.4	0.2	0.1	0.0	5.5	0.6	5.5	0.6	19.4	2.1
FB 0021	Currants, red, black, white	0.04	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
FB 0269	Grape (excl dried, excl juice, excl wine)	0.25	1.2	0.3	2.6	0.7	0.0	0.0	0.2	0.0	0.0	0.0	3.7	0.9	0.0	0.0
DF 0269	Grape, dried (= currants, raisins and sultanas)	0.28	0.0	0.0	0.2	0.1	0.2	0.1	0.0	0.0	0.3	0.1	0.4	0.1	2.6	0.7
JF 0269	Grape juice	0	0.0	0.0	0.1	0.0	1.0	0.0	0.0	0.0	0.6	0.0	0.4	0.0	3.6	0.0
-	Wine	0.011	1.0	0.0	0.9	0.0	6.8	0.1	0.1	0.0	3.4	0.0	3.6	0.0	31.0	0.3
FB 0275	Strawberry	0.72	0.0	0.0	1.8	1.3	0.1	0.1	0.0	0.0	0.3	0.2	6.2	4.5	5.9	4.2
VC 0046	Melons, except watermelon	0	7.5	0.0	6.1	0.0	0.7	0.0	1.4	0.0	2.5	0.0	6.9	0.0	12.4	0.0
VC 0424	Cucumber	0.125	7.9	1.0	0.6	0.1	0.2	0.0	0.0	0.0	0.4	0.1	5.5	0.7	5.3	0.7
VO 0448	Tomato (incl juice, incl paste, incl peeled)	0.09	23.5	2.1	31.7	2.9	15.0	1.4	16.2	1.5	35.6	3.2	9.9	0.9	103.0	9.3
MM 0095	Meat from mammals other than marine mammals	0	54.8	0.0	89.4	0.0	30.6	0.0	28.6	0.0	82.1	0.0	61.1	0.0	158.3	0.0
MO 0105	Edible offal (mammalian)	0.05	4.8	0.2	10.7	0.5	4.0	0.2	4.0	0.2	6.5	0.3	6.6	0.3	5.6	0.3
PM 0110	Poultry meat	0	17.6	0.0	131.3	0.0	25.1	0.0	4.7	0.0	145.9	0.0	27.7	0.0	115.1	0.0
PO 0111	Poultry, edible offal of	0	0.4	0.0	1.0	0.0	1.9	0.0	0.0	0.0	0.7	0.0	1.0	0.0	0.3	0.0
ML 0106	Milks (excl processed products)	0	66.0	0.0	121.1	0.0	81.6	0.0	102.4	0.0	207.7	0.0	57.0	0.0	287.9	0.0
PE 0112	Eggs	0	22.1	0.0	71.5	0.0	16.6	0.0	5.1	0.0	17.6	0.0	35.2	0.0	57.4	0.0
	Total intake (µg/person)=			6.6		10.5		2.8		2.7		10.4		11.4		21.2
	Bodyweight per region (kg bw) =			55		60		60		60		60		55		60
	ADI (µg/person)=			1100		1200		1200		1200		1200		1100		1200
	%ADI=			0.6%		0.9%		0.2%		0.2%		0.9%		1.0%		1.8%
	Rounded %ADI=			1%		1%		0%		0%		1%		1%		2%

CYFLUTHRIN (157)/BETA-CYFLUTHRIN (228) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0400 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
FP 0226	Apple (incl juice)	0.06	0.3	0.0	60.5	3.6	18.5	1.1	39.9	2.4	50.8	3.0	39.4	2.4
VB 0400	Broccoli	0.2	0.0	0.0	0.7	0.1	1.2	0.2	0.1	0.0	4.2	0.8	4.0	0.8
VB 0041	Cabbage, head	0.25	1.2	0.3	14.4	3.6	2.7	0.7	16.4	4.1	15.4	3.9	18.5	4.6
MO 1280	Cattle kidney	0.01	0.4	0.0	4.4	0.0	0.0	0.0	0.9	0.0	0.0	0.0	0.6	0.0
MO 1281	Cattle liver	0.01	0.4	0.0	4.4	0.0	1.7	0.0	0.9	0.0	1.0	0.0	0.6	0.0
VB 0404	Cauliflower	0.24	0.1	0.0	5.2	1.2	1.2	0.3	0.1	0.0	1.7	0.4	0.1	0.0
FC 0001	Citrus fruit (incl lemon juice, incl mandarin juice, incl orange juice, incl grapefruit juice, incl NES juice)	0.06	15.7	0.9	100.5	6.0	63.2	3.8	27.8	1.7	52.6	3.2	56.9	3.4
OR 0691	Cotton seed oil, edible	0.19	0.9	0.2	4.9	0.9	1.7	0.3	6.6	1.3	0.0	0.0	0.3	0.1
VO 0440	Egg plant (= aubergine)	0.06	1.7	0.1	17.5	1.1	12.3	0.7	1.7	0.1	0.8	0.0	0.4	0.0
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0.0378	5.5	0.2	23.3	0.9	7.7	0.3	11.0	0.4	18.0	0.7	26.3	1.0
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0.01	22.2	0.2	93.2	0.9	30.8	0.3	44.1	0.4	72.2	0.7	105.0	1.1
ML 0106	Milks (excl processed products)	0.0022	68.8	0.2	190.6	0.4	79.4	0.2	302.6	0.7	179.6	0.4	237.9	0.5
FP 0230	Pear	0.06	0.1	0.0	22.3	1.3	2.8	0.2	4.8	0.3	10.7	0.6	6.8	0.4
VO 0051	Peppers	0.06	1.4	0.1	29.9	1.8	13.0	0.8	6.3	0.4	6.2	0.4	4.0	0.2
VO 0444	Peppers, chilli	0.06	0.7	0.0	14.9	0.9	4.1	0.2	3.2	0.2	3.1	0.2	2.0	0.1
VR 0589	Potato (incl flour, frozen, starch, tapioca)	0	19.1	0.0	160.8	0.0	61.2	0.0	243.6	0.0	230.1	0.0	204.7	0.0
PM 0110	Poultry meat: 10% as fat	0	0.7	0.0	5.9	0.0	3.2	0.0	2.4	0.0	6.1	0.0	2.7	0.0
PM 0110	Poultry meat: 90% as muscle	0	6.4	0.0	52.7	0.0	28.7	0.0	21.6	0.0	54.9	0.0	24.6	0.0
PO 0111	Poultry, edible offal of	0	0.4	0.0	0.4	0.0	1.7	0.0	0.1	0.0	0.6	0.0	0.2	0.0
SO 0495	Rape seed (incl oil)	0.05	0.9	0.0	1.8	0.1	2.5	0.1	1.9	0.1	35.7	1.8	26.1	1.3
MO 1288	Sheep kidney	0.01	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
MO 1289	Sheep liver	0.01	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
VO 0448	Tomato (incl juice, incl paste, incl peeled)	0.07	11.8	0.8	185.0	13.0	118.0	8.3	60.7	4.2	31.6	2.2	40.9	2.9
	Total intake (µg/person)=			3.2		36.0		17.5		16.3		18.4		18.8
	Bodyweight per region (kg bw) =			60		60		60		60		60		60
	ADI (µg/person)=			2400		2400		2400		2400		2400		2400
	%ADI=			0.1%		1.5%		0.7%		0.7%		0.8%		0.8%
	Rounded %ADI=			0%		2%		1%		1%		1%		1%

Annex 3

CYFLUTHRIN (157) /BETA-CYFLUTHRIN (228) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0400 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day Intake = daily intake: µg/person													
			G		H		I		J		K		L		M	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
FP 0226	Apple (incl juice)	0.06	14.4	0.9	10.1	0.6	2.2	0.1	0.0	0.0	9.8	0.6	17.9	1.1	36.3	2.2
VB 0400	Broccoli	0.2	3.2	0.6	7.8	1.6	0.0	0.0	0.0	0.0	0.3	0.1	0.4	0.1	6.6	1.3
VB 0041	Cabbage, head	0.25	10.0	2.5	1.0	0.3	7.2	1.8	1.0	0.3	1.4	0.4	23.9	6.0	17.0	4.3
MO 1280	Cattle kidney	0.01	0.0	0.0	0.9	0.0	0.4	0.0	0.2	0.0	0.7	0.0	0.0	0.0	0.0	0.0
MO 1281	Cattle liver	0.01	0.0	0.0	0.9	0.0	0.4	0.0	0.2	0.0	0.7	0.0	0.0	0.0	0.4	0.0
VB 0404	Cauliflower	0.24	3.2	0.8	0.1	0.0	0.3	0.1	0.1	0.0	0.6	0.1	0.4	0.1	1.4	0.3
FC 0001	Citrus fruit (incl lemon juice, incl mandarin juice, incl orange juice, incl grapefruit juice, incl NES juice)	0.06	17.3	1.0	156.8	9.4	14.9	0.9	42.5	2.6	222.8	13.4	40.4	2.4	132.3	7.9
OR 0691	Cotton seed oil, edible	0.19	1.0	0.2	0.7	0.1	1.0	0.2	1.4	0.3	1.5	0.3	5.5	1.0	1.2	0.2
VO 0440	Egg plant (= aubergine)	0.06	20.1	1.2	0.1	0.0	0.6	0.0	6.3	0.4	0.5	0.0	6.3	0.4	0.7	0.0
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0.0378	11.0	0.4	17.9	0.7	6.1	0.2	5.7	0.2	16.4	0.6	12.2	0.5	31.7	1.2
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0.01	43.8	0.4	71.5	0.7	24.5	0.2	22.9	0.2	65.7	0.7	48.9	0.5	126.6	1.3
ML 0106	Milks (excl processed products)	0.0022	66.0	0.1	121.1	0.3	81.6	0.2	102.4	0.2	207.7	0.5	57.0	0.1	287.9	0.6
FP 0230	Pear	0.06	6.4	0.4	1.9	0.1	1.2	0.1	0.0	0.0	1.8	0.1	6.9	0.4	7.8	0.5
VO 0051	Peppers	0.06	8.7	0.5	22.4	1.3	8.4	0.5	9.4	0.6	3.3	0.2	5.3	0.3	8.9	0.5
VO 0444	Peppers, chilli	0.06	8.7	0.5	13.0	0.8	4.2	0.3	4.7	0.3	1.7	0.1	2.6	0.2	4.4	0.3
VR 0589	Potato (incl flour, frozen, starch, tapioca)	0	52.7	0.0	57.1	0.0	50.1	0.0	4.3	0.0	54.7	0.0	41.0	0.0	168.0	0.0
PM 0110	Poultry meat: 10% as fat	0	1.8	0.0	13.1	0.0	2.5	0.0	0.5	0.0	14.6	0.0	2.8	0.0	11.5	0.0
PM 0110	Poultry meat: 90% as muscle	0	15.8	0.0	118.2	0.0	22.6	0.0	4.2	0.0	131.3	0.0	24.9	0.0	103.6	0.0
PO 0111	Poultry, edible offal of	0	0.4	0.0	1.0	0.0	1.9	0.0	0.0	0.0	0.7	0.0	1.0	0.0	0.3	0.0
SO 0495	Rape seed (incl oil)	0.05	9.9	0.5	5.9	0.3	0.3	0.0	1.0	0.1	0.0	0.0	15.5	0.8	9.9	0.5
MO 1288	Sheep kidney	0.01	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
MO 1289	Sheep liver	0.01	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
VO 0448	Tomato (incl juice, incl paste, incl peeled)	0.07	23.5	1.6	31.7	2.2	15.0	1.1	16.2	1.1	35.6	2.5	9.9	0.7	103.0	7.2
	Total intake (µg/person)=			11.8		18.4		5.7		6.2		19.5		14.5		28.4
	Bodyweight per region (kg bw) =			55		60		60		60		60		55		60
	ADI (µg/person)=			2200		2400		2400		2400		2400		2200		2400
	%ADI=			0.5%		0.8%		0.2%		0.3%		0.8%		0.7%		1.2%
	Rounded %ADI=			1%		1%		0%		0%		1%		1%		1%

CYROMAZINE (169) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0600 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
VS 0620	Artichoke globe	1	0.0	0.0	10.0	10.0	2.1	2.1	0.1	0.1	0.8	0.8	0.1	0.1
VD 0071	Beans (dry)	1	15.8	15.8	6.1	6.1	1.7	1.7	6.3	6.3	1.8	1.8	5.0	5.0
VB 0400	Broccoli	0.15	0.0	0.0	0.7	0.1	1.2	0.2	0.1	0.0	4.2	0.6	4.0	0.6
VB 0403	Cabbage, Savoy	0.26	0.3	0.1	11.7	3.0	0.0	0.0	5.5	1.4	3.2	0.8	15.0	3.9
VS 0624	Celery	0.58	0.0	0.0	0.9	0.5	0.0	0.0	2.0	1.2	1.5	0.9	0.0	0.0
VC 0424	Cucumber	0.48	0.3	0.1	12.7	6.1	5.9	2.8	11.5	5.5	6.1	2.9	7.1	3.4
MO 0105	Edible offal (mammalian)	0.01	3.9	0.0	14.4	0.1	5.2	0.1	11.8	0.1	11.7	0.1	7.6	0.1
VO 0440	Egg plant	0.16	1.7	0.3	17.5	2.8	12.3	2.0	1.7	0.3	0.8	0.1	0.4	0.1
PE 0112	Eggs	0.07	2.5		29.7		25.1		24.5		37.8		27.4	
VL 0482	Lettuce, head	0.34	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
VL 0483	Lettuce, leaf	0.34	0.0	0.0	9.2	3.1	1.0	0.3	0.1	0.0	5.4	1.8	18.0	6.1
VP 0534	Lima bean (green pods and/or immature seeds)	0.23	0.0	0.0	0.0	0.0	0.0	0.0	0.9	0.2	0.0	0.0	0.1	0.0
MF 0100	Mammalian fats (except milk fats)	0	0.8	0.0	10.0	0.0	0.9	0.0	6.6	0.0	11.8	0.0	3.7	0.0
FI 0345	Mango (incl juice, pulp)	0.12	6.3	0.8	1.0	0.1	4.6	0.6	0.2	0.0	0.7	0.1	0.3	0.0
MM 0095	Meat from mammals other than marine mammals	0.01	27.7	0.3	116.5	1.2	38.5	0.4	55.1	0.6	90.2	0.9	131.3	1.3
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0	5.5	0.0	23.3	0.0	7.7	0.0	11.0	0.0	18.0	0.0	26.3	0.0
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0	22.2	0.0	93.2	0.0	30.8	0.0	44.1	0.0	72.2	0.0	105.0	0.0
VC 0046	Melons, except watermelon	0.04	3.6	0.1	26.7	1.1	22.6	0.9	11.5	0.5	5.6	0.2	2.0	0.1
ML 0106	Milks (excl processed products)	0.005	68.8	0.34	190.6	1.0	79.4	0.4	302.6	1.5	179.6	0.9	237.9	1.2
VL 0485	Mustard greens	2.7	0.3	0.8	0.3	0.8	0.0	0.0	5.5	14.9	0.0	0.0	1.9	5.1
VO 0442	Okra	0.16	3.9	0.6	1.0	0.2	5.3	0.8	0.1	0.0	0.0	0.0	0.0	0.0
VA 0385	Onion, bulb (= dry + green onion)	0.05	5.5	0.3	49.5	2.5	33.0	1.7	31.3	1.6	23.2	1.2	14.6	0.7
VO 0051	Peppers	0.16	1.4	0.2	29.9	4.8	13.0	2.1	6.3	1.0	6.2	1.0	4.0	0.6
PM 0110	Poultry meat	0.05	7.1	0.4	58.5	2.9	31.9	1.6	24.0	1.2	61.0	3.1	27.3	1.4
PM 0110	Poultry meat: 10% as fat	0	0.7	0.0	5.9	0.0	3.2	0.0	2.4	0.0	6.1	0.0	2.7	0.0
PM 0110	Poultry meat: 90% as muscle	0	6.4	0.0	52.7	0.0	28.7	0.0	21.6	0.0	54.9	0.0	24.6	0.0
PO 0111	Poultry, edible offal of	0.065	0.4	0.0	0.4	0.0	1.7	0.1	0.1	0.0	0.6	0.0	0.2	0.0
PF 0111	Poultry, fats	0	0.1	0.0	0.1	0.0	0.1	0.0	0.0	0.0	0.4	0.0	0.1	0.0

Annex 3

CYROMAZINE (169) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0600 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
VL 0502	Spinach	2	0.0	0.0	5.0	10.0	1.1	2.2	0.1	0.2	2.6	5.2	0.1	0.2
VA 0389	Spring onion	0.345	0.3	0.1	1.0	0.3	1.4	0.5	0.3	0.1	0.3	0.1	0.6	0.2
VC 0431	Squash, summer (= courgette)	0.16	0.0	0.0	8.3	1.4	11.4	1.8	7.3	1.2	3.2	0.5	0.3	0.1
VO 0448	Tomato (incl juice, paste, peeled)	0.16	11.8	1.9	185.0	29.6	118.0	18.9	60.7	9.7	31.6	5.1	40.9	6.5
JF 0448	Tomato juice	0.12	5.2	0.6	0.5	0.1	0.4	0.0	2.1	0.2	6.9	0.8	15.2	1.8
-d	Tomato paste	0.34	0.5	0.1	1.3	0.4	3.5	1.0	1.0	0.3	3.8	1.1	4.5	1.3
	Total intake (µg/person)=			25.6		88.3		42.5		48.4		39.2		39.8
	Bodyweight per region (kg bw) =			60		60		60		60		60		60
	ADI (µg/person)=			3600		3600		3600		3600		3600		3600
	%ADI=			0.7%		2.4%		1.2%		1.3%		1.1%		1.1%
	Rounded %ADI=			1%		2%		1%		1%		1%		1%

CYROMAZINE (169) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0600 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person													
			G		H		I		J		K		L		M	
			diet	intake	Diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
VS 0620	Artichoke globe	1	0.1	0.1	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.0	1.0
VD 0071	Beans (dry)	1	3.4	3.4	25.5	25.5	7.8	7.8	2.1	2.1	44.7	44.7	5.5	5.5	7.3	7.3
VB 0400	Broccoli	0.15	3.2	0.5	7.8	1.2	0.0	0.0	0.0	0.0	0.3	0.0	0.4	0.1	6.6	1.0
VB 0403	Cabbage, Savoy	0.26	3.4	0.9	0.4	0.1	2.4	0.6	0.3	0.1	0.4	0.1	7.9	2.1	5.8	1.5
VS 0624	Celery	0.58	0.0	0.0	0.3	0.2	0.0	0.0	0.0	0.0	1.0	0.6	0.0	0.0	4.2	2.0
VC 0424	Cucumber	0.48	7.9	3.8	0.6	0.3	0.2	0.1	0.0	0.0	0.4	0.2	5.5	2.6	5.3	2.5
MO 0105	Edible offal (mammalian)	0.01	4.8	0.0	10.7	0.1	4.0	0.0	4.0	0.0	6.5	0.1	6.6	0.1	5.6	0.1
VO 0440	Egg plant	0.16	20.1	3.2	0.1	0.0	0.6	0.1	6.3	1.0	0.5	0.1	6.3	1.0	0.7	0.1
PE 0112	Eggs	0.07	22.1		71.5		16.6		5.1		17.6		35.2		57.4	
VL 0482	Lettuce, head	0.34	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
VL 0483	Lettuce, leaf	0.34	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.5	0.9
VP 0534	Lima bean (green pods and/or immature seeds)	0.23	2.5	0.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.0	0.2
MF 0100	Mammalian fats (except milk fats)	0	2.2	0.0	18.6	0.0	0.5	0.0	0.8	0.0	5.7	0.0	4.5	0.0	18.2	0.0

CYROMAZINE (169) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0600 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day Intake = daily intake: µg/person													
			G		H		I		J		K		L		M	
			diet	intake	Diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
FI 0345	Mango (incl juice, pulp)	0.12	12.7	1.5	26.2	3.1	6.1	0.7	12.7	1.5	9.2	1.1	8.0	1.0	1.9	0.2
MM 0095	Meat from mammals other than marine mammals	0.01	54.8	0.5	89.4	0.9	30.6	0.3	28.6	0.3	82.1	0.8	61.1	0.6	158.3	1.6
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0	11.0	0.0	17.9	0.0	6.1	0.0	5.7	0.0	16.4	0.0	12.2	0.0	31.7	0.0
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0	43.8	0.0	71.5	0.0	24.5	0.0	22.9	0.0	65.7	0.0	48.9	0.0	126.6	0.0
VC 0046	Melons, except watermelon	0.04	7.5	0.3	6.1	0.2	0.7	0.0	1.4	0.1	2.5	0.1	6.9	0.3	12.4	0.5
ML 0106	Milks (excl processed products)	0.005	66.0	0.3	121.1	0.6	81.6	0.4	102.4	0.5	207.7	1.0	57.0	0.3	287.9	1.4
VL 0485	Mustard greens	2.7	3.4	9.2	0.4	1.1	2.4	6.5	0.3	0.8	0.5	1.4	7.9	21.3	0.3	0.8
VO 0442	Okra	0.16	4.1	0.7	1.0	0.2	7.0	1.1	15.9	2.5	1.1	0.2	3.9	0.6	0.2	0.0
VA 0385	Onion, bulb (= dry + green onion)	0.05	17.4	0.9	27.9	1.4	7.3	0.4	16.0	0.8	22.8	1.1	34.5	1.7	30.1	1.5
VO 0051	Peppers	0.16	8.7	1.4	22.4	3.6	8.4	1.3	9.4	1.5	3.3	0.5	5.3	0.8	8.9	1.4
PM 0110	Poultry meat	0.05	17.6	0.9	131.3	6.6	25.1	1.3	4.7	0.2	145.9	7.3	27.7	1.4	115.1	5.8
PM 0110	Poultry meat: 10% as fat	0	1.8	0.0	13.1	0.0	2.5	0.0	0.5	0.0	14.6	0.0	2.8	0.0	11.5	0.0
PM 0110	Poultry meat: 90% as muscle	0	15.8	0.0	118.2	0.0	22.6	0.0	4.2	0.0	131.3	0.0	24.9	0.0	103.6	0.0
PO 0111	Poultry, edible offal of	0.065	0.4	0.0	1.0	0.1	1.9	0.1	0.0	0.0	0.7	0.0	1.0	0.1	0.3	0.0
PF 0111	Poultry, fats	0	0.1	0.0	8.2	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.1	0.0	4.2	0.0
VL 0502	Spinach	2	9.4	18.8	0.4	0.8	0.0	0.0	0.0	0.0	0.2	0.4	4.3	8.6	2.0	4.0
VA 0389	Spring onion	0.345	0.1	0.0	4.8	1.7	0.1	0.0	1.0	0.3	1.0	0.3	2.7	0.9	0.6	0.2
VC 0431	Squash, summer (= courgette)	0.16	2.4	0.4	1.5	0.2	0.0	0.0	0.0	0.0	3.8	0.6	2.2	0.3	2.5	0.4
VO 0448	Tomato (incl juice, paste, peeled)	0.16	23.5	3.8	31.7	5.1	15.0	2.4	16.2	2.6	35.6	5.7	9.9	1.6	103.0	16.5
JF 0448	Tomato juice	0.12	0.0	0.0	0.8	0.1	0.1	0.0	7.2	0.7	0.0	0.0	2.4	0.2	45.2	4.5
-d	Tomato paste	0.34	0.1	0.0	2.1	0.7	0.6	0.2	0.4	0.1	0.6	0.2	1.4	0.6	1.2	0.4
	Total intake (µg/person)=			51.0		53.6		23.4		15.3		66.5		51.4		61.3
	Bodyweight per region (kg bw) =			55		60		60		60		60		55		60
	ADI (µg/person)=			3300		3600		3600		3600		3600		3300		3600
	%ADI=			1.4%		1.5%		0.6%		0.4%		1.8%		1.4%		1.7%
	Rounded %ADI=			1%		2%		1%		0%		2%		1%		2%

Annex 3

DIFENOCONAZOLE (224) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0100 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
JF 0226	Apple juice	0.0022	0.0	0.0	2.8	0.0	0.1	0.0	1.1	0.0	6.8	0.0	7.4	0.0
VS 0621	Asparagus	0.02	0.0	0.0	1.1	0.0	0.6	0.0	0.2	0.0	1.2	0.0	0.1	0.0
FI 0327	Banana	0.02	38.8	0.8	17.4	0.3	16.0	0.3	6.6	0.1	21.5	0.4	33.8	0.7
VB 0400	Broccoli	0.065	0.0	0.0	0.7	0.0	1.2	0.1	0.1	0.0	4.2	0.3	4.0	0.3
VB 0402	Brussels sprouts	0.065	0.0	0.0	0.1	0.0	2.8	0.2	5.5	0.4	1.5	0.1	1.9	0.1
VB 0041	Cabbage, head	0.035	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
VR 0577	Carrot	0.05	0.6	0.0	15.1	0.8	8.1	0.4	13.9	0.7	27.1	1.4	28.4	1.4
VB 0404	Cauliflower	0.02	0.1	0.0	5.2	0.1	1.2	0.0	0.1	0.0	1.7	0.0	0.1	0.0
VR 0578	Celeriac	0.12	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
VS 0624	Celery	0.14	0.0	0.0	0.9	0.1	0.0	0.0	2.0	0.3	1.5	0.2	0.0	0.0
FS 0013	Cherries	0.04	0.0	0.0	6.8	0.3	0.9	0.0	6.2	0.2	3.6	0.1	0.4	0.0
MO 0105	Edible offal (mammalian)	0.043	3.9	0.2	14.4	0.6	5.2	0.2	11.8	0.5	11.7	0.5	7.6	0.3
PE 0112	Eggs	0.0020	2.5		29.7		25.1		24.5		37.8		27.4	
VA 0381	Garlic	0	0.4	0.0	3.9	0.0	3.8	0.0	3.7	0.0	1.0	0.0	0.6	0.0
FB 0269	Grape (incl dried, juice, wine)	0.03	1.9	0.1	9.2	0.3	23.8	0.7	9.8	0.3	0.0	0.0	0.0	0.0
JF 0269	Grape juice	0.015	0.0	0.0	0.1	0.0	0.1	0.0	0.1	0.0	1.4	0.0	1.0	0.0
DF 0269	Grape, dried (= currants, raisins and sultanas)	0.036	0.0	0.0	2.9	0.1	0.4	0.0	0.4	0.0	2.3	0.1	1.7	0.1
VA 0384	Leek	0.08	0.3	0.0	5.3	0.4	0.0	0.0	0.2	0.0	4.6	0.4	1.5	0.1
-d	Lettuce and similar (incl witloof chicory sprouts)	0.41	0.2	0.1	23.8	9.8	3.6	1.5	0.6	0.2	11.9	4.9	18.0	7.4
FI 0345	Mango (incl juice, pulp)	0.03	6.3	0.2	1.0	0.0	4.6	0.1	0.2	0.0	0.7	0.0	0.3	0.0
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0.012	5.5	0.1	23.3	0.3	7.7	0.1	11.0	0.1	18.0	0.2	26.3	0.3
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0.01	22.2	0.2	93.2	0.9	30.8	0.3	44.1	0.4	72.2	0.7	105.0	1.1
ML 0106	Milks (excl processed products)	0.001	68.8	0.1	190.6	0.2	79.4	0.1	302.6	0.3	179.6	0.2	237.9	0.2
FS 0245	Nectarine	0.15	0.0	0.0	0.5	0.1	3.3	0.5	1.8	0.3	2.8	0.4	1.6	0.2
FT 0305	Olive (table olives, only)	0.465	0.0	0.0	4.8	2.2	0.8	0.4	0.4	0.2	1.0	0.5	0.8	0.4
OR 0305	Olive oil, refined	0.65	0.0	0.0	14.3	9.3	3.9	2.5	0.0	0.0	1.5	1.0	0.8	0.5
FI 0350	Papaya	0.01	5.1	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0
FS 0247	Peach	0.15	0.2	0.0	24.8	3.7	3.3	0.5	1.8	0.3	5.4	0.8	1.6	0.2
FS 0014	Plum (incl dried)	0.04	0.1	0.0	5.9	0.2	2.5	0.1	7.3	0.3	6.9	0.3	2.6	0.1
FP 0009	Pome fruit (incl apple juice)	0.11	0.5	0.1	79.9	8.8	21.8	2.4	43.6	4.8	51.5	5.7	35.1	3.9

DIFENOCONAZOLE (224) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0100 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
VR 0589	Potato (incl flour, frozen, starch, tapioca)	0.01	19.1	0.2	160.8	1.6	61.2	0.6	243.6	2.4	230.1	2.3	204.7	2.0
PM 0110	Poultry meat: 10% as fat	0.0002	0.7	0.0	5.9	0.0	3.2	0.0	2.4	0.0	6.1	0.0	2.7	0.0
PM 0110	Poultry meat: 90% as muscle	0.0002	6.4	0.0	52.7	0.0	28.7	0.0	21.6	0.0	54.9	0.0	24.6	0.0
PO 0111	Poultry, edible offal of	0.0002	0.4	0.0	0.4	0.0	1.7	0.0	0.1	0.0	0.6	0.0	0.2	0.0
SO 0495	Rape seed (incl oil)	0.02	0.9	0.0	1.8	0.0	2.5	0.1	1.9	0.0	35.7	0.7	26.1	0.5
-	Soya bean (immature seeds + dry seeds, incl oil)	0.02	9.9	0.2	36.4	0.7	34.3	0.7	22.4	0.4	35.3	0.7	39.2	0.8
VR 0596	Sugar beet	0.02	0.0	0.0	40.7	0.8	0.0	0.0	0.1	0.0	6.0	0.1	0.1	0.0
SO 0702	Sunflower seed (incl oil)	0.01	0.7	0.0	44.5	0.4	20.5	0.2	29.6	0.3	21.2	0.2	5.4	0.1
VO 0448	Tomato (incl juice, paste, peeled)	0.1	5.2	0.5	183.9	18.4	116.9	11.7	57.6	5.8	16.9	1.7	17.9	1.8
JF 0448	Tomato juice	0.022	5.2	0.1	0.5	0.0	0.4	0.0	2.1	0.0	6.9	0.2	15.2	0.3
-d	Tomato, peeled	0.0065	0.1	0.0	0.4	0.0	0.5	0.0	0.4	0.0	4.9	0.0	3.2	0.0
GC 0654	Wheat (incl bulgur wholemeal, flour)	0	88.4	0.0	396.3	0.0	426.5	0.0	390.2	0.0	236.3	0.0	216.0	0.0
-	Wine	0.0054	1.3	0.0	76.8	0.4	1.1	0.0	15.4	0.1	68.8	0.4	25.6	0.1
	Total intake (µg/person)=			2.9		61.1		23.8		18.6		24.5		23.1
	Bodyweight per region (kg bw) =			60		60		60		60		60		60
	ADI (µg/person)=			600		600		600		600		600		600
	%ADI=			0.5%		10.2%		4.0%		3.1%		4.1%		3.8%
	Rounded %ADI=			0%		10%		4%		3%		4%		4%

DIFENOCONAZOLE (224) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0100 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person													
			G		H		I		J		K		L		M	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
JF 0226	Apple juice	0.0022	0.1	0.0	0.5	0.0	0.1	0.0	0.0	0.0	0.7	0.0	0.9	0.0	5.7	0.0
VS 0621	Asparagus	0.02	3.7	0.1	0.3	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.5	0.0	1.1	0.0
FI 0327	Banana	0.02	21.4	0.4	36.6	0.7	11.4	0.2	9.2	0.2	70.2	1.4	40.5	0.8	32.6	0.7
VB 0400	Broccoli	0.065	3.2	0.2	7.8	0.5	0.0	0.0	0.0	0.0	0.3	0.0	0.4	0.0	6.6	0.4
VB 0402	Brussels sprouts	0.065	3.4	0.2	0.4	0.0	0.0	0.0	0.0	0.0	0.5	0.0	7.9	0.5	0.3	0.0
VB 0041	Cabbage, head	0.035	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-

Annex 3

DIFENOCONAZOLE (224) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0100 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day Intake = daily intake: µg/person													
			G		H		I		J		K		L		M	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
VR 0577	Carrot	0.05	5.4	0.3	7.9	0.4	2.5	0.1	3.5	0.2	4.1	0.2	8.6	0.4	19.4	1.0
VB 0404	Cauliflower	0.02	3.2	0.1	0.1	0.0	0.3	0.0	0.1	0.0	0.6	0.0	0.4	0.0	1.4	0.0
VR 0578	Celeriac	0.12	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
VS 0624	Celery	0.14	0.0	0.0	0.3	0.0	0.0	0.0	0.0	0.0	1.0	0.1	0.0	0.0	4.2	0.6
FS 0013	Cherries	0.04	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0	2.5	0.1
MO 0105	Edible offal (mammalian)	0.043	4.8	0.2	10.7	0.5	4.0	0.2	4.0	0.2	6.5	0.3	6.6	0.3	5.6	0.2
PE 0112	Eggs	0.0020	22.1		71.5		16.6		5.1		17.6		35.2		57.4	
VA 0381	Garlic	0	6.4	0.0	1.2	0.0	0.1	0.0	0.3	0.0	1.9	0.0	5.0	0.0	2.5	0.0
FB 0269	Grape (incl dried, juice, wine)	0.03	1.2	0.0	2.6	0.1	0.0	0.0	0.2	0.0	0.0	0.0	3.7	0.1	0.0	0.0
JF 0269	Grape juice	0.015	0.0	0.0	0.1	0.0	1.0	0.0	0.0	0.0	0.6	0.0	0.4	0.0	3.6	0.1
DF 0269	Grape, dried (= currants, raisins and sultanas)	0.036	0.0	0.0	0.2	0.0	0.2	0.0	0.0	0.0	0.3	0.0	0.4	0.0	2.6	0.1
VA 0384	Leek	0.08	0.8	0.1	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.1	0.0
-d	Lettuce and similar (incl witloof chicory sprouts)	0.41	7.1	2.9	7.0	2.9	0.6	0.2	1.9	0.8	2.0	0.8	7.1	2.9	30.6	12.5
FI 0345	Mango (incl juice, pulp)	0.03	12.7	0.4	26.2	0.8	6.1	0.2	12.7	0.4	9.2	0.3	8.0	0.2	1.9	0.1
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0.012	11.0	0.1	17.9	0.2	6.1	0.1	5.7	0.1	16.4	0.2	12.2	0.1	31.7	0.4
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0.01	43.8	0.4	71.5	0.7	24.5	0.2	22.9	0.2	65.7	0.7	48.9	0.5	126.6	1.3
ML 0106	Milks (excl processed products)	0.001	66.0	0.1	121.1	0.1	81.6	0.1	102.4	0.1	207.7	0.2	57.0	0.1	287.9	0.3
FS 0245	Nectarine	0.15	1.7	0.3	1.7	0.3	0.0	0.0	0.0	0.0	1.0	0.2	1.7	0.3	1.4	0.2
FT 0305	Olive (table olives, only)	0.465	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.6	0.3	0.0	0.0	1.0	0.5
OR 0305	Olive oil, refined	0.65	0.0	0.0	0.1	0.1	0.0	0.0	0.0	0.0	0.3	0.2	0.3	0.2	1.6	1.0
FI 0350	Papaya	0.01	1.3	0.0	11.5	0.1	1.6	0.0	13.7	0.1	14.5	0.1	1.0	0.0	0.6	0.0
FS 0247	Peach	0.15	1.7	0.3	1.7	0.3	1.1	0.2	0.1	0.0	1.0	0.2	1.7	0.3	10.2	1.5
FS 0014	Plum (incl dried)	0.04	3.3	0.1	1.4	0.1	0.1	0.0	0.0	0.0	0.6	0.0	1.5	0.1	2.2	0.1
FP 0009	Pome fruit (incl apple juice)	0.11	20.8	2.3	11.6	1.3	3.3	0.4	0.1	0.0	10.7	1.2	23.6	2.6	36.9	4.1
VR 0589	Potato (incl flour, frozen, starch, tapioca)	0.01	52.7	0.5	57.1	0.6	50.1	0.5	4.3	0.0	54.7	0.5	41.0	0.4	168.0	1.7
PM 0110	Poultry meat: 10% as fat	0.0002	1.8	0.0	13.1	0.0	2.5	0.0	0.5	0.0	14.6	0.0	2.8	0.0	11.5	0.0
PM 0110	Poultry meat: 90% as muscle	0.0002	15.8	0.0	118.2	0.0	22.6	0.0	4.2	0.0	131.3	0.0	24.9	0.0	103.6	0.0
PO 0111	Poultry, edible offal of	0.0002	0.4	0.0	1.0	0.0	1.9	0.0	0.0	0.0	0.7	0.0	1.0	0.0	0.3	0.0
SO 0495	Rape seed (incl oil)	0.02	9.9	0.2	5.9	0.1	0.3	0.0	1.0	0.0	0.0	0.0	15.5	0.3	9.9	0.2
-	Soya bean (immature seeds + dry seeds, incl oil)	0.02	25.9	0.5	59.4	1.2	11.2	0.2	11.0	0.2	109.3	2.2	51.5	1.0	123.2	2.5

DIFENOCONAZOLE (224) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0100 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person													
			G		H		I		J		K		L		M	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
VR 0596	Sugar beet	0.02	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.0	14.3	0.3
SO 0702	Sunflower seed (incl oil)	0.01	2.7	0.0	8.8	0.1	13.5	0.1	0.2	0.0	3.6	0.0	0.6	0.0	10.4	0.1
VO 0448	Tomato (incl juice, paste, peeled)	0.1	23.3	2.3	12.6	1.3	14.6	1.5	7.2	0.7	35.2	3.5	5.9	0.6	45.0	4.5
JF 0448	Tomato juice	0.022	0.0	0.0	0.8	0.0	0.1	0.0	7.2	0.2	0.0	0.0	2.4	0.1	45.2	1.0
-d	Tomato, peeled	0.0065	0.2	0.0	14.5	0.1	0.2	0.0	0.0	0.0	0.3	0.0	0.8	0.0	1.2	0.0
GC 0654	Wheat (incl bulgur wholemeal, flour)	0	172.9	0.0	79.0	0.0	68.1	0.0	41.9	0.0	114.1	0.0	103.4	0.0	234.2	0.0
-	Wine	0.0054	1.0	0.0	0.9	0.0	6.8	0.0	0.1	0.0	3.4	0.0	3.6	0.0	31.0	0.2
	Total intake (µg/person)=			12.0		12.4		4.3		3.4		12.7		11.9		35.6
	Bodyweight per region (kg bw) =			55		60		60		60		60		55		60
	ADI (µg/person)=			550		600		600		600		600		550		600
	%ADI=			2.2%		2.1%		0.7%		0.6%		2.1%		2.2%		5.9%
	Rounded %ADI=			2%		2%		1%		1%		2%		2%		6%

Notes

Pome fruit consumption (in diet columns) reduced by subtraction of 1.5 × apple juice consumption.

Grapes consumption (in diet columns) reduced by subtraction of 4 × dried grapes consumption and 1.4 × grape juice consumption and 1.4 × wine consumption.

Tomato consumption (in diet columns) reduced by subtraction of 1.25 × tomato juice consumption and 1.25 × peeled tomato consumption.

DIMETHOMORPH (225) International Estimated Daily Intake (IEDI) ADI = 0 - 0.2000 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
VB 0400	Broccoli	0.19	0.0	0.0	0.7	0.1	1.2	0.2	0.1	0.0	4.2	0.8	4.0	0.8
VB 0041	Cabbage, head	0.4	1.2	0.5	14.4	5.8	2.7	1.1	16.4	6.6	15.4	6.2	18.5	7.4
VC 0423	Chayote	0.02	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
VL 0470	Corn salad	3.4	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
VC 0424	Cucumber	0.15	0.3	0.0	12.7	1.9	5.9	0.9	11.5	1.7	6.1	0.9	7.1	1.1
MO 0105	Edible offal (mammalian)	0	3.9	0.0	14.4	0.0	5.2	0.0	11.8	0.0	11.7	0.0	7.6	0.0

Annex 3

DIMETHOMORPH (225) International Estimated Daily Intake (IEDI) ADI = 0 - 0.2000 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
VO 0440	Egg plant (= aubergine)	0.22	1.7	0.4	17.5	3.9	12.3	2.7	1.7	0.4	0.8	0.2	0.4	0.1
PE 0112	Eggs	0	2.5	0.0	29.7	0.0	25.1	0.0	24.5	0.0	37.8	0.0	27.4	0.0
VC 0425	Gherkin	0.15	0.3	0.0	12.7	1.9	5.9	0.9	11.5	1.7	6.1	0.9	7.1	1.1
FB 0269	Grape (excl dried, excl juice, excl wine)	0.39	1.9	0.7	9.2	3.6	23.8	9.3	9.8	3.8	0.0	0.0	0.0	0.0
DF 0269	Grape, dried (= currants, raisins and sultanas)	0.7	0.0	0.0	2.9	2.0	0.4	0.3	0.4	0.3	2.3	1.6	1.7	1.2
DH 1100	Hops, dry	26	0.1	2.6	0.1	2.6	0.1	2.6	0.1	2.6	0.3	7.8	0.1	2.6
VB 0405	Kohlrabi	0.02	0.3	0.0	0.1	0.0	0.0	0.0	5.5	0.1	12.3	0.2	1.9	0.0
VL 0482	Lettuce, head	3.6	0.1	0.4	12.3	44.3	1.3	4.7	0.1	0.4	0.1	0.4	0.0	0.0
MM 0095	Meat from mammals other than marine mammals	0	27.7	0.0	116.5	0.0	38.5	0.0	55.1	0.0	90.2	0.0	131.3	0.0
VC 0046	Melons, except watermelon	0.02	3.6	0.1	26.7	0.5	22.6	0.5	11.5	0.2	5.6	0.1	2.0	0.0
ML 0106	Milks (excl processed products)	0	68.8	0.0	190.6	0.0	79.4	0.0	302.6	0.0	179.6	0.0	237.9	0.0
VO 0442	Okra	0.22	3.9	0.9	1.0	0.2	5.3	1.2	0.1	0.0	0.0	0.0	0.0	0.0
VO 0051	Peppers	0.22	1.4	0.3	29.9	6.6	13.0	2.9	6.3	1.4	6.2	1.4	4.0	0.9
FI 0353	Pineapple (incl canned, incl juice)	0	3.8	0.0	6.2	0.0	0.6	0.0	0.9	0.0	7.7	0.0	8.2	0.0
VR 0589	Potato (incl flour, frozen, starch, tapioca)	0.02	19.1	0.4	160.8	3.2	61.2	1.2	243.6	4.9	230.1	4.6	204.7	4.1
PM 0110	Poultry meat	0	7.1	0.0	58.5	0.0	31.9	0.0	24.0	0.0	61.0	0.0	27.3	0.0
PO 0111	Poultry, edible offal of	0	0.4	0.0	0.4	0.0	1.7	0.0	0.1	0.0	0.6	0.0	0.2	0.0
VC 0431	Squash, summer (= courgette, zucchini)	0.15	0.0	0.0	8.3	1.2	11.4	1.7	7.3	1.1	3.2	0.5	0.3	0.0
-d	Squashes & pumpkins & gourds	0.02	16.3	0.3	12.3	0.2	14.4	0.3	21.9	0.4	3.2	0.1	1.0	0.0
FB 0275	Strawberry	0.01	0.0	0.0	5.0	0.1	2.0	0.0	1.7	0.0	5.2	0.1	4.1	0.0
VO 0448	Tomato (excl juice, excl paste, incl peeled)	0.22	3.3	0.7	179.2	39.4	103.5	22.8	54.1	11.9	7.8	1.7	3.9	0.9
JF 0448	Tomato juice	0.06	5.2	0.3	0.5	0.0	0.4	0.0	2.1	0.1	6.9	0.4	15.2	0.9
-d	Tomato paste	0.26	0.5	0.1	1.3	0.3	3.5	0.9	1.0	0.3	3.8	1.0	4.5	1.2
VC 0432	Watermelon	0.02	6.1	0.1	43.1	0.9	47.1	0.9	25.8	0.5	4.4	0.1	6.0	0.1
-	Wine	0.11	1.3	0.1	76.8	8.4	1.1	0.1	15.4	1.7	68.8	7.6	25.6	2.8
VC 0433	Winter squash (= pumpkin)	0.02	0.0	0.0	0.5	0.0	1.5	0.0	7.3	0.1	0.0	0.0	0.3	0.0
	Total intake (µg/person)=			8.0		127.3		55.2		40.3		36.4		25.2
	Bodyweight per region (kg bw) =			60		60		60		60		60		60
	ADI (µg/person)=			12000		12000		12000		12000		12000		12000

DIMETHOMORPH (225) International Estimated Daily Intake (IEDI) ADI = 0 - 0.2000 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day Intake = daily intake: µg/person A diet	A intake	B diet	B intake	C diet	C intake	D diet	D intake	E diet	E intake	F diet	F intake
	%ADI=			0.1%		1.1%		0.5%		0.3%		0.3%		0.2%
	Rounded %ADI=			0%		1%		0%		0%		0%		0%

DIMETHOMORPH (225) International Estimated Daily Intake (IEDI) ADI = 0 - 0.2000 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day Intake = daily intake: µg/person G diet	G intake	H diet	H intake	I diet	I intake	J diet	J intake	K diet	K intake	L diet	L intake	M diet	M intake
VB 0400	Broccoli	0.19	3.2	0.6	7.8	1.5	0.0	0.0	0.0	0.0	0.3	0.1	0.4	0.1	6.6	1.3
VB 0041	Cabbage, head	0.4	10.0	4.0	1.0	0.4	7.2	2.9	1.0	0.4	1.4	0.6	23.9	9.6	17.0	6.8
VC 0423	Chayote	0.02	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
VL 0470	Corn salad	3.4	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
VC 0424	Cucumber	0.15	7.9	1.2	0.6	0.1	0.2	0.0	0.0	0.0	0.4	0.1	5.5	0.8	5.3	0.8
MO 0105	Edible offal (mammalian)	0	4.8	0.0	10.7	0.0	4.0	0.0	4.0	0.0	6.5	0.0	6.6	0.0	5.6	0.0
VO 0440	Egg plant (= aubergine)	0.22	20.1	4.4	0.1	0.0	0.6	0.1	6.3	1.4	0.5	0.1	6.3	1.4	0.7	0.2
PE 0112	Eggs	0	22.1	0.0	71.5	0.0	16.6	0.0	5.1	0.0	17.6	0.0	35.2	0.0	57.4	0.0
VC 0425	Gherkin	0.15	7.9	1.2	0.6	0.1	0.2	0.0	0.0	0.0	0.4	0.1	5.5	0.8	5.3	0.8
FB 0269	Grape (excl dried, excl juice, excl wine)	0.39	1.2	0.5	2.6	1.0	0.0	0.0	0.2	0.1	0.0	0.0	3.7	1.4	0.0	0.0
DF 0269	Grape, dried (= currants, raisins and sultanas)	0.7	0.0	0.0	0.2	0.1	0.2	0.1	0.0	0.0	0.3	0.2	0.4	0.3	2.6	1.8
DH 1100	Hops, dry	26	0.0	0.0	0.1	2.6	0.1	2.6	0.1	2.6	0.1	2.6	0.1	2.6	0.6	15.6
VB 0405	Kohlrabi	0.02	3.4	0.1	0.0	0.0	0.0	0.0	0.3	0.0	0.5	0.0	7.9	0.2	0.7	0.0
VL 0482	Lettuce, head	3.6	2.4	8.6	7.0	25.2	0.2	0.7	0.6	2.2	2.0	7.2	2.4	8.6	15.7	56.5
MM 0095	Meat from mammals other than marine mammals	0	54.8	0.0	89.4	0.0	30.6	0.0	28.6	0.0	82.1	0.0	61.1	0.0	158.3	0.0
VC 0046	Melons, except watermelon	0.02	7.5	0.2	6.1	0.1	0.7	0.0	1.4	0.0	2.5	0.1	6.9	0.1	12.4	0.2
ML 0106	Milks (excl processed products)	0	66.0	0.0	121.1	0.0	81.6	0.0	102.4	0.0	207.7	0.0	57.0	0.0	287.9	0.0
VO 0442	Okra	0.22	4.1	0.9	1.0	0.2	7.0	1.5	15.9	3.5	1.1	0.2	3.9	0.9	0.2	0.0
VO 0051	Peppers	0.22	8.7	1.9	22.4	4.9	8.4	1.8	9.4	2.1	3.3	0.7	5.3	1.2	8.9	2.0
FI 0353	Pineapple (incl canned, incl juice)	0	3.9	0.0	11.7	0.0	12.6	0.0	11.1	0.0	16.6	0.0	21.4	0.0	22.6	0.0
VR 0589	Potato (incl flour, frozen, starch, tapioca)	0.02	52.7	1.1	57.1	1.1	50.1	1.0	4.3	0.1	54.7	1.1	41.0	0.8	168.0	3.4

Annex 3

DIMETHOMORPH (225) International Estimated Daily Intake (IEDI) ADI = 0 - 0.2000 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day Intake = daily intake: µg/person													
			G		H		I		J		K		L		M	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
PM 0110	Poultry meat	0	17.6	0.0	131.3	0.0	25.1	0.0	4.7	0.0	145.9	0.0	27.7	0.0	115.1	0.0
PO 0111	Poultry, edible offal of	0	0.4	0.0	1.0	0.0	1.9	0.0	0.0	0.0	0.7	0.0	1.0	0.0	0.3	0.0
VC 0431	Squash, summer (= courgette, zucchini)	0.15	2.4	0.4	1.5	0.2	0.0	0.0	0.0	0.0	3.8	0.6	2.2	0.3	2.5	0.4
-d	Squashes & pumpkins & gourds	0.02	7.1	0.1	4.6	0.1	11.3	0.2	3.0	0.1	7.0	0.1	6.7	0.1	7.6	0.2
FB 0275	Strawberry	0.01	0.0	0.0	1.8	0.0	0.1	0.0	0.0	0.0	0.3	0.0	6.2	0.1	5.9	0.1
VO 0448	Tomato (excl juice, excl paste, incl peeled)	0.22	23.1	5.1	22.3	4.9	12.5	2.7	5.6	1.2	33.2	7.3	1.3	0.3	41.7	9.2
JF 0448	Tomato juice	0.06	0.0	0.0	0.8	0.0	0.1	0.0	7.2	0.4	0.0	0.0	2.4	0.1	45.2	2.7
-d	Tomato paste	0.26	0.1	0.0	2.1	0.5	0.6	0.2	0.4	0.1	0.6	0.2	1.4	0.4	1.2	0.3
VC 0432	Watermelon	0.02	39.3	0.8	14.0	0.3	2.5	0.1	13.6	0.3	8.4	0.2	14.5	0.3	13.6	0.3
-	Wine	0.11	1.0	0.1	0.9	0.1	6.8	0.7	0.1	0.0	3.4	0.4	3.6	0.4	31.0	3.4
VC 0433	Winter squash (= pumpkin)	0.02	2.4	0.0	1.5	0.0	0.0	0.0	0.0	0.0	1.6	0.0	2.2	0.0	0.7	0.0
	Total intake (µg/person)=			31.2		43.7		14.9		14.4		21.7		30.8		105.8
	Bodyweight per region (kg bw) =			55		60		60		60		60		55		60
	ADI (µg/person)=			11000		12000		12000		12000		12000		11000		12000
	%ADI=			0.3%		0.4%		0.1%		0.1%		0.2%		0.3%		0.9%
	Rounded %ADI=			0%		0%		0%		0%		0%		0%		1%

FENITROTHION (37) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0060 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
FP 0226	Apple (incl juice)	0.04	0.3	0.0	60.5	2.4	18.5	0.7	39.9	1.6	50.8	2.0	39.4	1.6
GC 0640	Barley (excl pot, excl pearled, excl flour & grits, excl beer)	4.25	0.0	0.0	0.0	-0.1	0.2	0.7	0.0	0.0	0.0	-0.1	3.8	16.3
-	Barley beer*	0.85	18.3	15.6	84.1	71.5	4.1	3.5	66.0	56.1	243.1	206.6	161.3	137.1
-	Barley flour and grits	1	0.0	0.0	0.3	0.3	10.8	10.8	0.3	0.3	0.5	0.5	0.9	0.9
-	Barley, pearled	0.638	0.0	0.0	0.4	0.3	27.9	17.8	0.4	0.3	0.4	0.3	0.9	0.6
-	Barley, pot	2.72	29.0	78.9	0.0	0.0	11.9	32.4	4.0	10.9	2.0	5.4	12.5	34.0
GC 0641	Buckwheat (excl flour, excl bran)	4.25	0.0	0.0	0.1	0.4	0.0	0.0	0.0	0.0	0.0	0.2	0.1	0.4
-	Buckwheat bran	16.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

FENITROTHION (37) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0060 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
-	Buckwheat flour	1	0.0	0.0	0.0	0.0	0.0	0.0	1.3	1.3	1.2	1.2	0.0	0.0
MO 0105	Edible offal (mammalian)	0	3.9	0.0	14.4	0.0	5.2	0.0	11.8	0.0	11.7	0.0	7.6	0.0
PE 0112	Eggs	0	2.5	0.0	29.7	0.0	25.1	0.0	24.5	0.0	37.8	0.0	27.4	0.0
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0	5.5	0.0	23.3	0.0	7.7	0.0	11.0	0.0	18.0	0.0	26.3	0.0
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0	22.2	0.0	93.2	0.0	30.8	0.0	44.1	0.0	72.2	0.0	105.0	0.0
ML 0106	Milks (excl processed products)	0	68.8	0.0	190.6	0.0	79.4	0.0	302.6	0.0	179.6	0.0	237.9	0.0
GC 0646	Millet (excl flour, excl beer)	4.25	0.2	0.9	0.1	0.4	0.0	-0.2	0.0	-0.2	0.1	0.3	0.1	0.4
-	Millet beer	0.85	14.0	11.9	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.4	0.0	0.0
-	Millet flour	1	13.0	13.0	0.0	0.0	0.7	0.7	4.7	4.7	0.1	0.1	0.0	0.0
GC 0647	Oats (incl rolled)	4.25	1.4	6.0	0.6	2.6	0.2	0.9	4.2	17.9	5.7	24.2	8.9	37.8
PM 0110	Poultry meat: 10% as fat	0	0.7	0.0	5.9	0.0	3.2	0.0	2.4	0.0	6.1	0.0	2.7	0.0
PM 0110	Poultry meat: 90% as muscle	0	6.4	0.0	52.7	0.0	28.7	0.0	21.6	0.0	54.9	0.0	24.6	0.0
GC 0649	Rice (excl husked, excl polished)	4.25	0.0	0.1	0.0	0.0	0.0	0.1	0.1	0.3	0.0	0.0	0.0	0.1
CM 1206	Rice bran, unprocessed	30.6	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
CM 0649	Rice, husked (incl milled)	0.468	35.6	16.7	0.2	0.1	2.6	1.2	6.9	3.2	3.3	1.5	0.4	0.2
CM 1205	Rice, polished (incl flour)	0.17	29.8	5.1	20.9	3.6	60.8	10.3	16.1	2.7	5.6	1.0	8.1	1.4
GC 0650	Rye (excl flour)	4.25	0.1	0.4	0.1	0.3	0.0	0.2	0.0	0.0	0.1	0.3	0.0	0.2
CF 1250	Rye flour	1	0.0	0.0	2.8	2.8	0.2	0.2	18.7	18.7	19.8	19.8	35.2	35.2
GC 0651	Sorghum (excl flour, excl beer)	4.25	0.0	0.2	0.0	0.0	0.0	-0.1	0.0	0.0	0.0	0.0	0.0	0.0
-	Sorghum beer	0.85	62.3	53.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
-	Sorghum flour	1	33.5	33.5	0.0	0.0	9.3	9.3	0.0	0.0	0.0	0.0	0.0	0.0
VD 0541	Soya bean (dry, incl oil)	0.01	9.9	0.1	36.4	0.4	34.3	0.3	22.4	0.2	35.3	0.4	39.2	0.4
GC 0653	Triticale (excl flour)	4.25	0.0	0.0	0.0	-0.1	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0
-	Triticale flour	1	0.0	0.0	89.1	89.1	0.0	0.0	0.0	0.0	0.2	0.2	0.0	0.0
-d	Wheat bulgur wholemeal	1.615	5.5	8.9	10.2	16.5	0.7	1.1	0.2	0.3	0.1	0.2	0.0	0.0
-d	Wheat macaroni	0.425	0.8	0.3	1.1	0.5	0.8	0.3	1.8	0.8	4.6	2.0	7.6	3.2
-d	Wheat pastry	0.425	0.4	0.2	1.1	0.5	0.7	0.3	2.6	1.1	1.7	0.7	5.4	2.3
CP 1211	White bread	0.425	0.0	0.0	0.1	0.0	0.0	0.0	0.1	0.0	0.1	0.0	1.0	0.4
CP 1212	Wholemeal bread	1.615	0.0	0.0	0.1	0.2	0.0	0.0	0.1	0.2	0.1	0.2	1.0	1.6
	Total intake (µg/person)=			244.5		191.4		90.5		120.4		267.6		274.2

Annex 3

FENITROTHION (37) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0060 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
	Bodyweight per region (kg bw) =			60		60		60		60		60		60
	ADI (µg/person)=			360		360		360		360		360		360
	%ADI=			67.9%		53.2%		25.1%		33.5%		74.3%		76.2%
	Rounded %ADI=			70%		50%		30%		30%		70%		80%

* barley beer refers to the malt part of the beer, not the beer itself

FENITROTHION (37) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0060 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person													
			G		H		I		J		K		L		M	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
FP 0226	Apple (incl juice)	0.04	14.4	0.6	10.1	0.4	2.2	0.1	0.0	0.0	9.8	0.4	17.9	0.7	36.3	1.5
GC 0640	Barley (excl pot, excl pearled, excl flour & grits, excl beer)	4.25	1.5	6.5	0.0	-0.2	0.0	0.0	0.0	-0.1	0.0	0.1	0.4	1.5	0.0	0.2
-	Barley beer*	0.85	21.9	18.6	102.7	87.3	29.5	25.1	12.6	10.7	100.9	85.8	82.2	69.9	218.8	186.0
-	Barley flour and grits	1	0.4	0.4	0.0	0.0	0.1	0.1	0.0	0.0	1.0	1.0	0.8	0.8	0.0	0.0
-	Barley, pearled	0.638	0.5	0.3	0.1	0.1	0.0	0.0	0.0	0.0	0.7	0.4	0.0	0.0	0.1	0.1
-	Barley, pot	2.72	0.7	1.9	0.0	0.0	0.0	0.0	0.7	1.9	2.4	6.5	4.1	11.2	0.0	0.0
GC 0641	Buckwheat (excl flour, excl bran)	4.25	0.1	0.4	0.0	0.0	0.1	0.3	0.1	0.4	0.4	1.6	0.0	0.2	0.1	0.4
-	Buckwheat bran	16.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
-	Buckwheat flour	1	0.7	0.7	0.0	0.0	0.1	0.1	0.0	0.0	0.1	0.1	1.5	1.5	0.0	0.0
MO 0105	Edible offal (mammalian)	0	4.8	0.0	10.7	0.0	4.0	0.0	4.0	0.0	6.5	0.0	6.6	0.0	5.6	0.0
PE 0112	Eggs	0	22.1	0.0	71.5	0.0	16.6	0.0	5.1	0.0	17.6	0.0	35.2	0.0	57.4	0.0
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0	11.0	0.0	17.9	0.0	6.1	0.0	5.7	0.0	16.4	0.0	12.2	0.0	31.7	0.0
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0	43.8	0.0	71.5	0.0	24.5	0.0	22.9	0.0	65.7	0.0	48.9	0.0	126.6	0.0
ML 0106	Milks (excl processed products)	0	66.0	0.0	121.1	0.0	81.6	0.0	102.4	0.0	207.7	0.0	57.0	0.0	287.9	0.0
GC 0646	Millet (excl flour, excl beer)	4.25	0.0	0.2	0.0	0.0	0.0	0.1	3.9	16.6	0.0	0.0	0.0	0.2	0.0	0.0
-	Millet beer	0.85	0.0	0.0	0.0	0.0	22.5	19.1	8.8	7.5	0.0	0.0	0.0	0.0	0.0	0.0

FENITROTHION (37) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0060 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day Intake = daily intake: µg/person													
			G		H		I		J		K		L		M	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
-	Millet flour	1	10.8	10.8	0.0	0.0	6.9	6.9	77.5	77.5	0.0	0.0	0.3	0.3	0.0	0.0
GC 0647	Oats (incl rolled)	4.25	0.2	0.9	2.0	8.5	0.8	3.4	0.0	0.0	3.5	14.9	0.7	3.0	7.6	32.3
PM 0110	Poultry meat: 10% as fat	0	1.8	0.0	13.1	0.0	2.5	0.0	0.5	0.0	14.6	0.0	2.8	0.0	11.5	0.0
PM 0110	Poultry meat: 90% as muscle	0	15.8	0.0	118.2	0.0	22.6	0.0	4.2	0.0	131.3	0.0	24.9	0.0	103.6	0.0
GC 0649	Rice (excl husked, excl polished)	4.25	0.0	0.1	0.0	-0.2	0.0	-0.2	0.1	0.4	0.0	-0.2	0.1	0.2	0.0	0.0
CM 1206	Rice bran, unprocessed	30.6	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
CM 0649	Rice, husked (incl milled)	0.468	1.1	0.5	0.8	0.4	1.8	0.8	22.7	10.6	70.8	33.1	7.0	3.3	0.3	0.1
CM 1205	Rice, polished (incl flour)	0.17	250.3	42.6	42.2	7.2	23.8	4.0	29.8	5.1	97.6	16.6	248.1	42.2	22.8	3.9
GC 0650	Rye (excl flour)	4.25	0.0	0.0	0.0	0.0	0.1	0.3	0.1	0.4	0.0	-0.1	0.9	3.8	0.0	0.1
CF 1250	Rye flour	1	0.3	0.3	0.0	0.0	0.1	0.1	0.0	0.0	0.1	0.1	0.0	0.0	0.6	0.6
GC 0651	Sorghum (excl flour, excl beer)	4.25	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.3	0.0	0.0	2.2	9.5
-	Sorghum beer	0.85	0.0	0.0	0.0	0.0	35.1	29.8	28.6	24.3	0.1	0.1	0.0	0.0	3.3	2.8
-	Sorghum flour	1	8.9	8.9	18.1	18.1	16.9	16.9	102.1	102.1	0.0	0.0	3.0	3.0	0.7	0.7
VD 0541	Soya bean (dry, incl oil)	0.01	25.9	0.3	59.4	0.6	11.2	0.1	11.0	0.1	109.3	1.1	51.5	0.5	123.2	1.2
GC 0653	Triticale (excl flour)	4.25	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
-	Triticale flour	1	1.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
-d	Wheat bulgur wholemeal	1.615	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
-d	Wheat macaroni	0.425	1.7	0.7	3.6	1.5	0.5	0.2	0.2	0.1	0.3	0.1	1.7	0.7	2.0	0.9
-d	Wheat pastry	0.425	0.3	0.1	0.6	0.3	0.7	0.3	0.2	0.1	0.3	0.1	0.6	0.3	1.7	0.7
CP 1211	White bread	0.425	0.0	0.0	2.2	0.9	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
CP 1212	Wholemeal bread	1.615	0.0	0.0	2.2	3.6	0.1	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Total intake (µg/person)=			95.7		128.4		107.9		257.7		162.1		143.2		240.9
	Bodyweight per region (kg bw) =			55		60		60		60		60		55		60
	ADI (µg/person)=			330		360		360		360		360		330		360
	%ADI=			29.0%		35.7%		30.0%		71.6%		45.0%		43.4%		66.9%
	Rounded %ADI=			30%		40%		30%		70%		50%		40%		70%

* barley beer refers to the malt part of the beer, not the beer itself

Annex 3

FLUSILAZOLE (165) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0070 mg/kg bw 0.007

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
JF 0226	Apple juice	0.008	0.0	0.0	2.8	0.0	0.1	0.0	1.1	0.0	6.8	0.1	7.4	0.1
FS 0240	Apricot (excl dried)	0.05	0.3	0.0	4.2	0.2	3.6	0.2	2.9	0.1	1.3	0.1	0.1	0.0
FI 0327	Banana	0.01	38.8	0.4	17.4	0.2	16.0	0.2	6.6	0.1	21.5	0.2	33.8	0.3
GC 0640	Barley (incl pot, incl pearled, incl flour & grits, incl beer)	0.04	40.6	1.6	16.8	0.7	93.9	3.8	13.2	0.5	48.6	1.9	36.1	1.4
MO 0105	Edible offal (mammalian)	0.65	3.9	2.5	14.4	9.4	5.2	3.4	11.8	7.7	11.7	7.6	7.6	4.9
PE 0112	Eggs	0.02	2.5	0.1	29.7	0.6	25.1	0.5	24.5	0.5	37.8	0.8	27.4	0.5
FB 0269	Grape (excl dried, excl juice, excl wine)	0.03	1.9	0.1	9.2	0.3	23.8	0.7	9.8	0.3	0.0	0.0	0.0	0.0
FB 1236	Grape (for wine only: wine-grapes)	0.003	1.9	0.0	107.5	0.3	1.5	0.0	21.6	0.1	96.3	0.3	35.8	0.1
JF 0269	Grape juice	0.012	0.0	0.0	0.1	0.0	0.1	0.0	0.1	0.0	1.4	0.0	1.0	0.0
DF 0269	Grape, dried (= currants, raisins and sultanas)	0.054	0.0	0.0	2.9	0.2	0.4	0.0	0.4	0.0	2.3	0.1	1.7	0.1
GC 0645	Maize (incl flour, incl oil, incl beer)	0.04	82.7	3.3	148.4	5.9	135.9	5.4	31.8	1.3	33.3	1.3	7.5	0.3
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0.285	5.5	1.6	23.3	6.6	7.7	2.2	11.0	3.1	18.0	5.1	26.3	7.5
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0.02	22.2	0.4	93.2	1.9	30.8	0.6	44.1	0.9	72.2	1.4	105.0	2.1
ML 0106	Milks (excl processed products)	0.01	68.8	0.7	190.6	1.9	79.4	0.8	302.6	3.0	179.6	1.8	237.9	2.4
FS 0245	Nectarine	0.05	0.0	0.0	0.5	0.0	3.3	0.2	1.8	0.1	2.8	0.1	1.6	0.1
FS 0247	Peach	0.05	0.2	0.0	24.8	1.2	3.3	0.2	1.8	0.1	5.4	0.3	1.6	0.1
002	**POME FRUIT**		-	-	-	-	-	-	-	-	-	-	-	-
FP 0009	Pome fruit (excl apple juice)	0.04	0.5	0.0	79.9	3.2	21.8	0.9	43.6	1.7	51.5	2.1	35.1	1.4
PM 0110	Poultry meat: 10% as fat	0.05	0.7	0.0	5.9	0.3	3.2	0.2	2.4	0.1	6.1	0.3	2.7	0.1
PM 0110	Poultry meat: 90% as muscle	0.01	6.4	0.1	52.7	0.5	28.7	0.3	21.6	0.2	54.9	0.5	24.6	0.2
PO 0111	Poultry, edible offal of	0.02	0.4	0.0	0.4	0.0	1.7	0.0	0.1	0.0	0.6	0.0	0.2	0.0
SO 0495	Rape seed (incl oil)	0.01	0.9	0.0	1.8	0.0	2.5	0.0	1.9	0.0	35.7	0.4	26.1	0.3
GC 0650	Rye (incl flour)	0.04	0.1	0.0	3.7	0.1	0.3	0.0	24.3	1.0	25.8	1.0	45.8	1.8
VD 0541	Soya bean (dry, excl oil)	0.02	0.9	0.0	0.0	0.0	0.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0
OR 0541	Soya bean oil, refined	0.044	1.6	0.1	6.5	0.3	6.0	0.3	4.0	0.2	6.3	0.3	7.0	0.3
VR 0596	Sugar beet	0.01	0.0	0.0	40.7	0.4	0.0	0.0	0.1	0.0	6.0	0.1	0.1	0.0
SO 0702	Sunflower seed (incl oil)	0.01	0.7	0.0	44.5	0.4	20.5	0.2	29.6	0.3	21.2	0.2	5.4	0.1
VO 0447	Sweet corn (corn-on-the-cob)	0.01	7.3	0.1	1.0	0.0	0.1	0.0	0.5	0.0	3.3	0.0	3.6	0.0
GC 0654	Wheat (excl bulgur wholemeal, excl flour)	0.04	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0

FLUSILAZOLE (165) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0070 mg/kg bw 0.007

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day Intake = daily intake: µg/person A diet	A intake	B diet	B intake	C diet	C intake	D diet	D intake	E diet	E intake	F diet	F intake
CM 0654	Wheat bran, unprocessed	0.012	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
CF 1211	Wheat flour (incl macaroni, bread, pastry, starch, gluten)	0.036	63.4	2.3	296.3	10.7	327.5	11.8	300.0	10.8	181.6	6.5	166.2	6.0
-	Wine	0.002	1.3	0.0	76.8	0.2	1.1	0.0	15.4	0.0	68.8	0.1	25.6	0.1
	Total intake (µg/person)=			13.3		45.8		31.8		32.2		32.9		30.3
	Bodyweight per region (kg bw) =			60		60		60		60		60		60
	ADI (µg/person)=			420		420		420		420		420		420
	%ADI=			3.2%		10.9%		7.6%		7.7%		7.8%		7.2%
	Rounded %ADI=			3%		10%		8%		8%		8%		7%

FLUSILAZOLE (165) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0070 mg/kg bw 0.001

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day Intake = daily intake: µg/person G diet	G intake	H diet	H intake	I diet	I intake	J diet	J intake	K diet	K intake	L diet	L intake	M diet	M intake
JF 0226	Apple juice	0.008	0.1	0.0	0.5	0.0	0.1	0.0	0.0	0.0	0.7	0.0	0.9	0.0	5.7	0.0
FS 0240	Apricot (excl dried)	0.05	0.2	0.0	0.1	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.4	0.0
FI 0327	Banana	0.01	21.4	0.2	36.6	0.4	11.4	0.1	9.2	0.1	70.2	0.7	40.5	0.4	32.6	0.3
GC 0640	Barley (incl pot, incl pearled, incl flour & grits, incl beer)	0.04	5.9	0.2	20.5	0.8	5.9	0.2	2.5	0.1	20.2	0.8	16.8	0.7	43.8	1.8
MO 0105	Edible offal (mammalian)	0.65	4.8	3.1	10.7	7.0	4.0	2.6	4.0	2.6	6.5	4.2	6.6	4.3	5.6	3.6
PE 0112	Eggs	0.02	22.1	0.4	71.5	1.4	16.6	0.3	5.1	0.1	17.6	0.4	35.2	0.7	57.4	1.1
FB 0269	Grape (excl dried, excl juice, excl wine)	0.03	1.2	0.0	2.6	0.1	0.0	0.0	0.2	0.0	0.0	0.0	3.7	0.1	0.0	0.0
FB 1236	Grape (for wine only: wine-grapes)	0.003	1.4	0.0	1.3	0.0	9.5	0.0	0.2	0.0	4.8	0.0	5.0	0.0	43.4	0.1
JF 0269	Grape juice	0.012	0.0	0.0	0.1	0.0	1.0	0.0	0.0	0.0	0.6	0.0	0.4	0.0	3.6	0.0
DF 0269	Grape, dried (= currants, raisins and sultanas)	0.054	0.0	0.0	0.2	0.0	0.2	0.0	0.0	0.0	0.3	0.0	0.4	0.0	2.6	0.1
GC 0645	Maize (incl flour, incl oil, incl beer)	0.04	35.2	1.4	298.6	11.9	248.1	9.9	57.4	2.3	63.1	2.5	58.6	2.3	85.5	3.4
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0.285	11.0	3.1	17.9	5.1	6.1	1.7	5.7	1.6	16.4	4.7	12.2	3.5	31.7	9.0
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0.02	43.8	0.9	71.5	1.4	24.5	0.5	22.9	0.5	65.7	1.3	48.9	1.0	126.6	2.5

Annex 3

FLUSILAZOLE (165) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0070 mg/kg bw 0.001

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day Intake = daily intake: µg/person													
			G		H		I		J		K		L		M	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
ML 0106	Milks (excl processed products)	0.01	66.0	0.7	121.1	1.2	81.6	0.8	102.4	1.0	207.7	2.1	57.0	0.6	287.9	2.9
FS 0245	Nectarine	0.05	1.7	0.1	1.7	0.1	0.0	0.0	0.0	0.0	1.0	0.1	1.7	0.1	1.4	0.1
FS 0247	Peach	0.05	1.7	0.1	1.7	0.1	1.1	0.1	0.1	0.0	1.0	0.1	1.7	0.1	10.2	0.5
002	**POME FRUIT**		-	-	-	-	-	-	-	-	-	-	-	-	-	-
FP 0009	Pome fruit (excl apple juice)	0.04	20.8	0.8	11.6	0.5	3.3	0.1	0.1	0.0	10.7	0.4	23.6	0.9	36.9	1.5
PM 0110	Poultry meat: 10% as fat	0.05	1.8	0.1	13.1	0.7	2.5	0.1	0.5	0.0	14.6	0.7	2.8	0.1	11.5	0.6
PM 0110	Poultry meat: 90% as muscle	0.01	15.8	0.2	118.2	1.2	22.6	0.2	4.2	0.0	131.3	1.3	24.9	0.2	103.6	1.0
PO 0111	Poultry, edible offal of	0.02	0.4	0.0	1.0	0.0	1.9	0.0	0.0	0.0	0.7	0.0	1.0	0.0	0.3	0.0
SO 0495	Rape seed (incl oil)	0.01	9.9	0.1	5.9	0.1	0.3	0.0	1.0	0.0	0.0	0.0	15.5	0.2	9.9	0.1
GC 0650	Rye (incl flour)	0.04	0.4	0.0	0.0	0.0	0.2	0.0	0.1	0.0	0.1	0.0	0.9	0.0	0.8	0.0
VD 0541	Soya bean (dry, excl oil)	0.02	1.8	0.0	0.0	0.0	0.0	0.0	3.2	0.1	0.1	0.0	0.0	0.0	0.0	0.0
OR 0541	Soya bean oil, refined	0.044	4.3	0.2	10.6	0.5	2.0	0.1	1.4	0.1	19.5	0.9	9.2	0.4	22.0	1.0
VR 0596	Sugar beet	0.01	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.0	14.3	0.1
SO 0702	Sunflower seed (incl oil)	0.01	2.7	0.0	8.8	0.1	13.5	0.1	0.2	0.0	3.6	0.0	0.6	0.0	10.4	0.1
VO 0447	Sweet corn (corn-on-the-cob)	0.01	0.2	0.0	2.4	0.0	2.2	0.0	3.3	0.0	1.7	0.0	2.8	0.0	11.2	0.1
GC 0654	Wheat (excl bulgur wholemeal, excl flour)	0.04	0.0	0.0	0.9	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.1	0.0
CM 0654	Wheat bran, unprocessed	0.012	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-	ND	-
CF 1211	Wheat flour (incl macaroni, bread, pastry, starch, gluten)	0.036	133.0	4.8	60.1	2.2	52.4	1.9	32.2	1.2	87.7	3.2	79.6	2.9	180.1	6.5
-	Wine	0.002	1.0	0.0	0.9	0.0	6.8	0.0	0.1	0.0	3.4	0.0	3.6	0.0	31.0	0.1
	Total intake (µg/person)=			16.6		34.7		19.1		9.7		23.4		18.7		36.9
	Bodyweight per region (kg bw) =			55		60		60		60		60		55		60
	ADI (µg/person)=			385		420		420		420		420		385		420
	%ADI=			4.3%		8.3%		4.5%		2.3%		5.6%		4.8%		8.8%
	Rounded %ADI=			4%		8%		5%		2%		6%		5%		9%

PYRIMETHANIL (226) International Estimated Daily Intake (IEDI) ADI = 0 - 0.2000 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
TN 0660	Almond	0.05	0.0	0.0	1.9	0.1	1.0	0.1	0.0	0.0	1.0	0.1	0.8	0.0
JF 0226	Apple juice	0.32	0.0	0.0	2.8	0.9	0.1	0.0	1.1	0.4	6.8	2.2	7.4	2.4
FS 0240	Apricot (incl dried)	1.2	0.3	0.4	6.2	7.4	3.9	4.7	3.2	3.8	2.0	2.4	0.8	1.0
FI 0327	Banana	0.05	38.8	1.9	17.4	0.9	16.0	0.8	6.6	0.3	21.5	1.1	33.8	1.7
VR 0577	Carrot	0.14	0.6	0.1	15.1	2.1	8.1	1.1	13.9	1.9	27.1	3.8	28.4	4.0
FS 0013	Cherries	1.3	0.0	0.0	6.8	8.8	0.9	1.2	6.2	8.1	3.6	4.7	0.4	0.5
FC 0001	Citrus fruit (excl lemon juice, excl mandarin juice, excl orange juice, excl grapefruit juice, excl NES juice)	2.8	15.7	44.0	86.5	242.1	52.6	147.2	24.2	67.7	16.2	45.4	12.0	33.6
VP 0526	Common bean (green pods and/or immature seeds)	0.22	0.5	0.1	4.7	1.0	4.1	0.9	0.0	0.0	13.1	2.9	0.0	0.0
MO 0105	Edible offal (mammalian)	0.065	3.9	0.3	14.4	0.9	5.2	0.3	11.8	0.8	11.7	0.8	7.6	0.5
FB 0269	Grape (excl dried, excl juice, excl wine)	0.71	1.9	1.3	9.2	6.6	23.8	16.9	9.8	7.0	0.0	0.0	0.0	0.0
JF 0269	Grape juice	0.50	0.0	0.0	0.1	0.0	0.1	0.0	0.1	0.0	1.4	0.7	1.0	0.5
DF 0269	Grape, dried (= currants, raisins and sultanas)	1.1	0.0	0.0	2.9	3.2	0.4	0.4	0.4	0.4	2.3	2.5	1.7	1.7
JF 0203	Grapefruit juice	0.028	0.0	0.0	0.2	0.0	0.1	0.0	0.1	0.0	1.1	0.0	0.2	0.0
-d	Lemon juice	0.028	0.0	0.0	0.9	0.0	0.1	0.0	0.0	0.0	0.2	0.0	0.4	0.0
VL 0482	Lettuce, head	0.85	0.1	0.1	12.3	10.5	1.3	1.1	0.1	0.1	0.1	0.1	0.0	0.0
-	Mandarin + mandarin-like hybrid juice	0.028	0.0	0.0	1.4	0.0	0.9	0.0	0.4	0.0	0.7	0.0	0.9	0.0
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0	5.5	0.0	23.3	0.0	7.7	0.0	11.0	0.0	18.0	0.0	26.3	0.0
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0	22.2	0.0	93.2	0.0	30.8	0.0	44.1	0.0	72.2	0.0	105.0	0.0
ML 0106	Milks (excl processed products)	0.01	68.8	0.7	190.6	1.9	79.4	0.8	302.6	3.0	179.6	1.8	237.9	2.4
FS 0245	Nectarine	1.3	0.0	0.0	0.5	0.7	3.3	4.3	1.8	2.3	2.8	3.6	1.6	2.1
-	Onion, dry	0.062	4.3	0.3	45.6	2.8	27.4	1.7	30.2	1.9	22.1	1.4	12.2	0.8
-	Onion, green (= shallot, Welsh, spring onion, others)	0.38	1.2	0.5	3.9	1.5	5.6	2.1	1.1	0.4	1.1	0.4	2.4	0.9
JF 0004	Orange juice	0.028	0.0	0.0	2.1	0.1	4.4	0.1	1.4	0.0	16.2	0.5	22.6	0.6
FS 0247	Peach	1.3	0.2	0.3	24.8	32.2	3.3	4.3	1.8	2.3	5.4	7.0	1.6	2.1
FS 0014	Plum (excl dried)	0.59	0.1	0.1	5.3	3.1	2.5	1.5	7.0	4.1	5.5	3.2	0.9	0.5

Annex 3

PYRIMETHANIL (226) International Estimated Daily Intake (IEDI) ADI = 0 - 0.2000 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
DF 0014	Plum, dried (prunes)	0.48	0.0	0.0	0.2	0.1	0.0	0.0	0.1	0.0	0.5	0.2	0.6	0.3
FP 0009	Pome fruit (excl apple juice)	0.7	0.5	0.4	79.9	55.9	21.8	15.2	43.6	30.5	51.5	36.1	35.1	24.6
VR 0589	Potato (incl flour, frozen, starch, tapioca)	0.05	19.1	1.0	160.8	8.0	61.2	3.1	243.6	12.2	230.1	11.5	204.7	10.2
FB 0275	Strawberry	1.2	0.0	0.0	5.0	6.0	2.0	2.4	1.7	2.0	5.2	6.2	4.1	4.9
VO 0448	Tomato (incl juice, excl paste, incl peeled)	0.32	9.8	3.1	179.8	57.5	104.0	33.3	56.7	18.1	16.4	5.2	22.9	7.3
-d	Tomato paste	0.35	0.5	0.2	1.3	0.5	3.5	1.2	1.0	0.4	3.8	1.3	4.5	1.6
-	Wine	0.34	1.3	0.4	76.8	26.1	1.1	0.4	15.4	5.2	68.8	23.4	25.6	8.7
	Total intake (µg/person)=			54.9		480.8		245.1		172.9		168.5		112.8
	Bodyweight per region (kg bw) =			60		60		60		60		60		60
	ADI (µg/person)=			12000		12000		12000		12000		12000		12000
	%ADI=			0.5%		4.0%		2.0%		1.4%		1.4%		0.9%
	Rounded %ADI=			0%		4%		2%		1%		1%		1%

PYRIMETHANIL (226) International Estimated Daily Intake (IEDI) ADI = 0 - 0.2000 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person													
			G		H		I		J		K		L		M	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
TN 0660	Almond	0.05	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.3	0.0
JF 0226	Apple juice	0.32	0.1	0.0	0.5	0.2	0.1	0.0	0.0	0.0	0.7	0.2	0.9	0.3	5.7	1.8
FS 0240	Apricot (incl dried)	1.2	0.2	0.2	0.1	0.1	0.2	0.2	0.0	0.0	0.0	0.0	0.1	0.1	1.1	1.3
FI 0327	Banana	0.05	21.4	1.1	36.6	1.8	11.4	0.6	9.2	0.5	70.2	3.5	40.5	2.0	32.6	1.6
VR 0577	Carrot	0.14	5.4	0.8	7.9	1.1	2.5	0.4	3.5	0.5	4.1	0.6	8.6	1.2	19.4	2.7
FS 0013	Cherries	1.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.4	2.5	3.3
FC 0001	Citrus fruit (excl lemon juice, excl mandarin juice, excl orange juice, excl grapefruit juice, excl NES juice)	2.8	15.1	42.2	153.9	430.9	3.4	9.6	41.7	116.8	218.9	613.0	23.1	64.7	18.0	50.4

PYRIMETHANIL (226) International Estimated Daily Intake (IEDI) ADI = 0 - 0.2000 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day Intake = daily intake: µg/person G diet	G intake	H diet	H intake	I diet	I intake	J diet	J intake	K diet	K intake	L diet	L intake	M diet	M intake
VP 0526	Common bean (green pods and/or immature seeds)	0.22	0.0	0.0	1.9	0.4	0.0	0.0	0.0	0.0	0.3	0.1	1.8	0.4	8.0	1.8
MO 0105	Edible offal (mammalian)	0.065	4.8	0.3	10.7	0.7	4.0	0.3	4.0	0.3	6.5	0.4	6.6	0.4	5.6	0.4
FB 0269	Grape (excl dried, excl juice, excl wine)	0.71	1.2	0.9	2.6	1.8	0.0	0.0	0.2	0.1	0.0	0.0	3.7	2.6	0.0	0.0
JF 0269	Grape juice	0.506	0.0	0.0	0.1	0.0	1.0	0.5	0.0	0.0	0.6	0.3	0.4	0.2	3.6	1.8
DF 0269	Grape, dried (= currants, raisins and sultanas)	1.1	0.0	0.0	0.2	0.2	0.2	0.2	0.0	0.0	0.3	0.3	0.4	0.4	2.6	2.9
JF 0203	Grapefruit juice	0.028	0.0	0.0	0.0	0.0	0.5	0.0	0.0	0.0	0.0	0.0	0.3	0.0	2.4	0.1
-d	Lemon juice	0.028	0.3	0.0	0.0	0.0	1.0	0.0	0.3	0.0	0.0	0.0	0.5	0.0	2.6	0.1
VL 0482	Lettuce, head	0.85	2.4	2.0	7.0	6.0	0.2	0.2	0.6	0.5	2.0	1.7	2.4	2.0	15.7	13.3
-	Mandarin + mandarin-like hybrid juice	0.028	0.5	0.0	0.5	0.0	0.1	0.0	0.0	0.0	0.7	0.0	1.4	0.0	0.0	0.0
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0	11.0	0.0	17.9	0.0	6.1	0.0	5.7	0.0	16.4	0.0	12.2	0.0	31.7	0.0
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0	43.8	0.0	71.5	0.0	24.5	0.0	22.9	0.0	65.7	0.0	48.9	0.0	126.6	0.0
ML 0106	Milks (excl processed products)	0.01	66.0	0.7	121.1	1.2	81.6	0.8	102.4	1.0	207.7	2.1	57.0	0.6	287.9	2.9
FS 0245	Nectarine	1.3	1.7	2.2	1.7	2.2	0.0	0.0	0.0	0.0	1.0	1.3	1.7	2.2	1.4	1.8
-	Onion, dry	0.062	16.8	1.0	8.6	0.5	6.9	0.4	12.1	0.8	18.6	1.2	23.8	1.5	28.4	1.8
-	Onion, green (= shallot, Welsh, spring onion, others)	0.38	0.6	0.2	19.3	7.3	0.4	0.2	3.9	1.5	4.2	1.6	10.7	4.1	1.7	0.6
JF 0004	Orange juice	0.028	0.2	0.0	1.0	0.0	3.5	0.1	0.0	0.0	1.3	0.0	6.4	0.2	56.8	1.6
FS 0247	Peach	1.3	1.7	2.2	1.7	2.2	1.1	1.4	0.1	0.1	1.0	1.3	1.7	2.2	10.2	13.3
FS 0014	Plum (excl dried)	0.59	3.0	1.8	0.8	0.5	0.1	0.1	0.0	0.0	0.0	0.0	0.9	0.5	0.5	0.3
DF 0014	Plum, dried (prunes)	0.48	0.1	0.0	0.2	0.1	0.0	0.0	0.0	0.0	0.2	0.1	0.2	0.1	0.6	0.3
FP 0009	Pome fruit (excl apple juice)	0.7	20.8	14.5	11.6	8.1	3.3	2.3	0.1	0.1	10.7	7.5	23.6	16.5	36.9	25.8
VR 0589	Potato (incl flour, frozen, starch, tapioca)	0.05	52.7	2.6	57.1	2.9	50.1	2.5	4.3	0.2	54.7	2.7	41.0	2.1	168.0	8.4
FB 0275	Strawberry	1.2	0.0	0.0	1.8	2.2	0.1	0.1	0.0	0.0	0.3	0.4	6.2	7.4	5.9	7.1
VO 0448	Tomato (incl juice, excl paste, incl peeled)	0.32	23.1	7.4	23.3	7.5	12.6	4.0	14.6	4.7	33.2	10.6	4.3	1.4	98.2	31.4
-d	Tomato paste	0.35	0.1	0.0	2.1	0.7	0.6	0.2	0.4	0.1	0.6	0.2	1.4	0.5	1.2	0.4
-	Wine	0.34	1.0	0.3	0.9	0.3	6.8	2.3	0.1	0.0	3.4	1.2	3.6	1.2	31.0	10.5
	Total intake (µg/person)=			80.6		479.0		26.3		127.2		650.2		115.2		187.5
	Bodyweight per region (kg bw) =			55		60		60		60		60		55		60

Annex 3

PYRIMETHANIL (226) International Estimated Daily Intake (IEDI) ADI = 0 - 0.2000 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person													
			G		H		I		J		K		L		M	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
	ADI (µg/person)=			11000		12000		12000		12000		12000		11000		12000
	%ADI=			0.7%		4.0%		0.2%		1.1%		5.4%		1.0%		1.6%
	Rounded %ADI=			1%		4%		0%		1%		5%		1%		2%

PHOSMET (103) International Estimated Daily Intake (IEDI) ADI = 0 – 0.01 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
FS 0240	Apricot (incl dried)	1.6	0.3	0.5	6.2	9.9	3.9	6.2	3.2	5.1	2.0	3.2	0.8	1.3
FB 0020	Blueberries	4	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.8	0.3	1.2	0.8	3.2
FC 0001	Citrus fruit (incl juice)	0.21	15.7	3.3	100.5	21.1	63.2	13.3	27.8	5.8	52.6	11.0	56.9	11.9
SO 0691	Cotton seed (for oil processing only)	0	5.6	0.0	30.6	0.0	10.6	0.0	41.3	0.0	0.0	0.0	1.9	0.0
OR 0691	Cotton seed oil, edible	0	0.9	0.0	4.9	0.0	1.7	0.0	6.6	0.0	0.0	0.0	0.3	0.0
FB 0269	Grape (incl dried, juice, wine)	3.1	3.7	11.5	128.5	398.4	27.1	84.0	33.1	102.6	107.5	333.3	44.0	136.4
FS 0245	Nectarine	1.6	0.0	0.0	0.5	0.8	3.3	5.3	1.8	2.9	2.8	4.5	1.6	2.6
FS 0247	Peach	1.6	0.2	0.3	24.8	39.7	3.3	5.3	1.8	2.9	5.4	8.6	1.6	2.6
FP 0009	Pome fruit (incl apple juice)	0.38	0.5	0.2	84.1	32.0	21.9	8.3	45.2	17.2	61.7	23.4	46.2	17.6
VR 0589	Potato (incl flour, frozen, starch, tapioca)	0.05	19.1	1.0	160.8	8.0	61.2	3.1	243.6	12.2	230.1	11.5	204.7	10.2
TN 0085	Tree nuts	0.05	4.2	0.2	21.5	1.1	3.9	0.2	3.0	0.2	5.5	0.3	10.2	0.5
	Total intake (µg/person)=			16.9		510.9		125.7		149.6		397.0		186.3
	Bodyweight per region (kg bw) =			60		60		60		60		60		60
	ADI (µg/person)=			600		600		600		600		600		600
	%ADI=			2.8%		85.2%		20.9%		24.9%		66.2%		31.0%
	Rounded %ADI=			3%		90%		20%		20%		70%		30%

PHOSMET (103) International Estimated Daily Intake (IEDI) ADI = 0 – 0.01 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day Intake = daily intake: µg/person G diet	G intake	H diet	H intake	I diet	I intake	J diet	J intake	K diet	K intake	L diet	L intake	M diet	M intake
FS 0240	Apricot (incl dried)	1.6	0.2	0.3	0.1	0.2	0.2	0.3	0.0	0.0	0.0	0.0	0.1	0.2	1.1	1.8
FB 0020	Blueberries	4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.3	5.2
FC 0001	Citrus fruit (incl juice)	0.21	17.3	3.6	156.8	32.9	14.9	3.1	42.5	8.9	222.8	46.8	40.4	8.5	132.3	27.8
SO 0691	Cotton seed (for oil processing only)	0	6.3	0.0	4.4	0.0	6.3	0.0	8.8	0.0	9.4	0.0	34.4	0.0	7.5	0.0
OR 0691	Cotton seed oil, edible	0	1.0	0.0	0.7	0.0	1.0	0.0	1.4	0.0	1.5	0.0	5.5	0.0	1.2	0.0
FB 0269	Grape (incl dried, juice, wine)	3.1	2.6	8.1	4.8	14.9	11.7	36.3	0.3	0.9	6.8	21.1	10.9	33.8	58.8	182.3
FS 0245	Nectarine	1.6	1.7	2.7	1.7	2.7	0.0	0.0	0.0	0.0	1.0	1.6	1.7	2.7	1.4	2.2
FS 0247	Peach	1.6	1.7	2.7	1.7	2.7	1.1	1.8	0.1	0.2	1.0	1.6	1.7	2.7	10.2	16.3
FP 0009	Pome fruit (incl apple juice)	0.38	20.9	7.9	12.3	4.7	3.4	1.3	0.1	0.0	11.7	4.4	24.9	9.5	45.4	17.3
VR 0589	Potato (incl flour, frozen, starch, tapioca)	0.05	52.7	2.6	57.1	2.9	50.1	2.5	4.3	0.2	54.7	2.7	41.0	2.1	168.0	8.4
TN 0085	Tree nuts	0.05	16.3	0.8	15.7	0.8	9.7	0.5	1.9	0.1	19.1	1.0	29.0	1.5	5.6	0.3
	Total intake (µg/person)=			28.8		61.7		45.8		10.4		79.2		60.8		261.5
	Bodyweight per region (kg bw) =			55		60		60		60		60		55		60
	ADI (µg/person)=			550		600		600		600		600		550		600
	%ADI=			5.2%		10.3%		7.6%		1.7%		13.2%		11.1%		43.6%
	Rounded %ADI=			5%		10%		8%		2%		10%		10%		40%

TRIADIMEFON (133) / TRIADIMENOL (168) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0300 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day Intake = daily intake: µg/person A diet	A intake	B diet	B intake	C diet	C intake	D diet	D intake	E diet	E intake	F diet	F intake
FP 0226	Apple (excl juice)	0.06	0.3	0.0	56.3	3.4	18.4	1.1	38.3	2.3	40.6	2.4	28.3	1.7
JF 0226	Apple juice	0.04	0.0	0.0	2.8	0.1	0.1	0.0	1.1	0.0	6.8	0.3	7.4	0.3
FI 0327	Banana	0.04	38.8	1.6	17.4	0.7	16.0	0.6	6.6	0.3	21.5	0.9	33.8	1.4
GC 0640	Barley (including pot, including pearled, including flour & grits, including beer)	0.05	40.6	2.0	16.8	0.8	93.9	4.7	13.2	0.7	48.6	2.4	36.1	1.8
GC 0641	Buckwheat (including flour, including bran)	0.05	0.0	0.0	0.1	0.0	0.0	0.0	1.7	0.1	1.6	0.1	0.1	0.0
SB 0716	Coffee beans (including green, including extracts, excl roasted)	0.05	2.7	0.1	6.6	0.3	2.4	0.1	0.8	0.0	0.7	0.0	1.6	0.1

Annex 3

TRIADIMEFON (133) / TRIADIMENOL (168) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0300 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
SM 0716	Coffee beans, roasted	0.06	0.4	0.0	6.0	0.4	0.5	0.0	0.6	0.0	9.4	0.6	16.4	1.0
FB 0021	Currants, red, black, white	0.23	0.0	0.0	0.0	0.0	0.0	0.0	2.2	0.5	3.1	0.7	2.0	0.5
032	**EDIBLE OFFAL (MAMMALIAN)**	0	-	-	-	-	-	-	-	-	-	-	-	-
VO 0440	Egg plant (= aubergine)	0.15	1.7	0.3	17.5	2.6	12.3	1.8	1.7	0.3	0.8	0.1	0.4	0.1
PE 0112	Eggs	0.01	2.5	0.0	29.7	0.3	25.1	0.3	24,5	0,2	37.8	0.4	27.4	0.3
VC 0045	Fruiting vegetables, cucurbits	0.05	26.6	1.3	107.5	5.4	95.9	4.8	82.2	4.1	25.4	1.3	23.2	1.2
FB 0269	Grape (excl dried, excl juice, excl wine)	0.15	1.9	0.3	9.2	1.4	23.8	3.6	9.8	1.5	0.0	0.0	0.0	0.0
JF 0269	Grape juice	0.07	0.0	0.0	0.1	0.0	0.1	0.0	0.1	0.0	1.4	0.1	1.0	0.1
DF 0269	Grape, dried (= currants, raisins and sultanas)	0.47	0.0	0.0	2.9	1.4	0.4	0.2	0.4	0.2	2.3	1.1	1.7	0.8
031	**MAMMALIAN FATS**	0.01	-	-	-	-	-	-	-	-	-	-	-	-
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0.01	5.5	0.1	23.3	0.2	7.7	0.1	11.0	0.1	18.0	0.2	26.3	0.3
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0	22.2	0.0	93.2	0.0	30.8	0.0	44.1	0.0	72.2	0.0	105.0	0.0
033	**MILK AND MILK PRODUCTS**	0	-	-	-	-	-	-	-	-	-	-	-	-
GC 0646	Millet (including flour, including beer)	0.05	15.8	0.8	0.1	0.0	0.8	0.0	5.6	0.3	0.2	0.0	0.1	0.0
GC 0647	Oats (including rolled)	0.05	1.4	0.1	0.6	0.0	0.2	0.0	4.2	0.2	5.7	0.3	8.9	0.4
VO 0442	Okra	0.15	3.9	0.6	1.0	0.2	5.3	0.8	0.1	0.0	0.0	0.0	0.0	0.0
VO 0051	Peppers	0.15	1.4	0.2	29.9	4.5	13.0	2.0	6.3	0.9	6.2	0.9	4.0	0.6
FI 0353	Pineapple (including canned, including juice)	0.11	3.8	0.4	6.2	0.7	0.6	0.1	0.9	0.1	7.7	0.8	8.2	0.9
037	**POULTRY FATS**	0	-	-	-	-	-	-	-	-	-	-	-	-
036	**POULTRY MEAT**	0	-	-	-	-	-	-	-	-	-	-	-	-
038	**POULTRY, EDIBLE OFFAL OF**	0	-	-	-	-	-	-	-	-	-	-	-	-
GC 0650	Rye (including flour)	0.05	0.1	0.0	3.7	0.2	0.3	0.0	24.3	1.2	25.8	1.3	45.8	2.3
GC 0651	Sorghum (including flour, including beer)	0.05	36.9	1.8	0.0	0.0	10.2	0.5	0.0	0.0	0.0	0.0	0.0	0.0
FB 0275	Strawberry	0.265	0.0	0.0	5.0	1.3	2.0	0.5	1.7	0.5	5.2	1.4	4.1	1.1
VR 0596	Sugar beet	0.05	0.0	0.0	40.7	2.0	0.0	0.0	0.1	0.0	6.0	0.3	0.1	0.0
VO 0448	Tomato (excl juice, excl paste, including peeled)	0.15	3.3	0.5	179.2	26.9	103.5	15.5	54.1	8.1	7.8	1.2	3.9	0.6
JF 0448	Tomato juice	0.09	5.2	0.5	0.5	0.0	0.4	0.0	2.1	0.2	6.9	0.6	15.2	1.4
-d	Tomato paste	0.78	0.5	0.4	1.3	1.0	3.5	2.7	1.0	0.8	3.8	3.0	4.5	3.5
GC 0653	Triticale (including flour)	0.05	0.0	0.0	115.8	5.8	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.0
GC 0654	Wheat (including bulgur wholemeal, including	0.05	88.4	4.4	396.3	19.8	426.5	21.3	390.2	19.5	236.3	11.8	216.0	10.8

TRIADIMEFON (133) / TRIADIMENOL (168) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0300 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
	flour)													
-	Wine	0.06	1.3	0.1	76.8	4.6	1.1	0.1	15.4	0.9	68.8	4.1	25.6	1.5
	Total intake (µg/person)=			14.1		78.4		55.9		38.7		34.6		31.0
	Bodyweight per region (kg bw) =			60		60		60		60		60		60
	ADI (µg/person)=			1800		1800		1800		1800		1800		1800
	%ADI=			0.8%		4.4%		3.1%		2.1%		1.9%		1.7%
	Rounded %ADI=			1%		4%		3%		2%		2%		2%

TRIADIMEFON (133) / TRIADIMENOL (168) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0300 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person													
			G		H		I		J		K		L		M	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
FP 0226	Apple (excl juice)	0.06	14.3	0.9	9.4	0.6	2.1	0.1	0.0	0.0	8.8	0.5	16.6	1.0	27.8	1.7
JF 0226	Apple juice	0.04	0.1	0.0	0.5	0.0	0.1	0.0	0.0	0.0	0.7	0.0	0.9	0.0	5.7	0.2
FI 0327	Banana	0.04	21.4	0.9	36.6	1.5	11.4	0.5	9.2	0.4	70.2	2.8	40.5	1.6	32.6	1.3
GC 0640	Barley (including pot, including pearled, including flour & grits, including beer)	0.05	5.9	0.3	20.5	1.0	5.9	0.3	2.5	0.1	20.2	1.0	16.8	0.8	43.8	2.2
GC 0641	Buckwheat (including flour, including bran)	0.05	1.0	0.1	0.0	0.0	0.2	0.0	0.1	0.0	0.5	0.0	2.0	0.1	0.1	0.0
SB 0716	Coffee beans (including green, including extracts, excl roasted)	0.05	0.2	0.0	5.7	0.3	0.4	0.0	0.2	0.0	4.5	0.2	5.4	0.3	5.4	0.3
SM 0716	Coffee beans, roasted	0.06	0.0	0.0	1.3	0.1	0.1	0.0	0.0	0.0	0.8	0.0	0.3	0.0	7.0	0.4
FB 0021	Currants, red, black, white	0.23	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
032	**EDIBLE OFFAL (MAMMALIAN)**	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
VO 0440	Egg plant (= aubergine)	0.15	20.1	3.0	0.1	0.0	0.6	0.1	6.3	0.9	0.5	0.1	6.3	0.9	0.7	0.1
039	**EGGS**	0.01	22.1	0.2	71.5	0.7	16.6	0.2	5.1	0.1	17.6	0.2	35.2	0.4	57.4	0.6
011	**FRUITING VEGETABLES, CUCURBITS**	0.05	69.7	3.5	25.9	1.3	14.9	0.7	18.0	0.9	18.7	0.9	39.1	2.0	44.2	2.2
FB 0269	Grape (excl dried, excl juice, excl wine)	0.15	1.2	0.2	2.6	0.4	0.0	0.0	0.2	0.0	0.0	0.0	3.7	0.6	0.0	0.0
JF 0269	Grape juice	0.07	0.0	0.0	0.1	0.0	1.0	0.1	0.0	0.0	0.6	0.0	0.4	0.0	3.6	0.3

Annex 3

TRIADIMEFON (133) / TRIADIMENOL (168) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0300 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day Intake = daily intake: µg/person													
			G		H		I		J		K		L		M	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
DF 0269	Grape, dried (= currants, raisins and sultanas)	0.47	0.0	0.0	0.2	0.1	0.2	0.1	0.0	0.0	0.3	0.1	0.4	0.2	2.6	1.2
031	**MAMMALIAN FATS**	0.01	-	-	-	-	-	-	-	-	-	-	-	-	-	-
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0.01	11.0	0.1	17.9	0.2	6.1	0.1	5.7	0.1	16.4	0.2	12.2	0.1	31.7	0.3
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0	43.8	0.0	71.5	0.0	24.5	0.0	22.9	0.0	65.7	0.0	48.9	0.0	126.6	0.0
033	**MILK AND MILK PRODUCTS**	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
GC 0646	Millet (including flour, including beer)	0.05	13.0	0.7	0.0	0.0	8.3	0.4	96.9	4.8	0.0	0.0	0.4	0.0	0.0	0.0
GC 0647	Oats (including rolled)	0.05	0.2	0.0	2.0	0.1	0.8	0.0	0.0	0.0	3.5	0.2	0.7	0.0	7.6	0.4
VO 0442	Okra	0.15	4.1	0.6	1.0	0.2	7.0	1.1	15.9	2.4	1.1	0.2	3.9	0.6	0.2	0.0
VO 0051	Peppers	0.15	8.7	1.3	22.4	3.4	8.4	1.3	9.4	1.4	3.3	0.5	5.3	0.8	8.9	1.3
FI 0353	Pineapple (including canned, including juice)	0.11	3.9	0.4	11.7	1.3	12.6	1.4	11.1	1.2	16.6	1.8	21.4	2.4	22.6	2.5
037	**POULTRY FATS**	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
036	**POULTRY MEAT**	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
038	**POULTRY, EDIBLE OFFAL OF**	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
GC 0650	Rye (including flour)	0.05	0.4	0.0	0.0	0.0	0.2	0.0	0.1	0.0	0.1	0.0	0.9	0.0	0.8	0.0
GC 0651	Sorghum (including flour, including beer)	0.05	9.8	0.5	19.9	1.0	18.6	0.9	112.3	5.6	0.1	0.0	3.3	0.2	3.0	0.2
FB 0275	Strawberry	0.265	0.0	0.0	1.8	0.5	0.1	0.0	0.0	0.0	0.3	0.1	6.2	1.6	5.9	1.6
VR 0596	Sugar beet	0.05	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.0	14.3	0.7
VO 0448	Tomato (excl juice, excl paste, including peeled)	0.15	23.1	3.5	22.3	3.3	12.5	1.9	5.6	0.8	33.2	5.0	1.3	0.2	41.7	6.3
JF 0448	Tomato juice	0.09	0.0	0.0	0.8	0.1	0.1	0.0	7.2	0.6	0.0	0.0	2.4	0.2	45.2	4.1
-d	Tomato paste	0.78	0.1	0.1	2.1	1.6	0.6	0.5	0.4	0.3	0.6	0.5	1.4	1.1	1.2	0.9
GC 0653	Triticale (including flour)	0.05	1.3	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
GC 0654	Wheat (including bulgur wholemeal, including flour)	0.05	172.9	8.6	79.0	4.0	68.1	3.4	41.9	2.1	114.1	5.7	103.4	5.2	234.2	11.7
-	Wine	0.06	1.0	0.1	0.9	0.1	6.8	0.4	0.1	0.0	3.4	0.2	3.6	0.2	31.0	1.9
	Total intake (µg/person)=			21.2		19.6		12.5		20.9		19.2		18.2		39.5
	Bodyweight per region (kg bw) =			55		60		60		60		60		55		60
	ADI (µg/person)=			1650		1800		1800		1800		1800		1650		1800
	%ADI=			1.3%		1.1%		0.7%		1.2%		1.1%		1.1%		2.2%
	Rounded%ADI=			1%		1%		1%		1%		1%		1%		2%

TRIAZOPHOS (143) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0010 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
OR 0691	Cotton seed oil, edible	0.088	0.9	0.1	4.9	0.4	1.7	0.1	6.6	0.6	0.0	0.0	0.3	0.0
VP 0541	Soya bean (immature seeds only)	0.37	5.0	1.9	0.0	0.0	0.0	0.0	11.1	4.1	0.4	0.1	0.0	0.0
Total intake (µg/person)=				1.9		0.4		0.1		4.7		0.1		0.0
Bodyweight per region (kg bw) =				60		60		60		60		60		60
ADI (µg/person)=				60		60		60		60		60		60
%ADI=				3.2%		0.7%		0.2%		7.8%		0.2%		0.0%
Rounded %ADI=				3%		1%		0%		8%		0%		0%

TRIAZOPHOS (143) International Estimated Daily Intake (IEDI) ADI = 0 - 0.0010 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person													
			G		H		I		J		K		L		M	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
OR 0691	Cotton seed oil, edible	0.088	1.0	0.1	0.7	0.1	1.0	0.1	1.4	0.1	1.5	0.1	5.5	0.5	1.2	0.1
VP 0541	Soya bean (immature seeds only)	0.37	12.9	4.8	0.0	0.0	5.5	2.0	5.5	2.0	0.0	0.0	25.7	9.5	0.0	0.0
Total intake (µg/person)=				4.9		0.1		2.1		2.2		0.1		10.0		0.1
Bodyweight per region (kg bw) =				55		60		60		60		60		55		60
ADI (µg/person)=				55		60		60		60		60		55		60
%ADI=				8.8%		0.1%		3.5%		3.6%		0.2%		18.2%		0.2%
Rounded %ADI=				9%		0%		4%		4%		0%		20%		0%

Annex 3

ZOXAMIDE (227) International Estimated Daily Intake (IEDI) ADI = 0 - 0.5000 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			A		B		C		D		E		F	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
FB 0269	Grape (excl dried, excl juice, excl wine)	0.83	1.9	1.6	9.2	7.7	23.8	19.8	9.8	8.1	0.0	0.0	0.0	0.0
DF 0269	Grape, dried (= currants, raisins and sultanas)	2.4	0.0	0.0	2.9	7.0	0.4	1.0	0.4	1.0	2.3	5.5	1.7	4.1
JF 0269	Grape juice	0.11	0.0	0.0	0.1	0.0	0.1	0.0	0.1	0.0	1.4	0.2	1.0	0.1
-	Wine	0.02	1.3	0.0	76.8	1.5	1.1	0.0	15.4	0.3	68.8	1.4	25.6	0.5
VR 0589	Potato (incl flour, frozen, starch, tapioca)	0.02	19.1	0.4	160.8	3.2	61.2	1.2	243.6	4.9	230.1	4.6	204.7	4.1
VC 0424	Cucumber	0.06	0.3	0.0	12.7	0.8	5.9	0.4	11.5	0.7	6.1	0.4	7.1	0.4
VO 0448	Tomato (incl juice, excl paste, incl peeled)	0.195	9.8	1.9	179.8	35.1	104.0	20.3	56.7	11.1	16.4	3.2	22.9	4.5
-d	Tomato paste	0.19	0.5	0.1	1.3	0.2	3.5	0.7	1.0	0.2	3.8	0.7	4.5	0.9
	Total intake (µg/person)=			4.0		55.5		43.3		26.2		16.0		14.5
	Bodyweight per region (kg bw) =			60		60		60		60		60		60
	ADI (µg/person)=			30000		30000		30000		30000		30000		30000
	%ADI=			0.0%		0.2%		0.1%		0.1%		0.1%		0.0%
	Rounded %ADI=			0%		0%		0%		0%		0%		0%

ZOXAMIDE (227) International Estimated Daily Intake (IEDI) ADI = 0 - 0.5000 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day / Intake = daily intake: µg/person											
			G		H		I		J		K		L		M	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
FB 0269	Grape (excl dried, excl juice, excl wine)	0.83	1.2	1.0	2.6	2.2	0.0	0.0	0.2	0.1	0.0	0.0	3.7	3.1	0.0	0.0
DF 0269	Grape, dried (= currants, raisins and sultanas)	2.4	0.0	0.0	0.2	0.5	0.2	0.5	0.0	0.0	0.3	0.7	0.4	1.0	2.6	6.2
JF 0269	Grape juice	0.11	0.0	0.0	0.1	0.0	1.0	0.1	0.0	0.0	0.6	0.1	0.4	0.0	3.6	0.4
-	Wine	0.02	1.0	0.0	0.9	0.0	6.8	0.1	0.1	0.0	3.4	0.1	3.6	0.1	31.0	0.6
VR 0589	Potato (incl flour, frozen, starch, tapioca)	0.02	52.7	1.1	57.1	1.1	50.1	1.0	4.3	0.1	54.7	1.1	41.0	0.8	168.0	3.4
VC 0424	Cucumber	0.06	7.9	0.5	0.6	0.0	0.2	0.0	0.0	0.0	0.4	0.0	5.5	0.3	5.3	0.3
VO 0448	Tomato (incl juice, excl paste, incl peeled)	0.195	23.1	4.5	23.3	4.5	12.6	2.5	14.6	2.8	33.2	6.5	4.3	0.8	98.2	19.1
-d	Tomato paste	0.19	0.1	0.0	2.1	0.4	0.6	0.1	0.4	0.1	0.6	0.1	1.4	0.3	1.2	0.2
	Total intake (µg/person)=			7.1		8.8		4.3		3.1		8.6		6.4		30.3
	Bodyweight per region (kg bw) =			55		60		60		60		60		55		60

ZOXAMIDE (227) International Estimated Daily Intake (IEDI) ADI = 0 - 0.5000 mg/kg bw

Codex Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day Intake = daily intake: µg/person											
			G		H		I		J		K		L		M	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
	ADI (µg/person)=			27500		30000		30000		30000		30000		27500		30000
	%ADI=			0.0%		0.0%		0.0%		0.0%		0.0%		0.0%		0.1%
	Rounded %ADI=			0%		0%		0%		0%		0%		0%		0%

ANNEX 4: INTERNATIONAL ESTIMATES OF SHORT-TERM DIETARY INTAKES OF PESTICIDE RESIDUES

CARBARYL (008) International estimate of short term intake (IESTI) for **GENERAL POPULATION**

Acute RfD= 0.200 mg/kg bw (200 µg/kg bw)
Maximum %ARfD: 0%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
FB 0265	Cranberries	-	2.95	USA	65.0	229	-	-	ND	ND	ND	ND	-
VO 0444	Peppers, chilli	-	0.25	USA	65.0	90	45	USA	43	3	2a	0.68	0%

CARBARYL (008) International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS**

Acute RfD= 0.200 mg/kg bw (200 µg/kg bw)
Maximum %ARfD: 1%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
FB 0265	Cranberries	-	2.95	USA	15.0	102	-	-	ND	ND	ND	ND	-
VO 0444	Peppers, chilli	-	0.25	AUS	19.0	31	45	USA	43	3	2b	1.20	1%

CYFLUTHRIN (157)/
BETA-CYFLUTHRIN (228)

International estimate of short term intake (IESTI) for
GENERAL POPULATION

Acute RfD= 0.040 mg/kg bw (40 µg/kg bw)
Maximum %ARfD: 100%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
FP 0226	Apple	-	0.06	USA	65.0	1348	200	JPN	200	3	2a	1.61	4%
VB 0400	Broccoli	-	1.5	USA	65.0	376	608	USA	474	3	2b	26.06	70%
VB 0041	Cabbage, head	-	2.1	SAF	55.7	362	771	UNK	540	3	2b	40.95	100%
VB 0404	Cauliflower (head)	-	0.91	UNK	70.1	579	1500	JPN	1500	3	2b	22.55	60%
SO 0691	Cotton seed	0.19	-	USA	65.0	3	-	-	ND	ND	3	0.01	0%
VO 0440	Egg plant	-	0.12	AUS	67.0	487	80	JPN	80	3	2a	1.16	3%
PE 0112	Eggs	0	-	Thai	53.5	195	-	-	ND	ND	1	ND	-
FC 0203	Grapefruit	-	0.2	JPN	52.6	947	400	JPN	400	3	2a	6.64	20%
MO 0098	Kidney of cattle, goats, pigs and sheep	-	0.027	USA	65.0	788	-	-	ND	ND	1	0.33	1%
FC 0204	Lemon	-	0.2	FRA	62.3	115	100	FRA	64	3	2a	0.78	2%
FC 0205	Lime	-	0.2	AUS	67.0	590	67	USA	56	3	2a	2.10	5%
MO 0099	Liver of cattle, goats, pigs and sheep	-	0.021	USA	65.0	380	-	-	ND	ND	1	0.12	0%
FC 0206	Mandarin	-	0.2	JPN	52.6	409	100	FRA	72	3	2a	2.10	5%
MM 0097	Meat of cattle, pigs & sheep: 20% as fat	-	0.37	AUS	67.0	104	-	-	ND	ND	1	0.57	1%
MM 0097	Meat of cattle, pigs & sheep: 80% as muscle	-	0.01	AUS	67.0	416	-	-	ND	ND	1	0.06	0%
ML 0106	Milks	0.0022	-	USA	65.0	2466	-	-	ND	ND	3	0.08	0%
FC 0004	Orange, sweet, sour + orange-like hybrid	-	0.2	USA	65.0	564	200	JPN	200	3	2a	2.97	7%
FP 0230	Pear	-	0.06	USA	65.0	693	180	JPN	180	3	2a	0.97	2%
VO 0444	Peppers, chilli	-	0.12	USA	65.0	90	45	USA	43	3	2a	0.33	1%
FC 4020	Pomelo	-	0.2	Thai	53.5	554	-	-	ND	ND	ND	ND	-
PM 0110	Poultry meat: 10% as fat	-	0	AUS	67.0	43	-	-	ND	ND	1	0.00	0%
PM 0110	Poultry meat: 90% as muscle	-	0	AUS	67.0	388	-	-	ND	ND	1	0.00	0%
PO 0111	Poultry, edible offal of	-	0	USA	65.0	248	-	-	ND	ND	1	0.00	0%
OR 0495	Rape seed oil, edible	0.05	-	AUS	67.0	65	-	-	ND	ND	3	0.05	0%
FC 0005	Shaddock or pomelo + shaddock-like hybrid	-	0.2	Thai	53.5	554	230	UNK	161	3	2a	3.27	8%

Annex 4

CYFLUTHRIN (157)/
BETA-CYFLUTHRIN (228)

International estimate of short term intake (IESTI) for
GENERAL POPULATION

Acute RfD= 0.040 mg/kg bw (40 µg/kg bw)
Maximum %ARfD: 100%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
FC 4031	Tangelo	-	0.2	AUS	67.0	114	-	-	ND	ND	ND	ND	-
VO 0448	Tomato	-	0.1	USA	65.0	391	150	JPN	150	3	2a	1.06	3%

CYFLUTHRIN (157)/
BETA-CYFLUTHRIN (228)

International estimate of short term intake (IESTI) for
CHILDREN UP TO 6 YEARS

Acute RfD= 0.040 mg/kg bw (40 µg/kg bw)
Maximum %ARfD: 240%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
FC 0204	Lemon	-	0.2	JPN	15.9	88	100	FRA	64	3	2a	2.72	7%
FP 0226	Apple	-	0.06	USA	15.0	679	200	JPN	200	3	2a	4.32	10%
VB 0400	Broccoli	-	1.5	USA	15.0	164	608	USA	474	3	2b	49.28	120%
VB 0041	Cabbage, head	-	2.1	SAF	14.2	220	771	UNK	540	3	2b	97.65	240%
VB 0404	Cauliflower (head)	-	0.91	NLD	17.0	209	1500	JPN	1500	3	2b	33.61	80%
SO 0691	Cotton seed	0.19	-	USA	15.0	1	-	-	ND	ND	3	0.01	0%
VO 0440	Egg plant	-	0.12	JPN	15.9	219	80	JPN	80	3	2a	2.86	7%
PE 0112	Eggs	0	-	Thai	17.1	109	-	-	ND	ND	1	ND	-
FC 0203	Grapefruit	-	0.2	FRA	17.8	381	400	JPN	400	3	2b	12.86	30%
MO 0098	Kidney of cattle, goats, pigs and sheep	-	0.027	USA	15.0	187	-	-	ND	ND	1	0.34	1%
FC 0205	Lime	-	0.2	AUS	19.0	26	67	USA	56	3	2b	0.82	2%
MO 0099	Liver of cattle, goats, pigs and sheep	-	0.021	FRA	17.8	203	-	-	ND	ND	1	0.24	1%

CYFLUTHRIN (157)/
BETA-CYFLUTHRIN (228)

International estimate of short term intake (IESTI) for
CHILDREN UP TO 6 YEARS

Acute RfD= 0.040 mg/kg bw (40 µg/kg bw)
Maximum %ARfD: 240%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
FC 0206	Mandarin	-	0.2	JPN	15.9	353	100	FRA	72	3	2a	6.26	20%
MM 0097	Meat of cattle, pigs & sheep: 20% as fat	-	0.37	AUS	19.0	52	-	-	ND	ND	1	1.01	3%
MM 0097	Meat of cattle, pigs & sheep: 80% as muscle	-	0.01	AUS	19.0	208	-	-	ND	ND	1	0.11	0%
ML 0106	Milks	0.0022	-	USA	15.0	1286	-	-	ND	ND	3	0.19	0%
FC 0004	Orange, sweet, sour + orange-like hybrid	-	0.2	UNK	14.5	495	200	JPN	200	3	2a	12.35	30%
FP 0230	Pear	-	0.06	UNK	14.5	279	180	JPN	180	3	2a	2.64	7%
VO 0444	Peppers, chilli	-	0.12	AUS	19.0	31	45	USA	43	3	2b	0.58	1%
FC 4020	Pomelo	-	0.2	Thai	17.1	327	-	-	ND	ND	ND	ND	-
PM 0110	Poultry meat: 10% as fat	-	0	AUS	19.0	22	-	-	ND	ND	1	0.00	0%
PM 0110	Poultry meat: 90% as muscle	-	0	AUS	19.0	201	-	-	ND	ND	1	0.00	0%
PO 0111	Poultry, edible offal of	-	0	USA	15.0	37	-	-	ND	ND	1	0.00	0%
OR 0495	Rape seed oil, edible	0.05	-	AUS	19.0	18	-	-	ND	ND	3	0.05	0%
FC 0005	Shaddock or pomelo + shaddock-like hybrid	-	0.2	Thai	17.1	327	230	UNK	161	3	2a	7.59	20%
FC 4031	Tangelo	-	0.2	-	-	ND	-	-	ND	ND	ND	ND	-
VO 0448	Tomato	-	0.1	USA	15.0	159	150	JPN	150	3	2a	3.06	8%

Annex 4

CYROMAZINE (169) International estimate of short term intake (IESTI) for **GENERAL POPULATION**

Acute RfD= 0.100 mg/kg bw (100 µg/kg bw)

Maximum %ARfD: 130%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
VS 0620	Artichoke globe	-	1.3	FRA	62.3	534	128	USA	51	3	2a	13.28	10%
VD 0071	Beans (dry)	1	-	FRA	62.3	255	-	-	ND	ND	3	4.10	4%
VB 0400	Broccoli	-	0.51	USA	65.0	376	608	USA	474	3	2b	8.86	9%
VB 0041	Cabbage, head	-	6.1	SAF	55.7	362	908	USA	717	3	2b	118.95	120%
VS 0624	Celery (whole)	-	2.3	FRA	62.3	225	700	BEL	462	3	2b	24.91	20%
VC 0424	Cucumber	-	1.3	NLD	63.0	313	400	FRA	360	3	2b	19.38	20%
MO 0105	Edible offal (mammalian)	-	0.19	FRA	62.3	277	-	-	ND	ND	1	0.84	1%
VO 0440	Egg plant	-	0.58	AUS	67.0	487	548	USA	444	3	2a	11.90	10%
PE 0112	Eggs	-	0.16	Thai	53.5	195	-	-	ND	ND	1	0.58	1%
VL 0482	Lettuce, head	-	2	USA	65.0	213	539	USA	512	3	2b	19.62	20%
VL 0483	Lettuce, leaf	-	2	NLD	63.0	152	160	BEL	144	3	2a	13.96	10%
VP 0534	Lima bean (green pods & immature seeds)	-	0.58	USA	65.0	241	-	-	ND	ND	ND	ND	-
MF 0100	Mammalian fats (except milk fats)	-	0	-	-	ND	-	-	ND	ND	1	ND	-
FI 0345	Mango	-	0.25	FRA	62.3	567	207	USA	139	3	2a	3.39	3%
MM 0095	Meat from mammals other than marine mammals	-	0.2	AUS	67.0	521	-	-	ND	ND	1	1.56	2%
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0	AUS	67.0	104	-	-	ND	ND	1	0.00	0%
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0	AUS	67.0	417	-	-	ND	ND	1	0.00	0%
VC 0046	Melons, except watermelon	-	0.19	USA	65.0	655	1000	USA	630	3	2a	5.60	6%
ML 0106	Milks	-	0.005	USA	65.0	2466	-	-	ND	ND	3	ND	-
VO 0450	Mushrooms	-	4.2	FRA	62.3	219	21	UNK	20	1	1	14.74	10%
VL 0485	Mustard greens	-	7.4	USA	65.0	228	-	-	ND	ND	ND	ND	-
VO 0442	Okra	-	0.58	USA	65.0	235	10	JPN	10	1	1	2.10	2%
VA 0385	Onion, bulb	-	0.07	FRA	62.3	306	110	USA	100	3	2a	0.57	1%
VO 0051	Peppers	-	0.58	FRA	62.3	207	-	-	ND	ND	ND	ND	-
PM 0110	Poultry meat	-	0.05	AUS	67.0	431	-	-	ND	ND	1	0.32	0%

CYROMAZINE (169) International estimate of short term intake (IESTI) for **GENERAL POPULATION** Acute RfD= 0.100 mg/kg bw (100 µg/kg bw) Maximum %ARfD: 130%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
PM 0110	Poultry meat: 10% as fat	-	0	AUS	67.0	43	-	-	ND	ND	1	0.00	0%
PM 0110	Poultry meat: 90% as muscle	-	0	AUS	67.0	388	-	-	ND	ND	1	0.00	0%
PO 0111	Poultry, edible offal of	-	0.08	USA	65.0	248	-	-	ND	ND	1	0.30	0%
PF 0111	Poultry, fats	-	0	FRA	62.3	46	-	-	ND	ND	1	0.00	0%
VL 0502	Spinach (bunch)	-	6.1	NLD	63.0	820	340	USA	245	3	2a	126.77	130%
VA 0389	Spring onion	-	1.7	Thai	53.5	71	-	-	ND	ND	ND	ND	-
VC 0431	Squash, summer (= courgette)	-	1	FRA	62.3	343	300	FRA	270	3	2a	14.17	10%
VO 0448	Tomato	-	0.58	USA	65.0	391	123	USA	123	3	2a	5.68	6%
JF 0448	Tomato juice	0.1	-	-	-	ND	-	-	ND	ND	3	ND	-
-	Tomato paste	0.29	-	-	-	ND	-	-	ND	ND	ND	ND	-

CYROMAZINE (169) International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS** Acute RfD= 0.100 mg/kg bw (100 µg/kg bw) Maximum %ARfD: 390%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
VS 0620	Artichoke globe	-	1.3	FRA	17.8	89	128	USA	51	3	2a	13.98	10%
VD 0071	Beans (dry)	1	-	FRA	17.8	209	-	-	ND	ND	3	11.76	10%
VB 0400	Broccoli	-	0.51	USA	15.0	164	608	USA	474	3	2b	16.75	20%
VB 0041	Cabbage, head	-	6.1	SAF	14.2	220	908	USA	717	3	2b	283.65	280%
VS 0624	Celery (whole)	-	2.3	FRA	17.8	111	700	BEL	462	3	2b	43.13	40%
VC 0424	Cucumber	-	1.3	NLD	17.0	162	400	FRA	360	3	2b	37.17	40%
MO 0105	Edible offal (mammalian)	-	0.19	FRA	17.8	203	-	-	ND	ND	1	2.16	2%
VO 0440	Egg plant	-	0.58	JPN	15.9	219	548	USA	444	3	2b	23.99	20%

Annex 4

CYROMAZINE (169) International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS**

Acute RfD= 0.100 mg/kg bw (100 µg/kg bw)

Maximum %ARfD: 390%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
PE 0112	Eggs	-	0.16	Thai	17.1	109	-	-	ND	ND	1	1.02	1%
VL 0482	Lettuce, head	-	2	Thai	17.1	117	539	USA	512	3	2b	40.98	40%
VL 0483	Lettuce, leaf	-	2	NLD	17.0	102	160	BEL	144	3	2b	36.00	40%
VP 0534	Lima bean (green pods & immature seeds)	-	0.58	USA	15.0	117	-	-	ND	ND	ND	ND	-
MF 0100	Mammalian fats (except milk fats)	-	0	-	-	ND	-	-	ND	ND	1	ND	-
FI 0345	Mango	-	0.25	Thai	17.1	191	207	USA	139	3	2a	6.85	7%
MM 0095	Meat from mammals other than marine mammals	-	0.2	AUS	19.0	261	-	-	ND	ND	1	2.74	3%
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0	AUS	19.0	52	-	-	ND	ND	1	0.00	0%
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0	AUS	19.0	208	-	-	ND	ND	1	0.00	0%
VC 0046	Melons, except watermelon	-	0.19	AUS	19.0	413	1000	USA	630	3	2b	12.39	10%
ML 0106	Milks	-	0.005	USA	15.0	1286	-	-	ND	ND	3	ND	-
VO 0450	Mushrooms	-	4.2	Thai	17.1	94	21	UNK	20	1	1	22.97	20%
VL 0485	Mustard greens	-	7.4	USA	15.0	53	-	-	ND	ND	ND	ND	-
VO 0442	Okra	-	0.58	USA	15.0	203	10	JPN	10	1	1	7.83	8%
VA 0385	Onion, bulb	-	0.07	FRA	17.8	127	110	USA	100	3	2a	1.29	1%
VO 0051	Peppers	-	0.58	Thai	17.1	71	-	-	ND	ND	ND	ND	-
PM 0110	Poultry meat	-	0.05	AUS	19.0	224	-	-	ND	ND	1	0.59	1%
PM 0110	Poultry meat: 10% as fat	-	0	AUS	19.0	22	-	-	ND	ND	1	0.00	0%
PM 0110	Poultry meat: 90% as muscle	-	0	AUS	19.0	201	-	-	ND	ND	1	0.00	0%
PO 0111	Poultry, edible offal of	-	0.08	USA	15.0	37	-	-	ND	ND	1	0.20	0%
PF 0111	Poultry, fats	-	0	FRA	17.8	20	-	-	ND	ND	1	0.00	0%
VL 0502	Spinach (bunch)	-	6.1	SAF	14.2	420	340	USA	245	3	2a	390.88	390%
VA 0389	Spring onion	-	1.7	Thai	17.1	53	-	-	ND	ND	ND	ND	-
VC 0431	Squash, summer (= courgette)	-	1	AUS	19.0	219	300	FRA	270	3	2b	34.57	30%
VO 0448	Tomato	-	0.58	USA	15.0	159	123	USA	123	3	2a	15.66	20%

CYROMAZINE (169) International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS** Acute RfD= 0.100 mg/kg bw (100 µg/kg bw) Maximum %ARfD: 390%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
JF 0448	Tomato juice	0.1	-	-	-	ND	-	-	ND	ND	3	ND	-
-	Tomato paste	0.29	-	-	-	ND	-	-	ND	ND	ND	ND	-

DIFENOCONAZOLE (224) International estimate of short term intake (IESTI) for **GENERAL POPULATION** Acute RfD= 0.300 mg/kg bw (300 µg/kg bw) Maximum %ARfD: 7%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
FP 0226	Apple	-	0.28	USA	65.0	1348	155	BEL	140	3	2a	7.01	2%
VS 0621	Asparagus	-	0.02	NLD	63.0	398	25	FRA	13	3	2a	0.13	0%
FI 0327	Banana	-	0.02	SAF	55.7	613	708	USA	481	3	2a	0.57	0%
VB 0400	Broccoli	-	0.41	USA	65.0	376	310	BEL	186	3	2a	4.72	2%
VB 0402	Brussels sprouts	-	0.14	NLD	63.0	394	10	UNK	7	1	1	0.88	0%
VB 0041	Cabbage, head	-	0.19	SAF	55.7	362	1650	BEL	1403	3	2b	3.71	1%
VR 0577	Carrot	-	0.13	NLD	63.0	335	100	FRA	89	3	2a	1.06	0%
VB 0404	Cauliflower (head)	-	0.10	UNK	70.1	579	1000	BEL	640	3	2b	2.48	1%
VR 0578	Celeriac	-	0.22	FRA	62.3	374	1070	BEL	749	3	2b	3.96	1%
VS 0624	Celery (whole)	-	2	FRA	62.3	225	700	BEL	462	3	2b	21.66	7%
FS 0013	Cherries	-	0.1	FRA	62.3	375	5	FRA	4	1	1	0.60	0%
PE 0840	Chicken eggs	-	0.0054	FRA	62.3	219	-	-	ND	ND	1	0.02	0%
MO 0105	Edible offal (mammalian)	-	0.11	FRA	62.3	277	-	-	ND	ND	1	0.49	0%
VA 0381	Garlic	-	0	Thai	53.5	34	-	-	ND	ND	ND	ND	-
FB 0269	Grape (excl wine)	-	0.07	AUS	67.0	513	125	FRA	118	3	2a	0.78	0%
DF 0269	Grapes, dried (= currants, raisins and sultanas)	-	0.084	FRA	62.3	135	-	-	ND	ND	1	0.18	0%
VA 0384	Leek	-	0.21	FRA	62.3	374	140	UNK	80	3	2a	1.80	1%
VL 0482	Lettuce, head	-	1.0	USA	65.0	213	450	BEL	360	3	2b	9.81	3%
VL 0483	Lettuce, leaf	-	1.0	NLD	63.0	152	160	BEL	144	3	2a	6.98	2%

Annex 4

DIFENOCONAZOLE (224) International estimate of short term intake (IESTI) for **GENERAL POPULATION**

Acute RfD= 0.300 mg/kg bw (300 µg/kg bw)
Maximum %ARfD: 7%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Variability factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
FI 0345	Mango	-	0.04	FRA	62.3	567	207	USA	139	3	2a	0.54	0%
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.028	AUS	67.0	104	-	-	ND	ND	1	0.04	0%
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0.019	AUS	67.0	417	-	-	ND	ND	1	0.12	0%
ML 0106	Milks	0.001	-	USA	65.0	2466	-	-	ND	ND	3	0.04	0%
FS 0245	Nectarine	-	0.26	USA	65.0	590	110	FRA	99	3	2a	3.15	1%
FT 0305	Olive	-	1.2	NLD	63.0	63	-	-	ND	ND	ND	ND	-
OR 0305	Olive oil, refined	0.65	-	FRA	62.3	57	-	-	ND	ND	3	0.60	0%
FI 0350	Papaya	-	0.02	USA	65.0	567	304	USA	204	3	2a	0.30	0%
FS 0247	Peach	-	0.26	SAF	55.7	685	140	BEL	126	3	2a	4.37	1%
FP 0230	Pear	-	0.28	USA	65.0	693	187	UNK	170	3	2a	4.45	1%
FS 0014	Plum (incl dried)	-	0.1	Thai	53.5	480	59	BEL	55	3	2a	1.10	0%
VR 0589	Potato	-	0.01	NLD	63.0	687	216	UNK	216	3	2a	0.18	0%
PM 0110	Poultry meat	-	0.00054	AUS	67.0	431	-	-	ND	ND	1	0.00	0%
PO 0111	Poultry, edible offal of	-	0.00054	USA	65.0	248	-	-	ND	ND	1	0.00	0%
VD 0541	Soya bean (dry)	0.02	-	JPN	52.6	159	-	-	ND	ND	3	0.06	0%
VO 0448	Tomato	-	0.36	USA	65.0	391	150	BEL	143	3	2a	3.74	1%
GC 0654	Wheat	0	-	USA	65.0	383	-	-	ND	ND	3	0.00	0%
-	Wine	0.0054	-	AUS	67.0	1131	-	-	ND	ND	3	0.09	0%

DIFENOCONAZOLE (224) International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS**

Acute RfD= 0.300 mg/kg bw (300 µg/kg bw)
Maximum %ARfD: 10%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Variability factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
FP 0226	Apple	-	0.28	USA	15.0	679	155	BEL	140	3	2a	17.88	6%
VS 0621	Asparagus	-	0.02	USA	15.0	178	25	FRA	13	3	2a	0.27	0%
FI 0327	Banana	-	0.02	JPN	15.9	312	708	USA	481	3	2b	1.18	0%

DIFENOCONAZOLE (224) International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS**

Acute RfD= 0.300 mg/kg bw (300 µg/kg bw)
Maximum %ARfD: 10%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
VB 0400	Broccoli	-	0.41	USA	15.0	164	310	BEL	186	3	2b	13.47	4%
VB 0402	Brussels sprouts	-	0.14	NLD	17.0	213	10	UNK	7	1	1	1.75	1%
VB 0041	Cabbage, head	-	0.19	SAF	14.2	220	1650	BEL	1403	3	2b	8.84	3%
VR 0577	Carrot	-	0.13	FRA	17.8	205	100	FRA	89	3	2a	2.80	1%
VB 0404	Cauliflower (head)	-	0.10	NLD	17.0	209	1000	BEL	640	3	2b	3.69	1%
VR 0578	Celeriac	-	0.22	FRA	17.8	108	1070	BEL	749	3	2b	3.99	1%
VS 0624	Celery (whole)	-	2	FRA	17.8	111	700	BEL	462	3	2b	37.50	10%
FS 0013	Cherries	-	0.1	FRA	17.8	297	5	FRA	4	1	1	1.67	1%
PE 0840	Chicken eggs	-	0.0054	FRA	17.8	134	-	-	ND	ND	1	0.04	0%
MO 0105	Edible offal (mammalian)	-	0.11	FRA	17.8	203	-	-	ND	ND	1	1.25	0%
VA 0381	Garlic	-	0	FRA	17.8	30	-	-	ND	ND	ND	ND	-
FB 0269	Grape (excl wine)	-	0.07	AUS	19.0	342	125	FRA	118	3	2a	2.13	1%
DF 0269	Grapes, dried (= currants, raisins and sultanas)	-	0.084	USA	15.0	59	-	-	ND	ND	1	0.33	0%
VA 0384	Leek	-	0.21	FRA	17.8	121	140	UNK	80	3	2a	3.32	1%
VL 0482	Lettuce, head	-	1.0	Thai	17.1	117	450	BEL	360	3	2b	20.49	7%
VL 0483	Lettuce, leaf	-	1.0	NLD	17.0	102	160	BEL	144	3	2b	18.00	6%
FI 0345	Mango	-	0.04	Thai	17.1	191	207	USA	139	3	2a	1.10	0%
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.028	AUS	19.0	52	-	-	ND	ND	1	0.08	0%
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0.019	AUS	19.0	208	-	-	ND	ND	1	0.21	0%
ML 0106	Milks	0.001	-	USA	15.0	1286	-	-	ND	ND	3	0.09	0%
FS 0245	Nectarine	-	0.26	AUS	19.0	302	110	FRA	99	3	2a	6.84	2%
FT 0305	Olive	-	1.2	FRA	17.8	49	-	-	ND	ND	ND	ND	-
OR 0305	Olive oil, refined	0.65	-	FRA	17.8	63	-	-	ND	ND	3	2.29	1%
FI 0350	Papaya	-	0.02	USA	15.0	240	304	USA	204	3	2a	0.86	0%
FS 0247	Peach	-	0.26	AUS	19.0	315	140	BEL	126	3	2a	7.77	3%
FP 0230	Pear	-	0.28	UNK	14.5	279	187	UNK	170	3	2a	11.96	4%
FS 0014	Plum (incl dried)	-	0.1	Thai	17.1	377	59	BEL	55	3	2a	2.85	1%
VR 0589	Potato	-	0.01	SAF	14.2	300	216	UNK	216	3	2a	0.52	0%
PM 0110	Poultry meat	-	0.00054	AUS	19.0	224	-	-	ND	ND	1	0.01	0%
PO 0111	Poultry, edible offal of	-	0.00054	USA	15.0	37	-	-	ND	ND	1	0.00	0%
VD 0541	Soya bean (dry)	0.02	-	JPN	15.9	88	-	-	ND	ND	3	0.11	0%

Annex 4

DIFENOCONAZOLE (224) International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS**

Acute RfD= 0.300 mg/kg bw (300 µg/kg bw)
Maximum %ARfD: 10%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
VO 0448	Tomato	-	0.36	USA	15.0	159	150	BEL	143	3	2a	10.66	4%
GC 0654	Wheat	0	-	USA	15.0	151	-	-	ND	ND	3	0.00	0%
-	Wine	0.0054	-	AUS	19.0	4	-	-	ND	ND	3	0.00	0%

DIMETHOMORPH (225) International estimate of short term intake (IESTI) for **GENERAL POPULATION**

Acute RfD= 0.600 mg/kg bw (600 µg/kg bw)
Maximum %ARfD: 10%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
VC 0421	Balsam pear, stated as bitter gourd, VC 4195	-	0.05	Thai	53.5	120	-	-	ND	ND	ND	ND	-
VB 0400	Broccoli	-	0.52	USA	65.0	376	608	USA	474	3	2b	9.03	2%
VB 0041	Cabbage, head	-	1.4	SAF	55.7	362	908	USA	717	3	2b	27.30	5%
VC 0423	Chayote	-	0.05	AUS	67.0	196	-	-	ND	ND	ND	ND	-
PE 0840	Chicken eggs	-	0	FRA	62.3	219	-	-	ND	ND	1	0.00	0%
VL 0470	Corn salad	-	7.1	NLD	63.0	81	-	-	ND	ND	ND	ND	-
VC 0424	Cucumber	-	0.24	NLD	63.0	313	400	FRA	360	3	2b	3.58	1%
MO 0105	Edible offal (mammalian)	-	0	FRA	62.3	277	-	-	ND	ND	1	0.00	0%
VO 0440	Egg plant	-	0.56	AUS	67.0	487	548	USA	444	3	2a	11.49	2%
PE 0112	Eggs	-	0	Thai	53.5	195	-	-	ND	ND	1	0.00	0%
VC 0425	Gherkin	-	0.24	NLD	63.0	96	116	USA	81	3	2a	0.98	0%
FB 0269	Grape (excl wine)	-	1.7	AUS	67.0	513	456	SWE	438	3	2a	35.23	6%
DF 0269	Grapes, dried (= currants, raisins and sultanas)	-	3.1	FRA	62.3	135	-	-	ND	ND	1	6.73	1%
DH 1100	Hops, dry	26	-	USA	65.0	6	-	-	ND	ND	3	2.34	0%

DIMETHOMORPH (225) International estimate of short term intake (IESTI) for **GENERAL POPULATION** Acute RfD= 0.600 mg/kg bw (600 µg/kg bw)

Maximum %ARfD: 10%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
VB 0405	Kohlrabi	-	0.02	NLD	63.0	283	135	USA	99	3	2a	0.15	0%
VL 0482	Lettuce, head	-	7.2	USA	65.0	213	539	USA	512	3	2b	70.63	10%
VC 0427	Loofah, angled (= angled gourd)	-	0.05	Thai	53.5	215	-	-	ND	ND	ND	ND	-
MM 0095	Meat from mammals other than marine mammals	-	0	AUS	67.0	521	-	-	ND	ND	1	0.00	0%
VC 0046	Melons, except watermelon	-	0.05	USA	65.0	655	1000	USA	630	3	2a	1.47	0%
ML 0106	Milks	-	0	USA	65.0	2466	-	-	ND	ND	3	ND	-
VO 0051	Peppers	-	0.56	FRA	62.3	207	-	-	ND	ND	ND	ND	-
VO 0444	Peppers, chilli	-	0.56	USA	65.0	90	45	USA	43	3	2a	1.52	0%
VO 0445	Peppers, sweet (incl. pim(i)ento)	-	0.56	FRA	62.3	207	119	USA	98	3	2a	3.62	1%
FI 0353	Pineapple	-	0	JPN	52.6	371	2000	JPN	2000	3	2b	0.00	0%
VR 0589	Potato	-	0.05	NLD	63.0	687	200	FRA	160	3	2a	0.80	0%
PM 0110	Poultry meat	-	0	AUS	67.0	431	-	-	ND	ND	1	0.00	0%
PO 0111	Poultry, edible offal of	-	0	USA	65.0	248	-	-	ND	ND	1	0.00	0%
VC 0430	Snake gourd	-	0.05	Thai	53.5	215	-	-	ND	ND	ND	ND	-
VC 0431	Squash, summer (= courgette)	-	0.24	FRA	62.3	343	196	USA	186	3	2a	2.75	0%
FB 0275	Strawberry	-	0.02	FRA	62.3	346	16	BEL	15	1	1	0.11	0%
VO 0448	Tomato	-	0.56	USA	65.0	391	123	USA	123	3	2a	5.48	1%
JF 0448	Tomato juice	-	0.56	-	-	ND	-	-	ND	ND	3	ND	-
-	Tomato paste	-	0.56	-	-	ND	-	-	ND	ND	ND	ND	-
VC 0432	Watermelon	-	0.05	USA	65.0	1939	4518	USA	2078	3	2b	4.47	1%
-	Wine	0.11	-	AUS	67.0	1131	-	-	ND	ND	3	1.86	0%
VC 0433	Winter squash (= pumpkin)	-	0.05	USA	65.0	729	1000	JPN	1000	3	2b	1.68	0%

Annex 4

DIMETHOMORPH (225) International estimate of short term intake (IESTI) for Acute RfD= 0.600 mg/kg bw (600 µg/kg bw)

CHILDREN UP TO 6 YEARS Maximum %ARfD: 20%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
VC 0421	Balsam pear, stated as bitter gourd, VC 4195	-	0.05	Thai	17.1	87	-	-	ND	ND	ND	ND	-
VB 0400	Broccoli	-	0.52	USA	15.0	164	608	USA	474	3	2b	17.08	3%
VB 0041	Cabbage, head	-	1.4	SAF	14.2	220	908	USA	717	3	2b	65.10	10%
VC 0423	Chayote	-	0.05	AUS	19.0	105	-	-	ND	ND	ND	ND	-
PE 0840	Chicken eggs	-	0	FRA	17.8	134	-	-	ND	ND	1	0.00	0%
VL 0470	Corn salad	-	7.1	FRA	17.8	21	-	-	ND	ND	ND	ND	-
VC 0424	Cucumber	-	0.24	NLD	17.0	162	301	USA	286	3	2b	6.86	1%
MO 0105	Edible offal (mammalian)	-	0	FRA	17.8	203	-	-	ND	ND	1	0.00	0%
VO 0440	Egg plant	-	0.56	JPN	15.9	219	548	USA	444	3	2b	23.17	4%
PE 0112	Eggs	-	0	Thai	17.1	109	-	-	ND	ND	1	0.00	0%
VC 0425	Gherkin	-	0.24	NLD	17.0	56	116	USA	81	3	2b	2.35	0%
FB 0269	Grape (excl wine)	-	1.7	AUS	19.0	342	456	SWE	438	3	2b	91.80	20%
DF 0269	Grapes, dried (= currants, raisins and sultanas)	-	3.1	USA	15.0	59	-	-	ND	ND	1	12.25	2%
DH 1100	Hops, dry	26	-	JPN	15.9	0	-	-	ND	ND	3	0.78	0%
VB 0405	Kohlrabi	-	0.02	-	-	ND	135	USA	99	3	ND	ND	-
VL 0482	Lettuce, head	-	7.2	Thai	17.1	117	539	USA	512	3	2b	147.53	20%
VC 0427	Loofah, angled (= angled gourd)	-	0.05	Thai	17.1	130	-	-	ND	ND	ND	ND	-
MM 0095	Meat from mammals other than marine mammals	-	0	AUS	19.0	261	-	-	ND	ND	1	0.00	0%
VC 0046	Melons, except watermelon	-	0.05	AUS	19.0	413	1000	USA	630	3	2b	3.26	1%
ML 0106	Milks	-	0	USA	15.0	1286	-	-	ND	ND	3	ND	-
VO 0051	Peppers	-	0.56	Thai	17.1	71	-	-	ND	ND	ND	ND	-
VO 0444	Peppers, chilli	-	0.56	AUS	19.0	31	45	USA	43	3	2b	2.70	0%
VO 0445	Peppers, sweet (incl. pim(i)ento)	-	0.56	Thai	17.1	71	119	USA	98	3	2b	6.99	1%
FI 0353	Pineapple	-	0	JPN	15.9	216	2000	JPN	2000	3	2b	0.00	0%
VR 0589	Potato	-	0.05	SAF	14.2	300	216	UNK	216	3	2a	2.58	0%

DIMETHOMORPH (225) International estimate of short term intake (IESTI) for Acute RfD= 0.600 mg/kg bw (600 µg/kg bw)

CHILDREN UP TO 6 YEARS Maximum %ARfD: 20%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Variability factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
PM 0110	Poultry meat	-	0	AUS	19.0	224	-	-	ND	ND	1	0.00	0%
PO 0111	Poultry, edible offal of	-	0	USA	15.0	37	-	-	ND	ND	1	0.00	0%
VC 0430	Snake gourd	-	0.05	Thai	17.1	130	-	-	ND	ND	ND	ND	-
VC 0431	Squash, summer (= courgette)	-	0.24	AUS	19.0	219	196	USA	186	3	2a	7.47	1%
FB 0275	Strawberry	-	0.02	AUS	19.0	176	14	FRA	13	1	1	0.19	0%
VO 0448	Tomato	-	0.56	USA	15.0	159	123	USA	123	3	2a	15.12	3%
JF 0448	Tomato juice	-	0.56	-	-	ND	-	-	ND	ND	3	ND	-
-	Tomato paste	-	0.56	-	-	ND	-	-	ND	ND	ND	ND	-
VC 0432	Watermelon	-	0.05	AUS	19.0	1473	4518	USA	2078	3	2b	11.63	2%
-	Wine	0.11	-	AUS	19.0	4	-	-	ND	ND	3	0.02	0%
VC 0433	Winter squash (= pumpkin)	-	0.05	USA	15.0	169	1000	JPN	1000	3	2b	1.69	0%

FENITROTHION (37) International estimate of short term intake (IESTI) for Acute RfD= 0.040 mg/kg bw (40 µg/kg bw)

GENERAL POPULATION Maximum %ARfD: 80%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Variability factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
FP 0226	Apple	-	0.41	USA	65.0	1348	200	JPN	200	3	2a	11.03	30%
GC 0640	Barley	-	5.6	NLD	63.0	378	-	-	ND	ND	1	33.60	80%
GC 0640	Barley (beer only)*	0.85	-	AUS	67.0	528	-	-	ND	ND	3	6.70	20%
-	Barley flour and grits	1	-	-	-	ND	-	-	ND	ND	3	ND	-
-	Barley, pearled	0.638	-	-	-	ND	-	-	ND	ND	ND	ND	-
-	Barley, pot	2.72	-	-	-	ND	-	-	ND	ND	ND	ND	-

Annex 4

FENITROTHION (37) International estimate of short term intake (IESTI) for **GENERAL POPULATION**

Acute RfD= 0.040 mg/kg bw (40 µg/kg bw)
Maximum %ARfD: 80%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
CP 0179	Bread & other cooked cereal products	0.425	-	JPN	52.6	378	-	-	ND	ND	3	3.06	8%
GC 0641	Buckwheat	-	5.6	NLD	63.0	117	-	-	ND	ND	1	10.42	30%
-	Buckwheat flour	1	-	-	-	ND	-	-	ND	ND	3	ND	-
GC 0646	Millet	-	5.6	AUS	67.0	101	-	-	ND	ND	1	8.40	20%
-	Millet beer	0.85	-	-	-	ND	-	-	ND	ND	3	ND	-
-	Millet flour	1	-	-	-	ND	-	-	ND	ND	3	ND	-
GC 0647	Oats	-	5.6	FRA	62.3	305	-	-	ND	ND	1	27.44	70%
CM 1206	Rice bran, unprocessed	-	40.3	AUS	67.0	50	-	-	ND	ND	1	30.06	80%
-	Rice flour	1	-	-	-	ND	-	-	ND	ND	3	ND	-
CM 0649	Rice, husked	0.468	-	JPN	52.6	319	-	-	ND	ND	3	ND	-
CM 1205	Rice, polished	0.17	-	Thai	53.5	412	-	-	ND	ND	3	ND	-
GC 0650	Rye	-	5.6	NLD	63.0	77	-	-	ND	ND	1	6.83	20%
CP 1250	Rye bread	1.615	-	AUS	67.0	241	-	-	ND	ND	3	5.81	10%
CF 1250	Rye flour	1	-	FRA	62.3	115	-	-	ND	ND	3	1.84	5%
GC 0651	Sorghum	-	5.6	Thai	53.5	86	-	-	ND	ND	1	8.96	20%
-	Sorghum beer	0.85	-	-	-	ND	-	-	ND	ND	3	ND	-
-	Sorghum flour	1	-	-	-	ND	-	-	ND	ND	3	ND	-
GC 0653	Triticale	-	5.6	-	-	ND	-	-	ND	ND	1	ND	-
-	Triticale flour	1	-	-	-	ND	-	-	ND	ND	3	ND	-
CM 0654	Wheat bran, unprocessed	-	22.12	USA	65.0	80	-	-	ND	ND	1	27.21	70%
-	Wheat bulgur wholemeal	1.615	-	-	-	ND	-	-	ND	ND	ND	ND	-
CF 1211	Wheat flour	1	-	USA	65.0	365	-	-	ND	ND	3	5.62	10%
-	Wheat macaroni	0.425	-	-	-	ND	-	-	ND	ND	ND	ND	-
-	Wheat pastry	0.425	-	-	-	ND	-	-	ND	ND	ND	ND	-
CP 1211	White bread	0.425	-	SAF	55.7	479	-	-	ND	ND	3	3.66	9%
CP 1212	Wholemeal bread	1.615	-	SAF	55.7	395	-	-	ND	ND	3	11.47	30%

* barley beer refers to the malt part of the beer, not the beer itself

FENITROTHION (37) International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS**

Acute RfD= 0.040 mg/kg bw (40 µg/kg bw)
Maximum %ARfD: 110%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P g/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
FP 0226	Apple	-	0.41	USA	15.0	679	200	JPN	200	3	2a	29.49	70%
GC 0640	Barley	-	5.6	AUS	19.0	14	-	-	ND	ND	1	4.09	10%
GC 0640	Barley (beer only)*	0.85	-	AUS	19.0	12	-	-	ND	ND	3	0.52	1%
-	Barley flour and grits	1	-	-	-	ND	-	-	ND	ND	3	ND	-
-	Barley, pearled	0.638	-	-	-	ND	-	-	ND	ND	ND	ND	-
-	Barley, pot	2.72	-	-	-	ND	-	-	ND	ND	ND	ND	-
CP 0179	Bread & other cooked cereal products	0.425	-	JPN	15.9	227	-	-	ND	ND	3	6.06	20%
GC 0641	Buckwheat	-	5.6	NLD	17.0	59	-	-	ND	ND	1	19.38	50%
-	Buckwheat flour	1	-	-	-	ND	-	-	ND	ND	3	ND	-
GC 0646	Millet	-	5.6	-	-	ND	-	-	ND	ND	1	ND	-
-	Millet beer	0.85	-	-	-	ND	-	-	ND	ND	3	ND	-
-	Millet flour	1	-	-	-	ND	-	-	ND	ND	3	ND	-
GC 0647	Oats	-	5.6	USA	15.0	62	-	-	ND	ND	1	23.24	60%
CM 1206	Rice bran, unprocessed	-	40.3	USA	15.0	3	-	-	ND	ND	1	8.46	20%
-	Rice flour	1	-	-	-	ND	-	-	ND	ND	3	ND	-
CM 0649	Rice, husked	0.468	-	FRA	17.8	223	-	-	ND	ND	3	5.85	10%
CM 1205	Rice, polished	0.17	-	JPN	15.9	199	-	-	ND	ND	3	2.12	5%
GC 0650	Rye	-	5.6	NLD	17.0	37	-	-	ND	ND	1	12.15	30%
CP 1250	Rye bread	1.615	-	AUS	19.0	202	-	-	ND	ND	3	17.17	40%
CF 1250	Rye flour	1	-	USA	15.0	18	-	-	ND	ND	3	1.18	3%
GC 0651	Sorghum	-	5.6	Thai	17.1	30	-	-	ND	ND	1	9.91	20%
-	Sorghum beer	0.85	-	-	-	ND	-	-	ND	ND	3	ND	-
-	Sorghum flour	1	-	-	-	ND	-	-	ND	ND	3	ND	-
GC 0653	Triticale	-	5.6	-	-	ND	-	-	ND	ND	1	ND	-
-	Triticale flour	1	-	-	-	ND	-	-	ND	ND	3	ND	-

Annex 4

FENITROTHION (37) International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS** Acute RfD= 0.040 mg/kg bw (40 µg/kg bw) Maximum %ARfD: 110%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P g/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
CM 0654	Wheat bran, unprocessed	-	22.12	USA	15.0	30	-	-	ND	ND	1	43.80	110%
-	Wheat bulgur wholemeal	1.615	-	-	-	ND	-	-	ND	ND	ND	ND	-
CF 1211	Wheat flour	1	-	AUS	19.0	194	-	-	ND	ND	3	10.23	30%
-	Wheat macaroni	0.425	-	-	-	ND	-	-	ND	ND	ND	ND	-
-	Wheat pastry	0.425	-	-	-	ND	-	-	ND	ND	ND	ND	-
CP 1211	White bread	0.425	-	SAF	14.2	270	-	-	ND	ND	3	8.08	20%
CP 1212	Wholemeal bread	1.615	-	SAF	14.2	240	-	-	ND	ND	3	27.29	70%

* barley beer refers to the malt part of the beer, not the beer itself

FLUSILAZOLE (165) International estimate of short term intake (IESTI) for **GENERAL POPULATION** Acute RfD= 0.020 mg/kg bw (20 µg/kg bw) Maximum%ARfD: 40%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
FP 0226	Apple	-	0.13	USA	65.0	1348	200	JPN	200	3	2a	3.50	20%
FS 0240	Apricot	-	0.1	JPN	52.6	292	41	UNK	38	3	2a	0.70	3%
FI 0327	Banana	-	0.01	SAF	55.7	613	900	UNK	594	3	2a	0.32	2%
GC 0640	Barley	0.04	-	NLD	63.0	378	-	-	ND	ND	3	0.24	1%
MO 0105	Edible offal (mammalian)	-	1.68	FRA	62.3	277	-	-	ND	ND	1	7.46	40%
PE 0112	Eggs	-	0.07	Thai	53.5	195	-	-	ND	ND	1	0.25	1%
FB 0269	Grape (excl wine)	-	0.11	AUS	67.0	513	456	SWE	438	3	2a	2.28	10%

FLUSILAZOLE (165) International estimate of short term intake (IESTI) for **GENERAL POPULATION**

Acute RfD= 0.020 mg/kg bw (20 µg/kg bw)
Maximum%ARfD: 40%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
DF 0269	Grapes, dried (= currants, raisins and sultanas)	-	0.2	FRA	62.3	135	-	-	ND	ND	1	0.43	2%
GC 0645	Maize	0.04	-	FRA	62.3	260	-	-	ND	ND	3	0.17	1%
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.73	AUS	67.0	104	-	-	ND	ND	1	1.14	6%
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0.09	AUS	67.0	417	-	-	ND	ND	1	0.56	3%
ML 0106	Milks	0.01	-	USA	65.0	2466	-	-	ND	ND	3	0.38	2%
FS 0245	Nectarine	-	0.1	USA	65.0	590	136	USA	125	3	2a	1.29	6%
FS 0247	Peach	-	0.1	SAF	55.7	685	150	JPN	150	3	2a	1.77	9%
FP 0230	Pear	-	0.13	USA	65.0	693	180	JPN	180	3	2a	2.11	10%
PM 0110	Poultry meat: 10% as fat	-	0.13	AUS	67.0	43	-	-	ND	ND	1	0.08	0%
PM 0110	Poultry meat: 90% as muscle	-	0.03	AUS	67.0	388	-	-	ND	ND	1	0.17	1%
PO 0111	Poultry, edible offal of	-	0.09	USA	65.0	248	-	-	ND	ND	1	0.34	2%
FP 0231	Quince	-	0.13	AUS	67.0	175	92	USA	56	3	2a	0.56	3%
SO 0495	Rape seed	0.01	-	-	-	ND	-	-	ND	ND	3	ND	-
GC 0650	Rye	0.04	-	NLD	63.0	77	-	-	ND	ND	3	0.05	0%
VD 0541	Soya bean (dry)	0.02	-	JPN	52.6	159	-	-	ND	ND	3	0.06	0%
OR 0541	Soya bean oil, refined	0.044	-	USA	65.0	98	-	-	ND	ND	3	0.07	0%
VR 0596	Sugar beet	0.01	-	-	-	ND	-	-	ND	ND	ND	ND	-
OR 0702	Sunflower seed oil, edible	0.01	-	FRA	62.3	61	-	-	ND	ND	3	0.01	0%
VO 0447	Sweet corn (corn-on-the-cob)	-	0.01	Thai	53.5	383	200	JPN	200	3	2a	0.15	1%
GC 0654	Wheat	0.04	-	USA	65.0	383	-	-	ND	ND	3	0.24	1%
CM 0654	Wheat bran, unprocessed	0.012	-	USA	65.0	80	-	-	ND	ND	ND	ND	-
CF 1211	Wheat flour	0.036	-	USA	65.0	365	-	-	ND	ND	3	0.20	1%
-	Wine	0.003	-	AUS	67.0	1131	-	-	ND	ND	3	0.05	0%

Annex 4

FLUSILAZOLE (165) International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS**

Acute RfD= 0.020 mg/kg bw (20 µg/kg bw)
Maximum%ARfD: 100%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
FP 0226	Apple	-	0.13	USA	15.0	679	200	JPN	200	3	2a	9.35	50%
FS 0240	Apricot	-	0.1	AUS	19.0	414	41	UNK	38	3	2a	2.58	10%
FI 0327	Banana	-	0.01	JPN	15.9	312	900	UNK	594	3	2b	0.59	3%
GC 0640	Barley	0.04	-	AUS	19.0	14	-	-	ND	ND	3	0.03	0%
MO 0105	Edible offal (mammalian)	-	1.68	FRA	17.8	203	-	-	ND	ND	1	19.14	100%
PE 0112	Eggs	-	0.07	Thai	17.1	109	-	-	ND	ND	1	0.45	2%
FB 0269	Grape (excl wine)	-	0.11	AUS	19.0	342	456	SWE	438	3	2b	5.94	30%
DF 0269	Grapes, dried (= currants, raisins and sultanas)	-	0.2	USA	15.0	59	-	-	ND	ND	1	0.79	4%
GC 0645	Maize	0.04	-	FRA	17.8	148	-	-	ND	ND	3	0.33	2%
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.73	AUS	19.0	52	-	-	ND	ND	1	2.00	10%
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0.09	AUS	19.0	208	-	-	ND	ND	1	0.99	5%
ML 0106	Milks	0.01	-	USA	15.0	1286	-	-	ND	ND	3	0.86	4%
FS 0245	Nectarine	-	0.1	AUS	19.0	302	136	USA	125	3	2a	2.91	10%
FS 0247	Peach	-	0.1	AUS	19.0	315	150	JPN	150	3	2a	3.24	20%
FP 0230	Pear	-	0.13	UNK	14.5	279	180	JPN	180	3	2a	5.73	30%
PM 0110	Poultry meat: 10% as fat	-	0.13	AUS	19.0	22	-	-	ND	ND	1	0.15	1%
PM 0110	Poultry meat: 90% as muscle	-	0.03	AUS	19.0	201	-	-	ND	ND	1	0.32	2%
PO 0111	Poultry, edible offal of	-	0.09	USA	15.0	37	-	-	ND	ND	1	0.22	1%
FP 0231	Quince	-	0.13	NLD	17.0	1	92	USA	56	3	2b	0.02	0%
SO 0495	Rape seed	0.01	-	-	-	ND	-	-	ND	ND	3	ND	-
GC 0650	Rye	0.04	-	NLD	17.0	37	-	-	ND	ND	3	0.09	0%
VD 0541	Soya bean (dry)	0.02	-	JPN	15.9	88	-	-	ND	ND	3	0.11	1%
OR 0541	Soya bean oil, refined	0.044	-	USA	15.0	35	-	-	ND	ND	3	0.10	1%

FLUSILAZOLE (165) International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS** Acute RfD= 0.020 mg/kg bw (20 µg/kg bw) Maximum%ARfD: 100%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
VR 0596	Sugar beet	0.01	-	-	-	ND	-	-	ND	ND	ND	ND	-
OR 0702	Sunflower seed oil, edible	0.01	-	FRA	17.8	37	-	-	ND	ND	3	0.02	0%
VO 0447	Sweet corn (corn-on-the-cob)	-	0.01	Thai	17.1	197	200	JPN	200	3	2b	0.35	2%
GC 0654	Wheat	0.04	-	USA	15.0	151	-	-	ND	ND	3	0.40	2%
CM 0654	Wheat bran, unprocessed	0.012	-	USA	15.0	30	-	-	ND	ND	ND	ND	-
CF 1211	Wheat flour	0.036	-	AUS	19.0	194	-	-	ND	ND	3	0.37	2%
-	Wine	0.003	-	AUS	19.0	4	-	-	ND	ND	3	0.00	0%

INDOXACARB (216) International estimate of short term intake (IESTI) for **GENERAL POPULATION** Acute RfD= 0.100 mg/kg bw (100 µg/kg bw) Maximum %ARfD: 40%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
VB 0041	Cabbage, head	-	2.0	SAF	55.7	362	908	USA	717	3	2b	39.00	40%

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INDOXACARB (216) International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS** Acute RfD= 0.100 mg/kg bw (100 µg/kg bw) Maximum %ARfD: 90%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Variability factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
VB 0041	Cabbage, head	-	2.0	SAF	14.2	220	908	USA	717	3	2b	93.00	90%

PHOSMET (103) International estimate of short term intake (IESTI) for **GENERAL POPULATION** Acute RfD= 0.2 mg/kg bw (200 µg/kg bw) Maximum %ARfD: 50%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Variability factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
FP 0226	Apple	-	1.8	USA	65.0	1348	138	USA	127	3	2a	44.36	20%
FS 0240	Apricot	-	6.8	JPN	52.6	292	35	USA	34	3	2a	46.43	20%
FB 0020	Blueberries	-	9.9	AUS	67.0	158	-	-	ND	1	1	23.36	10%
FC 0203	Grapefruit	-	0.52	JPN	52.6	947	300	BEL	210	3	2a	13.51	7%
FC 0204	Lemon	-	0.52	FRA	62.3	115	100	FRA	64	3	2a	2.03	1%
FC 0206	Mandarin	-	0.52	JPN	52.6	409	100	FRA	72	3	2a	5.46	3%
FS 0245	Nectarine	-	6.8	USA	65.0	590	136	USA	125	3	2a	87.92	40%
FC 0004	Orange, sweet, sour + orange-like hybrid	-	0.52	USA	65.0	564	190	FRA	137	3	2a	6.70	3%
FS 0247	Peach	-	6.8	SAF	55.7	685	98	USA	85	3	2a	104.46	50%
FP 0230	Pear	-	1.8	USA	65.0	693	166	USA	151	3	2a	27.55	10%
FP 0231	Quince	-	1.8	AUS	67.0	175	92	USA	56	3	2a	7.71	4%
FC 0005	Shaddock or pomelo + shaddock-like hybrid	-	0.52	USA	65.0	448	210	FRA	126	3	2a	5.60	3%

PHOSMET (103) International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS** Acute RfD= 0.2 mg/kg bw (200 µg/kg bw) Maximum %ARfD: 100%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
FC 0204	Lemon	-	0.52	JPN	15.9	88	100	FRA	64	3	2a	7.08	4%
FP 0226	Apple	-	1.8	USA	15.0	679	138	USA	127	3	2a	111.92	60%
FS 0240	Apricot	-	6.8	AUS	19.0	414	35	USA	34	3	2a	172.36	90%
FB 0020	Blueberries	-	9.9	FRA	17.8	138	-	-	ND	ND	1	76.92	40%
FC 0203	Grapefruit	-	0.52	FRA	17.8	381	300	BEL	210	3	2a	23.41	10%
FC 0206	Mandarin	-	0.52	JPN	15.9	353	100	FRA	72	3	2a	16.26	8%
FS 0245	Nectarine	-	6.8	AUS	19.0	302	136	USA	125	3	2a	197.68	100%
FC 0004	Orange, sweet, sour + orange-like hybrid	-	0.52	UNK	14.5	495	190	FRA	137	3	2a	27.56	10%
FS 0247	Peach	-	6.8	AUS	19.0	315	98	USA	85	3	2a	173.94	90%
FP 0230	Pear	-	1.8	UNK	14.5	279	166	USA	151	3	2a	72.14	40%
FP 0231	Quince	-	1.8	NLD	17.0	1	92	USA	56	3	2b	0.32	0%
FC 0005	Shaddock or pomelo + shaddock-like hybrid	-	0.52	FRA	17.8	381	210	FRA	126	3	2a	18.51	9%

TRIADIMEFON (133)/ TRIADIMENOL (168) **International estimate of short term intake (IESTI) for GENERAL POPULATION** **Acute RfD= 0.080 mg/kg bw (80 µg/kg bw)** **Maximum%ARfD:** 80%

Codex Code	**Commodity**	**STMR or STMR-P mg/kg**	**HR or HR-P mg/kg**	**Large portion diet**			**Unit weight**			**Varia-bility factor**	**Case**	**IESTI µg/kg bw per day**	**% acute RfD rounded**
				Country	**Body weight (kg)**	**Large portion, g/person**	**Unit weight, g**	**Country**	**Unit weight, edible portion, g**				
FP 0226	Apple	-	0.18	USA	65.0	1348	162	SWE	149	3	2a	4.56	6%
FI 0327	Banana	-	0.3	SAF	55.7	613	**1218**	SWE	767	3	2b	9.90	10%
GC 0640	Barley	0.05	-	NLD	63.0	378	-	-	ND	ND	3	0.30	0%
CM 0081	Bran, unprocessed of cereal grain (except buckwheat, canihua, quinoa)	0.05	-	AUS	67.0	37	-	-	ND	ND	ND	ND	-

TRIADIMEFON (133)/
TRIADIMENOL (168)

International estimate of short term intake (IESTI) for
GENERAL POPULATION

Acute RfD= 0.080 mg/kg bw (80 µg/kg bw)
Maximum%ARfD: 80%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
GC 0641	Buckwheat	0.05	-	NLD	63.0	117	-	-	ND	ND	3	0.09	0%
MF 0812	Cattle fat	-	0.01	USA	65.0	60	-	-	ND	ND	1	0.01	0%
PE 0840	Chicken eggs	-	0.01	FRA	62.3	219	-	-	ND	ND	1	0.04	0%
SB 0716	Coffee beans	0.05	-	NLD	63.0	66	-	-	ND	ND	3	0.05	0%
VC 0424	Cucumber	-	0.2	NLD	63.0	313	410	BEL	385	3	2b	2.98	4%
FB 0021	Currants, red, black, white	-	0.23	FRA	62.3	153	-	-	ND	ND	1	0.57	1%
PE 0841	Duck eggs	-	0.01	AUS	67.0	135	-	-	ND	ND	1	0.02	0%
032	**EDIBLE OFFAL (MAMMALIAN)**	-	0	-	-	-	-	-	-	-	-	-	-
VO 0440	Egg plant	-	0.68	AUS	67.0	487	330	BEL	281	3	2a	10.64	10%
PE 0112	Eggs	-	0.01	Thai	53.5	195	-	-	ND	ND	1	0.04	0%
VC 0425	Gherkin	-	0.2	NLD	63.0	96	59	UKN	55	3	2a	0.66	1%
MF 0814	Goat fat	-	0.01	USA	65.0	18	-	-	ND	ND	1	0.00	0%
FB 0269	Grape (excl wine)	-	3.2	AUS	67.0	513	456	SWE	438	3	2a	66.32	80%
JF 0269	Grape juice	0.07	-	-	-	ND	-	-	ND	ND	3	ND	-
DF 0269	Grapes, dried (= currants, raisins and sultanas)	-	9.9	FRA	62.3	135	-	-	ND	ND	1	21.48	30%
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.01	AUS	67.0	104	-	-	ND	ND	1	0.02	0%
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0	AUS	67.0	417	-	-	ND	ND	1	0.00	0%
VC 0046	Melons, except watermelon	-	0.2	USA	65.0	655	720	BEL	540	3	2a	5.34	7%
033	**MILK AND MILK PRODUCTS**	-	0	-	-	-	-	-	-	-	-	-	-
086	**MILK FATS**	-	0	-	-	-	-	-	-	-	-	-	-
GC 0646	Millet	0.05	-	AUS	67.0	101	-	-	ND	ND	3	0.08	0%
GC 0647	Oats	0.05	-	FRA	62.3	305	-	-	ND	ND	3	0.25	0%
VO 0442	Okra	-	0.68	USA	65.0	235	10	JPN	10	1	1	2.46	3%
VO 0444	Peppers, chilli	-	0.68	USA	65.0	90	45	USA	43	3	2a	1.85	2%
VO 0445	Peppers, sweet (incl. pim(i)ento)	-	0.68	FRA	62.3	207	185	BEL	148	3	2a	5.50	7%

TRIADIMEFON (133)/
TRIADIMENOL (168)

International estimate of short term intake (IESTI) for GENERAL POPULATION

Acute RfD= 0.080 mg/kg bw (80 µg/kg bw)
Maximum%ARfD: 80%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
MF 0818	Pig fat	-	0.01	AUS	67.0	144	-	-	ND	ND	1	0.02	0%
FI 0353	Pineapple	-	0.16	JPN	52.6	371	2000	JPN	2000	3	2b	3.39	4%
037	**POULTRY FATS**	-	0	-	-	-	-	-	-	-	-	-	-
036	**POULTRY MEAT**	-	0	-	-	-	-	-	-	-	-	-	-
038	**POULTRY, EDIBLE OFFAL OF**	-	0	-	-	-	-	-	-	-	-	-	-
GC 0650	Rye	0.05	-	NLD	63.0	77	-	-	ND	ND	3	0.06	0%
MF 0822	Sheep fat	-	0.01	USA	65.0	54	-	-	ND	ND	1	0.01	0%
GC 0651	Sorghum	0.05	-	Thai	53.5	86	-	-	ND	ND	3	0.08	0%
VC 0431	Squash, summer (= courgette)	-	0.2	FRA	62.3	343	300	FRA	270	3	2a	2.83	4%
FB 0275	Strawberry	-	0.41	FRA	62.3	346	16	BEL	15	1	1	2.28	3%
VO 0448	Tomato	-	0.68	USA	65.0	391	150	BEL	143	3	2a	7.07	9%
GC 0653	Triticale	0.05	-	-	-	ND	-	-	ND	ND	3	ND	-
VC 0432	Watermelon	-	0.2	USA	65.0	1939	4518	USA	2078	3	2b	17.90	20%
GC 0654	Wheat	0.05	-	USA	65.0	383	-	-	ND	ND	3	0.29	0%
-	Wine	0.06	-	AUS	67.0	1131	-	-	ND	ND	3	1.01	1%
VC 0433	Winter squash (= pumpkin)	-	0.2	USA	65.0	729	1000	JPN	1000	3	2b	6.73	8%
VC 0433	Winter squash (= pumpkin), stated as pumpkin, VC 0429	-	0.2	SAF	55.7	1003	1000	JPN	1000	3	2a	10.78	10%

TRIADIMEFON (133) / TRIADIMENOL (168)

International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS**

Acute RfD= 0.080 mg/kg bw (80 µg/kg bw)

Maximum%ARfD: 220%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
FP 0226	Apple	-	0.18	USA	15.0	679	162	SWE	149	3	2a	11.72	10%
FI 0327	Banana	-	0.3	JPN	15.9	312	1218	SWE	767	3	2b	17.65	20%
GC 0640	Barley	0.05	-	AUS	19.0	14	-	-	ND	ND	3	0.04	0%
CM 0081	Bran, unprocessed of cereal grain (except buckwheat, canihua, quinoa)	0.05	-	AUS	19.0	13	-	-	ND	ND	ND	ND	-
GC 0641	Buckwheat	0.05	-	NLD	17.0	59	-	-	ND	ND	3	0.17	0%
MF 0812	Cattle fat	-	0.01	USA	15.0	27	-	-	ND	ND	1	0.02	0%
PE 0840	Chicken eggs	-	0.01	FRA	17.8	134	-	-	ND	ND	1	0.08	0%
SB 0716	Coffee beans	0.05	-	NLD	17.0	19	-	-	ND	ND	3	0.06	0%
VC 0424	Cucumber	-	0.2	NLD	17.0	162	410	BEL	385	3	2b	5.72	7%
FB 0021	Currants, red, black, white	-	0.23	AUS	19.0	584	-	-	ND	ND	1	7.07	9%
PE 0841	Duck eggs	-	0.01	-	-	ND	-	-	ND	ND	1	ND	-
032	**EDIBLE OFFAL (MAMMALIAN)**	-	0	-	-	-	-	-	-	-	-	-	-
VO 0440	Egg plant	-	0.68	JPN	15.9	219	330	BEL	281	3	2b	28.13	40%
PE 0112	Eggs	-	0.01	Thai	17.1	109	-	-	ND	ND	1	0.06	0%
VC 0425	Gherkin	-	0.2	NLD	17.0	56	59	UKN	55	3	2a	1.96	2%
MF 0814	Goat fat	-	0.01	USA	15.0	3	-	-	ND	ND	1	0.00	0%
FB 0269	Grape (excl wine)	-	3.2	AUS	19.0	342	456	SWE	438	3	2b	172.80	220%
JF 0269	Grape juice	0.07	-	-	-	ND	-	-	ND	ND	3	ND	-
DF 0269	Grapes, dried (= currants, raisins and sultanas)	-	9.9	USA	15.0	59	-	-	ND	ND	1	39.11	50%
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.01	AUS	19.0	52	-	-	ND	ND	1	0.03	0%
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0	AUS	19.0	208	-	-	ND	ND	1	0.00	0%
VC 0046	Melons, except watermelon	-	0.2	AUS	19.0	413	720	BEL	540	3	2b	13.04	20%
033	**MILK AND MILK PRODUCTS**	-	0	-	-	-	-	-	-	-	-	-	-
086	**MILK FATS**	-	0	-	-	-	-	-	-	-	-	-	-

TRIADIMEFON (133) / TRIADIMENOL (168)

International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS**

Acute RfD= 0.080 mg/kg bw (80 µg/kg bw)

Maximum%ARfD: 220%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
GC 0646	Millet	0.05	-	-	-	ND	-	-	ND	ND	3	ND	-
GC 0647	Oats	0.05	-	USA	15.0	62	-	-	ND	ND	3	0.21	0%
VO 0442	Okra	-	0.68	USA	15.0	203	10	JPN	10	1	1	9.18	10%
VO 0444	Peppers, chilli	-	0.68	AUS	19.0	31	45	USA	43	3	2b	3.27	4%
VO 0445	Peppers, sweet (incl. pim(i)ento)	-	0.68	Thai	17.1	71	185	BEL	148	3	2b	8.49	10%
MF 0818	Pig fat	-	0.01	FRA	17.8	85	-	-	ND	ND	1	0.05	0%
FI 0353	Pineapple	-	0.16	JPN	15.9	216	2000	JPN	2000	3	2b	6.53	8%
037	**POULTRY FATS**	-	0	-	-	-	-	-	-	-	-	-	-
036	**POULTRY MEAT**	-	0	-	-	-	-	-	-	-	-	-	-
038	**POULTRY, EDIBLE OFFAL OF**	-	0	-	-	-	-	-	-	-	-	-	-
GC 0650	Rye	0.05	-	NLD	17.0	37	-	-	ND	ND	3	0.11	0%
MF 0822	Sheep fat	-	0.01	USA	15.0	28	-	-	ND	ND	1	0.02	0%
GC 0651	Sorghum	0.05	-	Thai	17.1	30	-	-	ND	ND	3	0.09	0%
VC 0431	Squash, summer (= courgette)	-	0.2	AUS	19.0	219	300	FRA	270	3	2b	6.91	9%
FB 0275	Strawberry	-	0.41	AUS	19.0	176	16	BEL	15	1	1	3.80	5%
VO 0448	Tomato	-	0.68	USA	15.0	159	150	BEL	143	3	2a	20.13	30%
GC 0653	Triticale	0.05	-	-	-	ND	-	-	ND	ND	3	ND	-
VC 0432	Watermelon	-	0.2	AUS	19.0	1473	4518	USA	2078	3	2b	46.50	60%
GC 0654	Wheat	0.05	-	USA	15.0	151	-	-	ND	ND	3	0.50	1%
-	Wine	0.06	-	AUS	19.0	4	-	-	ND	ND	3	0.01	0%
VC 0433	Winter squash (= pumpkin)	-	0.2	USA	15.0	169	1000	JPN	1000	3	2b	6.74	8%
VC 0433	Winter squash (= pumpkin), stated as pumpkin, VC 0429	-	0.2	SAF	14.2	224	1000	JPN	1000	3	2b	9.48	10%

Annex 4

TRIAZOPHOS (143) International estimate of short term intake (IESTI) for **GENERAL POPULATION**

Acute RfD= 0.001 mg/kg bw (1 µg/kg bw)
Maximum %ARfD: 140%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
VP 0541	Soya bean (immature seeds)	-	0.6	Thai	53.5	129	129	-	129	3	1	1.45	140%
OR 0691	Cotton seed oil, edible	0.088	-	USA	65.0	9	-	-	ND	ND	3	0.01	1%

TRIAZOPHOS (143) International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS**

Acute RfD= 0.001 mg/kg bw (1 µg/kg bw)
Maximum %ARfD: 230%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight			Varia-bility factor	Case	IESTI µg/kg bw per day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
VP 0541	Soya bean (immature seeds)	-	0.6	Thai	17.1	66	-	-	ND	ND	1	2.32	230%
OR 0691	Cotton seed oil, edible	0.088	-	USA	15.0	6	-	-	ND	ND	3	0.04	4%

ANNEX 5: REPORTS AND OTHER DOCUMENTS RESULTING FROM PREVIOUS JOINT MEETINGS

OF THE FAO PANEL OF EXPERTS ON PESTICIDE RESIDUES IN FOOD AND THE ENVIRONMENT AND THE WHO EXPERT GROUPS ON PESTICIDE RESIDUES

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2. Evaluation of the toxicity of pesticide residues in food. Report of a Joint Meeting of the FAO Committee on Pesticides in Agriculture and the WHO Expert Committee on Pesticide Residues. FAO Meeting Report, No. PL/1963/13; WHO/Food Add./23, 1964.
3. Evaluation of the toxicity of pesticide residues in food. Report of the Second Joint Meeting of the FAO Committee on Pesticides in Agriculture and the WHO Expert Committee on Pesticide Residues. FAO Meeting Report, No. PL/1965/10; WHO/Food Add./26.65, 1965.
4. Evaluation of the toxicity of pesticide residues in food. FAO Meeting Report, No. PL/1965/10/1; WHO/Food Add./27.65, 1965.
5. Evaluation of the hazards to consumers resulting from the use of fumigants in the protection of food. FAO Meeting Report, No. PL/1965/10/2; WHO/Food Add./28.65, 1965.
6. Pesticide residues in food. Joint report of the FAO Working Party on Pesticide Residues and the WHO Expert Committee on Pesticide Residues. FAO Agricultural Studies, No. 73; WHO Technical Report Series, No. 370, 1967.
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ANNEX 6. LIVESTOCK DIETARY BURDEN

Cyromazine

BEEF CATTLE MAX

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Cabbage heads, leaves	VC	6.1	HR	15	40.667		*20*			8.13	
Beans, seed	VD	1.8	highest residue	88	2.045	*15*	*20*	*50*	0.31	0.41	1.02
Total						*15*	*40*	*50*	0.31	8.54	1.02

DAIRY CATTLE MAX

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Cabbage heads, leaves	VC	6.1	HR	15	40.667		*20*			8.13	
Beans, seed	VD	1.8	highest residue	88	2.045	*15*	*20*	*15*	0.31	0.41	0.31
Total						*15*	*40*	*15*	0.31	8.54	0.31

POULTRY - BROILER AND LAYER MAX

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Cabbage heads, leaves	VC	6.1	HR	15	40.667		*5*			2.03	
Beans, seed	VD	1.8	highest residue	88	2.045	*20*	*20*	*70*	0.41	0.41	1.43
Total						*20*	*20*	*70*	0.409	2.4424	1.432

Cyromazine

Estimated mean dietary burden of farm animals

BEEF CATTLE MAX

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Cabbage heads, leaves	VC	0.26	STMR	15	1.733		*20*			0.35	
Beans, seed	VD	1	STMR	88	1.136	*15*	*20*	*50*	0.17	0.23	0.57
Total						*15*	*40*	*50*	0.17	0.57	0.57

DAIRY CATTLE MAX

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Cabbage heads, leaves	VC	0.26	STMR	15	1.733		*20*			0.35	
Beans, seed	VD	1	STMR	88	1.136	*15*	*20*	*15*	0.17	0.23	0.17
Total						*15*	*40*	*15*	0.17	0.57	0.17

POULTRY - BROILER AND LAYER MAX

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Cabbage heads, leaves	VC	0.26	STMR	15	1.733		*5*			0.09	
Beans, seed	VD	0.26	STMR	88	0.295	*20*	*20*	*70*	0.06	0.06	0.21
Total						*20*	*20*	*70*	0.059	0.1458	0.207

Difenoconazole

Estimated maximum dietary burden

BEEF CATTLE MAX

Commodity	Commod group	Residue mg/kg	Basis	% Dry matter	Residue dw mg/kg	*Diet content (%)* *US-CAN*	*EU*	*AU*	Residue contribution (ppm) US-CAN	EU	AU
Sugar beet leaves or tops	AM AV	0.95	highest residue	23	4.130		*20*			0.83	
Apple pomace, dry	AB	1.65	STMR-P	100	1.650	*20*	*20*	*20*	0.33	0.33	0.33
Wheat straw and fodder	AS	1.2	highest residue	88	1.364	*10*	*20*	*80*	0.14	0.27	1.09
Cabbage heads, leaves	VC	0.19	HR	15	1.267		*20*			0.25	
Carrot culls	VR	0.13	HR	12	1.083	*10*	*15*		0.11	0.16	
Oilseed rape fodder	AM AV	0.14	highest residue	100	0.140	*20*			0.03		
Potato culls	VR	0.01	HR	20	0.050	*20*	*5*		0.01	0.00	
Rape seed (for meal)	SO	0.02	STMR	88	0.023	*15*			0.00		
Soya bean seed	VD	0.02	STMR	89	0.022	*5*			0.00		
Total						*100*	*100*	*10 0*	0.62	1.85	1.42

DAIRY CATTLE MAX

Commodity	Commod group	Residue mg/kg	Basis	% Dry matter	Residue dw mg/kg	*Diet content (%)* *US-CAN*	*EU*	*AU*	Residue contribution (ppm) US-CAN	EU	AU
Sugar beet leaves or tops	AM AV	0.95	highest residue	23	4.130		*30*			1.24	
Apple pomace, dry	AB	1.65	STMR-P	100	1.650	*10*	*10*	*10*	0.17	0.17	0.17
Wheat straw and fodder	AS	1.2	highest residue	88	1.364	*10*	*20*	*20*	0.14	0.27	0.27
Cabbage heads, leaves	VC	0.19	HR	15	1.267		*20*			0.25	
Carrot culls	VR	0.13	HR	12	1.083	*10*	*15*	*5*	0.11	0.16	0.05
Grape pomace, dry	AB	0.36	STMR-P	100	0.360			*10*			0.04
Oilseed rape fodder	AM AV	0.14	highest residue	100	0.140	*20*		*40*	0.03		0.06
Potato culls	VR	0.01	HR	20	0.050		*5*	*5*		0.00	0.00
Rape seed (for meal)	SO	0.02	STMR	88	0.023	*15*		*10*	0.00		0.00
Soya bean seed	VD	0.02	STMR	89	0.022	*15*			0.00		
Total						*80*	*100*	*10 0*	0.44	2.10	0.59

POULTRY - BROILER MAX

Commodity	Commod group	Residue mg/kg	Basis	% Dry matter	Residue dw mg/kg	*Diet content (%)* *US-CAN*	*EU*	*AU*	Residue contribution (ppm) US-CAN	EU	AU
Carrot culls	VR	0.13	HR	12	1.083		*10*			0.11	
Potato culls	VR	0.01	HR	20	0.050		*10*			0.01	
Rape seed (for meal)	SO	0.02	STMR	88	0.023	*15*		*5*	0.00		0.00
Soya bean seed	VD	0.02	STMR	89	0.022	*20*	*20*	*15*	0.00	0.00	0.00
Sunflower seed (for meal)	SO	0.01	STMR	92	0.011	*30*	*10*	*15*	0.00	0.00	0.00
Total						*65*	*50*	*35*	0.01	0.12	0.01

POULTRY - LAYER MAX

Commodity	Commod group	Residue mg/kg	Basis	% Dry matter	Residue dw mg/kg	*Diet content (%)* *US-CAN*	*EU*	*AU*	Residue contribution (ppm) US-CAN	EU	AU
Sugar beet leaves or tops	AM AV	0.95	highest residue	23	4.130		*5*			0.21	
Wheat straw and fodder	AS	1.2	highest residue	88	1.364		*10*			0.14	
Cabbage heads, leaves	VC	0.19	HR	15	1.267		*5*			0.06	
Carrot culls	VR	0.13	HR	12	1.083		*10*			0.11	
Oilseed rape fodder	AM AV	0.14	highest residue	100	0.140		*10*			0.01	
Potato culls	VR	0.01	HR	20	0.050		*10*			0.01	
Rape seed (for meal)	SO	0.02	STMR	88	0.023	*15*	*10*	*5*	0.00	0.00	0.00
Soya bean seed	VD	0.02	STMR	89	0.022	*20*	*15*	*15*	0.00	0.00	0.00
Sunflower seed (for meal)	SO	0.01	STMR	92	0.011	*25*	*10*	*15*	0.00	0.00	0.00
Total						*60*	*85*	*35*	0.01	0.54	0.01

Difenoconazole

Estimated mean dietary burden

BEEF CATTLE MEAN

Commodity	Commod group	Residue mg/kg	Basis	% Dry matter	Residue dw mg/kg	*Diet content (%)*			Residue contribution (ppm)		
						US-CAN	*EU*	*AU*	US-CAN	EU	AU
Apple pomace, dry	AB	1.65	STMR-P	100	1.650	*20*	*20*	*20*	0.33	0.33	0.33
Sugar beet leaves or tops	AM AV	0.25	STMR	23	1.087		*20*			0.22	
Wheat straw and fodder	AS	0.685	STMR	88	0.778	*10*	*20*	*80*	0.08	0.16	0.62
Carrot culls	VR	0.05	STMR	12	0.417	*10*	*15*		0.04	0.06	
Grape pomace	AB	0.36	STMR-P	100	0.360						
Cabbage heads, leaves	VC	0.035	STMR	15	0.233		*20*			0.05	
Oilseed rape fodder	AM AV	0.06	STMR	100	0.060	*20*			0.01		
Potato culls	VR	0.01	STMR	20	0.050	*20*	*5*		0.01	0.00	
Rape seed (for meal)	SO	0.02	STMR	88	0.023	*15*			0.00		
Soya bean seed	VD	0.02	STMR	89	0.022	*5*			0.00		
Total						*100*	*100*	*100*	0.48	0.81	0.95

DAIRY CATTLE MEAN

Commodity	Commod group	Residue mg/kg	Basis	% Dry matter	Residue dw mg/kg	*Diet content (%)*			Residue contribution (ppm)		
						US-CAN	*EU*	*AU*	US-CAN	EU	AU
Apple pomace, dry	AB	1.65	STMR-P	100	1.650	*10*	*10*	*10*	0.17	0.17	0.17
Sugar beet leaves or tops	AM AV	0.25	STMR	23	1.087		*30*			0.33	
Wheat straw and fodder	AS	0.685	STMR	88	0.778	*10*	*20*	*20*	0.08	0.16	0.16
Carrot culls	VR	0.05	STMR	12	0.417	*10*	*15*	*5*	0.04	0.06	0.02
Grape pomace	AB	0.36	STMR-P	100	0.360			*20*			0.07
Cabbage heads, leaves	VC	0.035	STMR	15	0.233		*20*			0.05	
Oilseed rape fodder	AM AV	0.06	STMR	100	0.060	*20*		*40*	0.01		0.02
Potato culls	VR	0.01	STMR	20	0.050		*5*	*5*		0.00	0.00
Rape seed (for meal)	SO	0.02	STMR	88	0.023	*15*			0.00		
Soya bean seed	VD	0.02	STMR	89	0.022	*15*			0.00		
Total						*80*	*100*	*100*	0.30	0.76	0.44

POULTRY - BROILER MEAN

Commodity	Commod group	Residue mg/kg	Basis	% Dry matter	Residue dw mg/kg	*Diet content (%)*			Residue contribution (ppm)		
						US-CAN	*EU*	*AU*	US-CAN	EU	AU
Carrot culls	VR	0.05	STMR	12	0.417		*10*			0.04	
Potato culls	VR	0.01	STMR	20	0.050		*10*			0.01	
Rape seed (for meal)	SO	0.02	STMR	88	0.023	*15*		*5*	0.00		0.00
Soya bean seed	VD	0.02	STMR	89	0.022	*20*	*20*	*15*	0.00	0.00	0.00
Sunflower seed (for meal)	SO	0.01	STMR	92	0.011	*30*	*10*	*15*	0.00	0.00	0.00
Total						*65*	*50*	*35*	0.01	0.05	0.01

POULTRY - LAYER MEAN

Commodity	Commod group	Residue mg/kg	Basis	% Dry matter	Residue dw mg/kg	*Diet content (%)*			Residue contribution (ppm)		
						US-CAN	*EU*	*AU*	US-CAN	EU	AU
Sugar beet leaves or tops	AM AV	0.25	STMR	23	1.087		*5*			0.05	
Wheat straw and fodder	AS	0.685	STMR	88	0.778		*10*			0.08	
Carrot culls	VR	0.05	STMR	12	0.417		*10*			0.04	
Cabbage heads, leaves	VC	0.035	STMR	15	0.233		*5*			0.01	
Oilseed rape fodder	AM AV	0.06	STMR	100	0.060		*10*			0.01	
Potato culls	VR	0.01	STMR	20	0.050		*10*			0.01	
Rape seed (for meal)	SO	0.02	STMR	88	0.023	*15*	*10*	*5*	0.00	0.00	0.00
Soya bean seed	VD	0.02	STMR	89	0.022	*20*	*15*	*15*	0.00	0.00	0.00
Sunflower seed (for meal)	SO	0.01	STMR	92	0.011	*25*	*10*	*15*	0.00	0.00	0.00
Total						*60*	*85*	*35*	0.01	0.20	0.01

Dimethomorph

Estimated maximum dietary burden

BEEF CATTLE MAX

Commodity	CC	Residue mg/kg	Basis	DM %	Residue dw mg/kg	Diet content (%) US-CAN	EU	AU	Residue contribution (ppm) US-CAN	EU	AU
Grape pomace	AB	1.07	STMR-P	15	7.13			20			1.43
Cabbage heads, leaves	VC	1.4	HR	15	9.33		20			1.87	
Potato process waste	VR	0.128	STMR-P	12	1.07	30	40	5	0.32	0.43	0.05
Total						30	50	30	0.32	2.30	1.48

DAIRY CATTLE MAX

Commodity	CC	Residue mg/kg	Basis	DM %	Residue dw mg/kg	Diet content (%) US-CAN	EU	AU	Residue contribution (ppm) US-CAN	EU	AU
Grape pomace	AB	1.07	STMR-P	15	7.33			20			1.43
Cabbage heads, leaves	VC	1.4	HR	15	9.33		20			1.87	
Potato process waste	VR	0.128	STMR-P	12	1.07	10	30		0.11	0.32	
Total						30	50	30	0.11	2.19	1.43

POULTRY - BROILER MAX

Commodity	CC	Residue mg/kg	Basis	DM %	Residue dw mg/kg	Diet content (%) US-CAN	EU	AU	Residue contribution (ppm) US-CAN	EU	AU
Potato culls	VR	0.05	HR	20	0.25		10			0.03	
Total						0	10	0	0.00	0.03	0.00

POULTRY - LAYER MAX

Commodity	CC	Residue mg/kg	Basis	DM %	Residue dw mg/kg	Diet content (%) US-CAN	EU	AU	Residue contribution (ppm) US-CAN	EU	AU
Cabbage heads, leaves	VC	1.4	HR	15	9.33		5			0.47	
Potato culls	VR	0.05	HR	20	0.25		10			0.03	
Total						0	15	0	0.00	0.5	0.00

Dimethomorph

Estimated mean dietary burden of farm animals

BEEF CATTLE MEAN

Commodity	CC	Residue mg/kg	Basis	DM %	Residue dw mg/kg	Diet content (%) US-CAN	EU	AU	Residue contribution (ppm) US-CAN	EU	AU
Grape pomace	AB	1.07	STMR-P	15	7.13			20			1.43
Cabbage heads, leaves	VC	0.4	STMR	15	2.67		20			0.53	
Potato process waste	VR	0.128	STMR-P	12	1.07	30	40	5	0.32	0.43	0.05
Total						30	50	30	0.32	0.96	1.48

DAIRY CATTLE MEAN

Commodity	CC	Residue mg/kg	Basis	DM %	Residue dw mg/kg	Diet content (%) US-CAN	EU	AU	Residue contribution (ppm) US-CAN	EU	AU
Grape pomace	AB	1.07	STMR-P	15	7.13			20			1.43
Cabbage heads, leaves	VC	0.4	STMR	15	2.67		20			0.53	
Potato process waste	VR	0.128	STMR-P	12	1.07	10	30		0.11	0.32	
Total						30	50	30	0.11	0.85	1.43

POULTRY - BROILER MEAN

Commodity	CC	Residue mg/kg	Basis	DM %	Residue dw mg/kg	Diet content (%) US-CAN	EU	AU	Residue contribution (ppm) US-CAN	EU	AU
Potato culls	VR	0.02	STMR	20	0.1		10			0.01	
Total						0	10	0	0.00	0.01	0.00

POULTRY - LAYER MEAN

Commodity	CC	Residue mg/kg	Basis	DM %	Residue dw mg/kg	Diet content (%) US-CAN	EU	AU	Residue contribution (ppm) US-CAN	EU	AU
Cabbage heads, leaves	VC	0.4	STMR	15	2.67		5			0.13	
Potato culls	VR	0.02	STMR	20	0.1		10			0.01	
Total						0	15	0	0.00	0.14	0.00

Fenitrothion

Estimated maximum dietary burden of farm animals

BEEF CATTLE MAX

Commodity	CC	Residue mg/kg	Basis	DM %	Residue dw mg/kg	*Diet content (%)* *US-CAN*	*EU*	*AU*	Residue contribution (ppm) US-CAN	EU	AU
Apple pomace, wet	AB?	0.04	STMR-P	40	0.100		*20*			0.02	
Rice bran	CM	30.6	STMR	90	34.000			*40*			13.60
Rice hulls	CM	42.5	STMR	90	47.222	*10*		*5*	4.72		2.36
Soya bean	VD	0.1	STMR	89	0.112	*10*	*10*		0.01	0.01	
Wheat milled byproducts	CF	16.79	STMR	88	19.080	*40*	*30*	*40*	7.63	5.72	7.63
Wheat grain	GC	5.6	HR	89	6.292	*40*	*20*	*15*	2.52	1.26	0.94
Total						*100*	*80*	*100*	14.88	7.01	24.54

DAIRY CATTLE MAX

Commodity	CC	Residue mg/kg	Basis	DM %	Residue dw mg/kg	*Diet content (%)* *US-CAN*	*EU*	*AU*	Residue contribution (ppm) US-CAN	EU	AU
Apple pomace, wet	AB?	0.04	STMR-P	40	0.100	*10*			0.01		
Rice bran	CM	30.6	STMR	90	34.000	*15*	*20*	*40*	5.10	6.80	13.60
Rice hulls	CM	42.5	STMR	90	47.222						
Soya bean	VD	0.1	STMR	89	0.112	*15*	*10*		0.02	0.01	
Wheat milled byproducts	CF	16.79	STMR	88	19.080	*40*	*30*	*40*	7.63	5.72	7.63
Wheat grain	GC	5.6	HR	89	6.292	*20*	*40*	*20*	1.26	2.52	1.26
Total						*100*	*100*	*100*	14,02	15,05	22,49

POULTRY - BROILER MAX

Commodity	CC	Residue mg/kg	Basis	DM %	Residue dw mg/kg	*Diet content (%)* *US-CAN*	*EU*	*AU*	Residue contribution (ppm) US-CAN	EU	AU
Apple pomace, wet	AB?	0.04	STMR-P	40	0.100						
Rice bran	CM	30.6	STMR	90	34.000	*25*	*10*	*20*	8.50	3.40	6.80
Rice hulls	CM	42.5	STMR	90	47.222						
Soya bean	VD	0.1	STMR	89	0.112						
Wheat milled byproducts	CF	16.79	STMR	88	19.080	*50*	*20*	*20*	9.54	3.82	3.82
Wheat grain	GC	5.6	HR	89	6.292	*25*	*70*	*60*	1.57	4.40	3.78
Total						*100*	*100*	*100*	19.61	11.62	14.39

POULTRY - LAYER MAX

Commodity	CC	Residue mg/kg	Basis	DM %	Residue dw mg/kg	*Diet content (%)* *US-CAN*	*EU*	*AU*	Residue contribution (ppm) US-CAN	EU	AU
Apple pomace, wet	AB?	0.04	STMR-P	40	0.100						
Rice bran	CM	30.6	STMR	90	34.000	*25*	*5*	*20*	8.50	1.70	6.80
Rice hulls	CM	42.5	STMR	90	47.222						
Soya bean	VD	0.1	STMR	89	0.112		*5*	*5*		0.01	0.01
Wheat milled byproducts	CF	16.79	STMR	88	19.080	*50*	*20*	*20*	9.54	3.82	3.82
Wheat grain	GC	4.25	HR	89	4.775	*25*	*70*	*55*	1.57	4.40	3.46
Total						*100*	*100*	*100*	19.61	9.93	14.08

Fenitrothion

Estimated mean dietary burden of farm animals

BEEF CATTLE MEAN

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Apple pomace, wet	AB ?	0.04	STMR-P	40	0.100		*20*			0.02	
Rice bran	CM	30.6	STMR	90	34.000			*40*			13.60
Rice hulls	CM	42.5	STMR	90	47.222	*10*			4,72		
Soya bean	VD	0.1	STMR	89	0.112	*10*	*10*		0.01	0.01	
Wheat milled byproducts	CF	16.79	STMR	88	19.080	*40*	*30*	*40*	7.63	5.72	7.63
Wheat grain	GC	4.25	STMR	89	4.775	*40*	*20*	*20*	1.91	0.96	0.96
Total						*100*	*80*	*100*	14.28	6.71	22.19

DAIRY CATTLE MEAN

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Apple pomace, wet	AB ?	0.04	STMR-P	40	0.100	*10*	*10*		0.01	0.01	
Rice bran	CM	30.6	STMR	90	34.000	*15*	*20*	*40*	5.10	6.80	13.60
Rice hulls	CM	42.5	STMR	90	47.222						
Soya bean	VD	0.1	STMR	89	0.112	*15*	*10*		0.02	0.01	
Wheat milled byproducts	CF	16.79	STMR	88	19.080	*40*	*30*	*40*	7.63	5.72	7.63
Wheat grain	GC	4.25	STMR	89	4.775	*20*	*40*	*20*	0.96	1.91	0.96
Total						*100*	*110*	*100*	13.71	14.46	22.19

POULTRY - BROILER MEAN

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Apple pomace, wet	AB ?	0.04	STMR-P	40	0.100						
Rice bran	CM	30.6	STMR	90	34.000	*25*	*10*	*20*	8.50	3.40	6.80
Rice hulls	CM	42.5	STMR	90	47.222						
Soya bean	VD	0.1	STMR	89	0.112						
Wheat milled byproducts	CF	16.79	STMR	88	19.080	*50*	*20*	*20*	9.54	3.82	3.82
Wheat grain	GC	4.25	STMR	89	4.775	*25*	*70*	*60*	1.19	3.34	2.87
Total						*100*	*100*	*100*	19.23	10.56	13.48

POULTRY - LAYER MEAN

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Apple pomace, wet	AB ?	0.04	STMR-P	40	0.100						
Rice bran	CM	30.6	STMR	90	34.000	*25*	*5*	*20*	8.50	1.70	6.80
Rice hulls	CM	42.5	STMR	90	47.222						
Soya bean	VD	0.1	STMR	89	0.112		*5*	*5*		0.01	0.01
Wheat milled byproducts	CF	16.79	STMR	88	19.080	*50*	*20*	*20*	9.54	3.82	3.82
Wheat grain	GC	4.25	STMR	89	4.775	*25*	*70*	*55*	1.19	3.34	2.63
Total						*100*	*100*	*100*	19.23	8.86	13.25

Flusilazole

Estimated maximum dietary burden of farm animals

BEEF CATTLE MAX

Commodity	CC	Residue (mg/kg)	Basis	DM (%)	Residue dw (mg/kg)	Diet content (%)			Residue contribution (mg/kg)		
						US-CAN	EU	AU	US-CAN	EU	AU
Apple pomace, wet	AB	0.094	STMR-P	40	0.24	20	20		0.05	0.05	
Barley forage	AF	4.5	HR	30	15		30			4.5	
Barley straw	AS	2.5	HR	89	2.8		30			0.84	
Barley grain	GC	0.04	STMR	88	0.045	30			0.01		
Sugar beet leaves or tops	AV	1.0	HR	23	4.3		20			0.87	
Wheat forage	AF	4.5	HR	25	18	40		100	7.2		18
Wheat straw	AS	2.5	HR	88	2.8	10			0.28		
Total						100	100	100	7.5	6.3	18

DAIRY CATTLE MAX

Commodity	CC	Residue (mg/kg)	Basis	DM (%)	Residue dw (mg/kg)	Diet content (%)			Residue contribution (mg/kg)		
						US-CAN	EU	AU	US-CAN	EU	AU
Apple pomace, wet	AB	0.094	STMR-P	40	0.24	10	10		0.02	0.02	
Barley forage	AF	4.5	HR	30	15		30			4.5	
Barley grain	GC	0.04	STMR	88	0.045	40			0.02		
Barley straw	AS	2.5	HR	89	2.8		30			0.84	
Grape pomace, wet	AB	0.108	STMR-P	15	0.72			20			0.14
Sugar beet leaves or tops	AV	1.0	HR	23	4.3		30			1.3	
Wheat forage	AF	4.5	HR	25	18	40		60	7.2		10.8
Wheat straw	AS	2.5	HR	88	2.8	10		20	0.28		0.57
Total						100	100	100	7.5	6.7	11.5

POULTRY - BROILER MAX

Commodity	CC	Residue (mg/kg)	Basis	DM (%)	Residue dw (mg/kg)	Diet content (%)			Residue contribution (mg/kg)		
						US-CAN	EU	AU	US-CAN	EU	AU
Barley grain	GC	0.04	STMR	88	0.045	75	70		0.034	0.032	
Rye grain	GC	0.04	STMR	88	0.045			50			0.023
Soya bean hulls	AB	0.022	STMR-P	90	0.024	20	10	5	0.004	0.002	0.001
Soya bean meal	AB	0.008	STMR-P	92	0.009			10			0.001
Soya bean seed	VD	0.02	STMR	89	0.022	5	20	15	0.001	0.004	0.003
Wheat milled by-products	CF CM	0.024	STMR-P	88	0.027			20			0.005
Total						100	100	100	0.04	0.04	0.03

POULTRY - LAYER MAX

Commodity	CC	Residue (mg/kg)	Basis	DM (%)	Residue dw (mg/kg)	Diet content (%)			Residue contribution (mg/kg)		
						US-CAN	EU	AU	US-CAN	EU	AU
Barley grain	GC	0.04	STMR	88	0.045	70	75		0.032	0.034	
Rye grain	GC	0.04	STMR	88	0.045			35			0.016
Soya bean hulls	AB	0.022	STMR-P	90	0.024	10		5	0.002		0.001
Soya bean meal	AB	0.008	STMR-P	92	0.009			25			0.002
Soya bean seed	VD	0.02	STMR	89	0.022	20		15	0.004		0.003
Sugar beet leaves or tops	AV	1.0	HR	23	4.3		5			0.22	
Wheat forage	AF	4.5	HR	25	18		10			1.8	
Wheat straw	AS	2.5	HR	88	2.8		10			0.28	
Wheat milled by-products	CF CM	0.024	STMR-P	88	0.027			20			0.005
Total						100	100	100	0.04	2.3	0.02

Flusilazole

Estimated maximum dietary burden of farm animals

Flusilazole

Estimated mean dietary burden of farm animals

BEEF CATTLE — Mean

Commodity	CC	Residue (mg/kg)	Basis	DM (%)	Residue dw (mg/kg)	Diet content (%)			Residue contribution (mg/kg)		
						US-CAN	EU	AU	US-CAN	EU	AU
Apple pomace, wet	AB	0.094	STMR-P	40	0.24	20	20		0.05	0.05	
Barley straw	AS	1.6	STMR	89	1.8		30			0.54	
Barley forage	AF	2.0	STMR	30	6.7	30	30		2.0	2.0	
Barley grain	GC	0.04	STMR	88	0.045	40			0.02		
Sugar beet leaves or tops	AV	0.29	STMR	23	1.3		20			0.25	
Wheat forage	AF	2.0	STMR	25	8			100			8.0
Wheat straw	AS	1.6	STMR	88	1.8	10			0.18		
Total						100	100	100	2.25	2.9	8.0

DAIRY CATTLE — Mean

Commodity	CC	Residue (mg/kg)	Basis	DM (%)	Residue dw (mg/kg)	Diet content (%)			Residue contribution (mg/kg)		
						US-CAN	EU	AU	US-CAN	EU	AU
Apple pomace, wet	AB	0.094	STMR-P	40	0.24	10	10		0.02	0.02	
Barley forage	AF	2.0	STMR	30	6.7		30			2.0	
Barley grain	GC	0.04	STMR	88	0.045	40			0.02		
Barley straw	AS	1.6	STMR	89	1.8		30			0.54	
Grape pomace, wet	AB	0.108	STMR-P	15	0.72			20			0.14
Sugar beet leaves or tops	AV	0.29	STMR	23	1.3		30			0.38	
Wheat forage	AF	2.0	STMR	25	8.0	40		60	3.2		4.8
Wheat straw	AS	1.6	STMR	88	1.8	10		20	0.18		0.36
Total						100	100	100	3.4	2.9	5.3

POULTRY BROILER — Mean

Commodity	CC	Residue (mg/kg)	Basis	DM (%)	Residue dw (mg/kg)	Diet content (%)			Residue contribution (mg/kg)		
						US-CAN	EU	AU	US-CAN	EU	AU
Barley grain	GC	0.04	STMR	88	0.045	75	70		0.034	0.032	
Rye grain	GC	0.04	STMR	88	0.045			50			0.023
Soya bean hulls	AB	0.022	STMR-P	90	0.024	20	10	5	0.004	0.002	0.001
Soya bean meal	AB	0.008	STMR-P	92	0.009			25			0.002
Soya bean seed	VD	0.02	STMR	89	0.022	5	20		0.001	0.004	
Wheat milled by-	CF	0.024	STMR-P	88	0.027			20			0.005
Total						100	100	100	0.04	0.04	0.03

POULTRY - LAYER — Mean

Commodity	CC	Residue (mg/kg)	Basis	DM (%)	Residue dw (mg/kg)	Diet content (%)			Residue contribution (mg/kg)		
						US-CAN	EU	AU	US-CAN	EU	AU
Barley grain	GC	0.04	STMR	88	0.045	70	75		0.032	0.034	
Rye grain	GC	0.04	STMR	88	0.045			35			0.016
Soya bean hulls	AB	0.022	STMR-P	90	0.024			5			0.001
Soya bean meal	AB	0.008	STMR-P	92	0.009			25			0.002
Soya bean seed	VD	0.02	STMR	89	0.022	10		15	0.002		0.003

Flusilazole

Estimated maximum dietary burden of farm animals

Sugar beet leaves or tops	AV	0.29	STMR	23	1.3		5			0.063		
Wheat forage	AF	2.0	STMR	25	8.0		10			0.80		
Wheat milled by-products	CF CM	0.024	STMR-P	88	0.027	20		20	0.005		0.005	
Wheat straw	AS	1.6	STMR	88	1.8		10			0.18		
Total						100	100	100	0.04	1.1	0.02	

Propiconazole

Estimated max dietary burden of farm animals

BEEF CATTLE MAX

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Wheat grain	CC	0.02	STMR	89	0.022						
Sugar beet leaves or tops	AM AV	0.5	HR	23	2.174		*20*			0.43	
Wheat straw	AS	2	HR	88	2.273	*10*	*20*	*80*	0.23	0.45	1.82
Barley straw		2	HR	89	2.247	*10*	*30*	*20*	0.22	0.67	0.45
Corn, field, grain		0.05	STMR	88	0.057	*80*	*30*		0.05	0.02	
Rape seed (for meal)	SO	0.02	STMR	88	0.023						
Soya been seed	VD	0.01	STMR	89	0.011						
Total						*100*	*100*	*100*	0.50	1.58	2.27

DAIRY CATTLE MAX

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Wheat grain	CC	0.02	STMR	89	0.022	*20*		*25*	0.00		0.01
Sugar beet leaves or tops	AM AV	0.5	HR	23	2.174		*30*			0.65	
Wheat straw	AS	2	HR	88	2.273	*10*	*20*	*20*	0.23	0.45	0.45
Barley straw		2	HR	89	2.247	*10*	*30*	*20*	0.22	0.67	0.45
Corn, field, grain		0.05	STMR	88	0.057	*45*	*20*	*20*	0.03	0.01	0.01
Rape seed (for meal)	SO	0.02	STMR	88	0.023	*15*		*15*	0.00		0.00
Soya been seed	VD	0.01	STMR	89	0.011						
Total						*100*	*100*	*100*	0.49	1.79	0.92

POULTRY - BROILER MAX

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Wheat grain	CC	0.02	STMR	89	0.022						
Sugar beet leaves or tops	AM AV	0.5	HR	23	2.174						
Wheat straw	AS	2	HR	88	2.273						
Barley straw		2	HR	89	2.247						
Corn, field, grain		0.05	STMR	88	0.057	*80*	*70*		0.05	0.04	
Rape seed (for meal)	SO	0.02	STMR	88	0.023	*15*		*5*	0.00		0.00
Soya been seed	VD	0.01	STMR	89	0.011	*5*	*20*	*15*	0.00	0.00	0.00
Total						*100*	*90*	*20*	0.05	0.04	0.00

POULTRY - LAYER MAX

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Wheat grain	CC	0.02	STMR	89	0.022						

Propiconazole

Estimated max dietary burden of farm animals

Sugar beet leaves or tops	AM AV	0.5	HR	23	2.174		*5*			0.11	
Wheat straw	AS	2	HR	88	2.273		*10*			0.23	
Barley straw		2	HR	89	2.247		*5*			0.11	
Corn, field, grain		0.05	STMR	88	0.057	*70*	*70*		0.04	0.04	
Rape seed (for meal)	SO	0.02	STMR	88	0.023	*15*	*10*	*5*	0.00	0.00	0.00
Soya been seed	VD	0.01	STMR	89	0.011	*15*		*15*	0.00		0.00
Total						*100*	*100*	*20*	0.04	0,49	0.00

Propiconazole

Estimated mean dietary burden of farm animals

BEEF CATTLE MEAN

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Wheat grain	CC	0.02	STMR	89	0.022						
Sugar beet leaves or tops	AM AV	0.1	STMR	23	0.435		*20*			0.09	
Wheat straw	AS	0.32	STMR	88	0.364	*10*	*20*	*80*	0.04	0.07	0.29
Barley straw		0.145	STMR	89	0.163		*30*	*20*		0.05	0.03
Corn, field, grain		0.05	STMR	88	0.057	*80*	*30*		0.05	0.02	
Rape seed (for meal)	SO	0.02	STMR	88	0.023	*10*			0.00		
Soya been seed	VD	0.01	STMR	89	0.011						
Total						*100*	*100*	*100*	0.08	0.23	0.32

DAIRY CATTLE MEAN

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Wheat grain	CC	0.02	STMR	89	0.022	*20*		*25*	0.00		0.01
Sugar beet leaves or tops	AM AV	0.1	STMR	23	0.435		*30*			0.13	
Wheat straw	AS	0.32	STMR	88	0.364	*10*	*20*	*20*	0.04	0.07	0.07
Barley straw		0.145	STMR	89	0.163	*10*	*30*	*20*	0.02	0.05	0.03
Corn, field, grain		0.05	STMR	88	0.057	*45*	*20*	*20*	0.03	0.01	0.01
Rape seed (for meal)	SO	0.02	STMR	88	0.023	*15*		*15*	0.00		0.00
Soya been seed	VD	0.01	STMR	89	0.011						
Total						*100*	*100*	*100*	0,09	0,26	0,13

POULTRY - BROILER MEAN

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Wheat grain	CC	0.02	STMR	89	0.022						
Sugar beet leaves or tops	AM AV	0.1	STMR	23	0.435						
Wheat straw and fodder	AS	0.32	STMR	88	0.364						
Barley straw		0.145	STMR	89	0.163						
Corn, field, grain		0.05	STMR	88	0.057	*80*	*70*		0.05	0.04	
Rape seed (for meal)	SO	0.02	STMR	88	0.023	*15*		*5*	0.00		0.00
Soya been seed	VD	0.01	STMR	89	0.011	*5*	*20*	*15*	0.00	0.00	0.00
Total						*100*	*90*	*20*	0.05	0.04	0.00

POULTRY - LAYER MEAN

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Wheat grain	CC	0.02	STMR	89	0.022						
Sugar beet leaves or tops	AM AV	0.1	STMR	23	0.435		*5*			0.02	
Wheat straw and fodder	AS	0.32	STMR	88	0.364		*10*			0.04	

Propiconazole

Estimated mean dietary burden of farm animals

Barley straw		0.145	STMR	89	0.163		*5*			0.01	
Corn, field, grain		0.05	STMR	88	0.057	*70*	*70*		0.04	0.04	
Rape seed (for meal)	SO	0.02	STMR	88	0.023	*15*	*10*	*5*	0.00	0.00	0.00
Soya been seed	VD	0.01	STMR	89	0.011	*15*		*15*	0.00		0.00
Total						*100*	*100*	*20*	0.04	0.11	0.00

Pyrimethanil

Estimated maximum dietary burden of livestock

BEEF CATTLE MEAN

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Apple pomace, wet	AB	2.9	STMR-P	40	7.250	*20*	*20*	*0*	1.45	1.45	
Almond hulls	TN	2.6	STMR	90	2.889	*10*	*0*	*10*	0.29		0.29
Carrot culls	VR	0.14	STMR	12	1.167	*10*	*15*	*5*	0.12	0.18	0.06
Grape pomace wet	AB	1.7	STMR	15	11.63	*0*	*0*	*20*			2.26
Pea seed	VD	0.09	STMR	90	0.100	*0*	*20*	*0*		0.02	
Pea straw	AM	0.2	STMR	88	0.227	*20*	*25*	*65*	0.05	0.06	0.15
Total						*60*	*80*	*100*	1.90	1.70	2.76

DAIRY CATTLE MEAN

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Apple pomace, wet	AB	2.9	STMR-P	40	7.250	*10*	*10*	*0*	0.73	0.73	
Almond hulls	TN	2.6	STMR	90	2.889	*10*	*0*	*10*	0.29		0.29
Carrot culls	VR	0.14	STMR	12	1.167	*10*	*10*	*15*	0.12	0.12	0.18
Grape pomace wet	AB	1.7	STMR	15	11.3	*0*	*0*	*20*			2.26
Pea seed	VD	0.09	STMR	90	0.100	*0*	*20*	*0*		0.02	
Pea straw	AM	0.2	STMR	88	0.227	*20*	*30*	*55*	0.05	0.07	0.13
Total						*50*	*70*	*100*	1.18	0.93	2.86

Pyrimethanil

Estimated maximum livestock dietary burden

BEEF CATTLE MAX

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Apple pomace, wet	AB	2.9	STMR-P	40	7.250	*20*	*20*	*0*	1.45	1.45	
Almond hulls	TN	2.6	STMR	90	2.889	*10*	*0*	*10*	0.29		0.29
Carrot culls	VR	0.54	highest residue	12	4.500	*10*	*15*	*5*	0.45	0.68	0.23
Grape pomace wet	AB	1.7	STMR-P	15	11.3	*0*	*0*	*20*			2.26
Pea seed	VD	0.09	STMR-P	90	0.100	*0*	*20*	*0*		0.02	
Pea straw	AM	1	highest residue	88	1.136	*20*	*30*	*65*	0.23	0.34	0.74
Total						*60*	*85*	*100*	2.42	2.49	3.52

DAIRY CATTLE MAX

Commodity	CC	Residue	Basis	DM	Residue dw	*Diet content (%)*			Residue contribution (ppm)		
		mg/kg		%	mg/kg	*US-CAN*	*EU*	*AU*	US-CAN	EU	AU
Apple pomace, wet	AB	2.9	STMR-P	40	7.250	*10*	*10*	*0*	0.73	0.73	

Pyrimethanil

Estimated maximum livestock dietary burden

Almond hulls	TN	2.6	STMR	90	2.889	*10*	*0*	*10*	0.29		0.29
Carrot culls	VR	0.54	highest residue	12	4.500	*10*	*15*	*5*	0.45	0.68	0.23
Grape pomace wet	AB	1.7	STMR-P	15	11.3	*0*	*0*	*20*			2.26
Pea seed	VD	0.09	STMR-P	90	0.100	*0*	*20*	*0*		0.02	
Pea straw	AM	1	highest residue	88	1.136	*20*	*30*	*65*	0.23	0.34	0.74
Potato culls	VR	0.05	highest residue	20	0.250	*0*	*0*	*0*			
Potato process waste	AB	0.05	STMR-P	12	0.417	*0*	*0*	*0*			
Total						*50*	*75*	*100*	1.69	1.76	3.52

Triadimefon/Triadimenol

Estimated maximum dietary burden of farm animals

BEEF CATTLE MAX

Commodity	CC	Residue	Basis	DM	Residue dw	Diet content (%)			Residue contribution (ppm)		
		mg/kg		%	mg/kg	US-CAN	EU	AU	US-CAN	EU	AU
Grape pomace, wet	AB	0.5	STMR-P	15	3.333	0	0	0			
Sugar beet leaves or tops	AM AV	0.42	highest residue	23	1.826	0	20	0		0.37	
Wheat straw and fodder	AS	4.1	highest residue	88	4.659	10	20	0	0.47	0.93	
Wheat hay		0.98	highest residue	88	1.114	25	20	0	0.28	0.22	
Wheat forage	AF	10	highest residue	25	40.000	25	20	100	10.00	8.00	40.00
Pineapple, process waste	AM	1.95	STMR-P	25	7.800	10		0	0.78		
Wheat	GC	0.15	highest residue	89	0.169	20	20	0	0.03	0.03	
Total						90	100	100	11.56	9.55	40.00

DAIRY CATTLE MAX

Commodity	CC	Residue	Basis	DM	Residue dw	Diet content (%)			Residue contribution (ppm)		
		mg/kg		%	mg/kg	US-CAN	EU	AU	US-CAN	EU	AU
Grape pomace, wet	AB	0.5	STMR-P	15	3.333	0	0	0			
Sugar beet leaves or tops	AM AV	0.42	highest residue	23	1.826	0	30	0		0.55	
Wheat straw and fodder	AS	4.1	highest residue	88	4.659	10	20	10	0.47	0.93	0.47
Wheat hay		0.98	highest residue	88	1.114	40	20	0	0.45	0.22	
Wheat forage	AF	10	highest residue	25	40.000	40	20	60	16.00	8.00	24.00
Pineapple, process waste	AM	1.95	STMR-P	25	7.800	10		30	0.78		2.34
Wheat	GC	0.15	highest residue	89	0.169	0	10	0		0.02	
Total						100	100	100	17.69	9.72	26.81

POULTRY - BROILER MAX

Commodity	CC	Residue	Basis	DM	Residue dw	Diet content (%)			Residue contribution (ppm)		
		mg/kg		%	mg/kg	US-CAN	EU	AU	US-CAN	EU	AU
Grape pomace, wet	AB	0.5	STMR-P	15	3.333	0	0	0			
Sugar beet leaves or tops	AM AV	0.42	highest residue	23	1.826	0	0	0			
Wheat straw and fodder	AS	4.1	highest residue	88	4.659	0	0	0			
Wheat hay		0.98	highest residue	88	1.114	0	0	0			
Wheat forage	AF	10	highest residue	25	40.000	0	0	0			
Pineapple, process waste	AM	1.95	STMR-P	25	7.800	0	0	0			
Wheat	GC	0.15	highest residue	89	0.169	80	70	70	0.13	0.12	0.12
Total						80	70	70	0.13	0.12	0.12

POULTRY - LAYER MAX

Commodity	CC	Residue	Basis	DM	Residue dw	Diet content (%)			Residue contribution (ppm)		
		mg/kg		%	mg/kg	US-CAN	EU	AU	US-CAN	EU	AU
Grape pomace, wet	AB	0.5	STMR-P	15	3.333	0	0	0			

Triadimefon/Triadimenol

Estimated maximum dietary burden of farm animals

BEEF CATTLE MAX

Commodity	CC	Residue	Basis	DM	Residue dw	Diet content (%)			Residue contribution (ppm)		
		mg/kg		%	mg/kg	US-CAN	EU	AU	US-CAN	EU	AU
Sugar beet leaves or tops	AM AV	0.42	highest residue	23	1.826	0	0	5			0.09
Wheat straw and fodder	AS	4.1	highest residue	88	4.659	0	10	0		0.47	
Wheat hay		0.98	highest residue	88	1.114	0	10	0		0.11	
Wheat forage	AF	10	highest residue	25	40.000	0	10	0		4.00	
Pineapple, process waste	AM	1.95	STMR-P	25	7.800	0	0	0			
Wheat	GC	0.15	highest residue	89	0.169	70	70	55	0.12	0.12	0.09
Total						70	100	60	0.12	4.70	0.18

Estimated mean dietary burden of farm animals

BEEF CATTLE MEAN

Commodity	CC	Residue	Basis	DM	Residue dw	Diet content (%)			Residue contribution (ppm)		
		mg/kg		%	mg/kg	US-CAN	EU	AU	US-CAN	EU	AU
Grape pomace, wet	AB	0.5	STMR-P	15	3.333	0	0	0			
Sugar beet leaves or tops	AM AV	0.14	STMR	23	0.609	0	20	0		0.12	
Wheat straw and fodder	AS	0.65	STMR	88	0.739	10	20	0	0.07	0.15	
Wheat hay		0.06	STMR	88	0.068	25	20	0	0.02	0.01	
Wheat forage	AF	2.2	STMR	25	8.800	25	20	100	2.20	1.76	8.80
Pineapple, process waste	AM	1.95	STMR-P	25	7.800	10		0	0.78		
Wheat	GC	0.05	STMR	89	0.056	20	20	0	0.01	0.01	
Total						90	100	100	3.08	2.05	8.80

DAIRY CATTLE MEAN

Commodity	CC	Residue	Basis	DM	Residue dw	Diet content (%)			Residue contribution (ppm)		
		mg/kg		%	mg/kg	US-CAN	EU	AU	US-CAN	EU	AU
Grape pomace, wet	AB	0.5	STMR-P	15	3.333	0	0	0			
Sugar beet leaves or tops	AM AV	0.14	STMR	23	0.609	0	30	0		0.18	
Wheat straw and fodder	AS	0.65	STMR	88	0.739	10	20	10	0.07	0.15	0.07
Wheat hay		0.06	STMR	88	0.068	40	20	0	0.03	0.01	
Wheat forage	AF	2.2	STMR	25	8.800	40	20	60	3.52	1.76	5.28
Pineapple, process waste	AM	1.95	STMR-P	25	7.800	10		30	0.78		2.34
Wheat	GC	0.05	STMR	89	0.056	0	10	0		0.01	
Total						100	100	100	4.40	2.11	7.69

POULTRY - BROILER MEAN

Commodity	CC	Residue	Basis	DM	Residue dw	Diet content (%)			Residue contribution (ppm)		
		mg/kg		%	mg/kg	US-CAN	EU	AU	US-CAN	EU	AU
Grape pomace, wet	AB	0.5	STMR-P	15	3.333	0	0	0			
Sugar beet leaves or tops	AM AV	0.14	STMR	23	0.609	0	0	0			
Wheat straw and fodder	AS	0.65	STMR	88	0.739	0	0	0			
Wheat hay		0.06	STMR	88	0.068	0	0	0			
Wheat forage	AF	2.2	STMR	25	8.800	0	0	0			
Pineapple, process waste	AM	1.95	STMR-P	25	7.800	0	0	0			
Wheat	GC	0.05	STMR	89	0.056	80	70	70	0.04	0.04	0.04
Total						80	70	70	0.04	0.04	0.04

POULTRY - LAYER MEAN

Commodity	CC	Residue	Basis	DM	Residue dw	Diet content (%)			Residue contribution (ppm)		
		mg/kg		%	mg/kg	US-CAN	EU	AU	US-CAN	EU	AU
Grape pomace, wet	AB	0.5	STMR-P	15	3.333	0	0	0			
Sugar beet leaves or tops	AM AV	0.14	STMR	23	0.609	0	0	5			0.03

Triadimefon/Triadimenol

Estimated maximum dietary burden of farm animals

BEEF CATTLE MAX

Commodity	CC	Residue mg/kg	Basis	DM %	Residue dw mg/kg	Diet content (%) US-CAN	EU	AU	Residue contribution (ppm) US-CAN	EU	AU
Wheat straw and fodder	AS	0.65	STMR	88	0.739	0	10	0		0.07	
Wheat hay		0.06	STMR	88	0.068	0	10	0		0.01	
Wheat forage	AF	2.2	STMR	25	8.800	0	10	0		0.88	
Pineapple, process waste	AM	1.95	STMR-P	25	7.800	0	0	0			
Wheat	GC	0.05	STMR	89	0.056	70	70	55	0.04	0.04	0.03
Total						70	100	60	0.04	1.00	0.06

Zoxamide

Estimated dietary burden of farm animals

BEEF CATTLE MEAN/ MAXIMUM

Commodity	CC	Residue mg/kg	Basis	DM %	Residue dw mg/kg	Diet content (%) US-CAN	EU	AU	Residue contribution (ppm) US-CAN	EU	AU
Grape pomace, wet	AB	1.1	STMR-P	15	7.333			20			1.47
Potato culls	VR	0.06	STMR	20	0.300	30	30	10	0.03	0.09	0.03
Total						30	30	30	0.03	0.09	1.50

DAIRY CATTLE MEAN /MAXIMUM

Commodity	CC	Residue mg/kg	Basis	DM %	Residue dw mg/kg	Diet content (%) US-CAN	EU	AU	Residue contribution (ppm) US-CAN	EU	AU
Grape pomace, wet	AB	1.1	STMR-P	15	7.333			20			1.47
Potato culls	VR	0.06	STMR	20	0.300	10	30	10	0.03	0.09	0.03
Total						10	30	30	0.03	0.09	1.50

POULTRY - BROILER MEAN /MAXIMUM

Commodity	CC	Residue mg/kg	Basis	DM %	Residue dw mg/kg	Diet content (%) US-CAN	EU	AU	Residue contribution (ppm) US-CAN	EU	AU
Grape pomace, wet	AB	1.1	STMR-P	15	7.333			10			0.73
Potato culls	VR	0.06	STMR	20	0.300		10			0.03	
Total						0	10	10	0.00	0.03	0.73

POULTRY - LAYER MEAN /MAXIMUM

Commodity	CC	Residue mg/kg	Basis	DM %	Residue dw mg/kg	Diet content (%) US-CAN	EU	AU	Residue contribution (ppm) US-CAN	EU	AU
Grape pomace, wet	AB	1.1	STMR-P	15	7.333						
Potato culls	VR	0.06	STMR	20	0.300		10			0.03	
Total						0	10	0	0.00	0.03	0.00

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The annual Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues was held in Geneva, Switzerland, from 18 to 27 September 2007. The FAO Panel of Experts had met in Preparatory Sessions from 13 to 17 September. The Meeting was held in pursuance of recommendations made by previous meetings and accepted by the governing bodies of FAO and WHO that studies should be undertaken jointly by experts to evaluate possible hazards to humans arising from the occurrence of pesticide residues in foods. During the meeting the FAO Panel of Experts was responsible for reviewing pesticide use patterns (good agricultural practices), data on the chemistry and composition of the pesticides and methods of analysis for pesticide residues and for estimating the maximum residue levels that might occur as a result of the use of the pesticides according to good agricultural practices. The WHO Core Assessment Group was responsible for reviewing toxicological and related data and for estimating, where possible and appropriate, acceptable daily intakes (ADIs) and acute reference doses (ARfDs) of the pesticides for humans. This report contains information on ADIs, ARfDs, maximum residue levels, and general principles for the evaluation of pesticides. The recommendations of the Joint Meeting, including further research and information, are proposed for use by Member governments of the respective agencies and other interested parties.

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