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Pesticide residues in food 2003

**Joint FAO/WHO Meeting on
Pesticide Residues**

REPORT 2003

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T- toxicological evaluation; R-residue and analytical aspects

*New compound

** Evaluated within the Periodic Review Programme of the Codex Committee on Pesticide Residues

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ABBREVIATIONS

(Well-known abbreviations in general use are not included)

ADI	acceptable daily intake
AFI(D)	alkali flame-ionization (detector)
ai	active ingredient
AR	applied radioactivity
bw	body weight
CA	Chemical Abstracts
CAC	Codex Alimentarius Commission
CAS	Chemical Abstracts Services
CCN	Codex classification number (for compounds or commodities)
CCPR	Codex Committee on Pesticide Residues
CCRVDF	Codex Committee on Residue of Veterinary Drugs in Food
CI	chemical ionization
CV	coefficient of variation
CXL	Codex Maximum Residue Limit (Codex MRL). See MRL
2,4-D IPE	(2,4-dichlorophenoxy)acetic acid isopropyl ester
DFG	Deutsche Forschungsgemeinschaft
DT ₅₀	time for 50% decomposition (i.e. half-life)
DT ₉₀	time for 90% decomposition
EC	(1) emulsifiable concentrate (2) electron capture
ECD	electron capture detection or detector
EI	electron-impact
EPA	Environmental Protection Agency
F ₁	first filial generation
F ₂	second filial generation
FAO	Food and Agriculture Organization of the United Nations
FDA	Food and Drug Administration
FI(D)	flame-ionization (detector)
FP(D)	flame-photometric (detector)
GAP	good agricultural practice(s)
GC	gas chromatography
GC-MS	gas chromatography – mass spectrometry
GC-MSD	gas chromatography with mass-selective detection
GLC	gas–liquid chromatography
GPC	gel-permeation chromatography
GEMS/Food	Global Environment Monitoring System–Food Contamination Monitoring and Assessment Programme
GLP	good laboratory practice
GPC	gel-permeation chromatograph or chromatography
GSH	glutathione
HPLC	high-performance liquid chromatography
HPLC-MS	high-performance liquid chromatography – mass spectrometry
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
IARC	International Agency for Research on Cancer
IEDI	international estimated daily intake
IESTI	international estimate of short-term dietary intake
IPCS	International Programme on Chemical Safety
ITD	ion-trap detector or detection
JECFA	Joint Expert Committee on Food Additives
JMPR	Joint Meeting on Pesticide Residues
LC	liquid chromatography
LC-MS	liquid chromatography – mass spectrometry
LC ₅₀	median lethal concentration
LD ₅₀	median lethal dose
LOAEL	lowest-observed-adverse-effect level
LOAEC	lowest-observed-adverse-effect concentration
LOD	limit of detection
LOQ	limit of quantification
LSC	liquid scintillation counting or counter
MRL	Maximum Residue Limit. MRLs include <u>draft</u> MRLs and <u>Codex</u> MRLs (CXLs). The MRLs recommended by the JMPR on the basis of its estimates of maximum residue levels enter the Codex procedure as draft MRLs. They become Codex MRLs when they have passed through the procedure and have been adopted by the Codex Alimentarius Commission.
MSD	mass-selective detection or detector
MS/MS	tandem mass spectrometry
NOAEL	no-observed-adverse-effect level
NP(D)	nitrogen–phosphorus (detector)
OECD	Organisation for Economic Co-operation and Development
PF	processing factor
PHI	pre-harvest interval
ppm	parts per million. (Used only with reference to the concentration of a pesticide in a diet. In all other contexts the terms mg/kg or mg/l are used.)
P _{ow}	octanol–water partition coefficient
RAC	raw agricultural commodity
r.d.	relative density (formerly called specific gravity)
RfD	reference dose (usually in phrase “acute RfD”)
RSD	relative standard deviation
SC	suspension concentrate (= flowable concentrate)
SD	standard deviation
SPE	solid-phase extraction
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
t	tonne (metric ton)

TLC	thin-layer chromatography
TRR	total radioactive residue
TMDI	theoretical maximum daily intake
US FDA	US Food and Drug Administration
UV	ultraviolet (radiation)
W	the previous recommendation is withdrawn, or withdrawal of the existing Codex or draft MRL is recommended
WP	wettable powder
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 2003 JOINT FAO/WHO MEETING OF EXPERTS

1. INTRODUCTION

A Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group (JMPR) was held at WHO Headquarters, Geneva (Switzerland) from 15 to 24 September 2003. The Panel Members of FAO and WHO had met in preparatory sessions from 10 to 14 September.

The Meeting was opened by Dr Maged Younes, Senior Adviser, Health and Environment, Department of Protection of the Human Environment, WHO. On behalf of FAO and WHO, Dr Younes thanked the participants for providing their expertise and for the significant time and effort put into this important activity. He noted that on the Meeting agenda there were a number of important issues for consideration, that would result in recommendations to the Codex Committee on Pesticide Residues (CCPR), as well as to Member States.

Dr Younes referred to resolution WHA56.23 of the last World Health Assembly, 2003, which noted that the rise in global distribution of food is linked to an increased need for internationally agreed assessments and guidelines related to food safety and nutrition. The resolution emphasized the lead responsibility of WHO, in collaboration with the FAO, for the provision of sound scientific assessments of food hazards, as a basis for risk management on a national and international level. Dr Younes stressed that this was a clear recognition of the importance and relevance of the work of the JMPR.

Closing remarks were made by Dr Margaret Chan, Director of the Department of Protection of the Human Environment, WHO, who congratulated the participants on a successful Meeting and emphasized the importance of the output of this Meeting, not only for work at the Codex Alimentarius Commission, but also for national public health authorities.

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 Joint Meetings (see Annex 5) contain information on acceptable daily intakes (ADIs), 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 maximum residue levels and supervised trials median residues (STMR) values for commodities of animal origin was elaborated. The WHO Core Assessment Group was responsible for reviewing toxicological and related data and for estimating acceptable daily intakes (ADIs), and if necessary acute reference doses (RfD), where possible.

The Meeting evaluated 23 pesticides, including four new compounds and nine compounds that were re-evaluated within the periodic review programme of the Codex Committee on Pesticide Residues (CCPR) for toxicity or residues, or both.

The Meeting allocated ADIs and acute reference doses (RfDs), 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 devoted particular attention to estimating the dietary intakes (both short-term and long-term) of the pesticides reviewed in relation to their ADIs or acute RfDs. In particular, for compounds undergoing a complete evaluation or re-evaluation, it distinguished between those for which the estimated intake is below the ADI and those for which the intake might exceed the ADI. Footnotes are used to indicate those pesticides for which the available information indicates that the ADI might be exceeded, and footnotes are used to denote specific commodities in which the available information indicates that the acute RfD of the pesticide might be exceeded. A proposal to make this distinction and its rationale 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).

2. GENERAL CONSIDERATIONS

2.1 THE WHO CLASSIFICATION OF PESTICIDES BY HAZARD

“The WHO recommended classification of pesticides by hazard” (IPCS, 2002) is prepared for and refers to “the acute risk to health that might be encountered accidentally by any person handling the product”.

The classification is generally based on the oral and/or dermal LD₅₀ in rats, but exceptions apply (for a complete discussion of the criteria of this classification see Part I of the document).

As such, the criteria guiding and the purpose of this classification are distinct from the considerations and procedures that are required when assessing acute dietary risk, including the derivation of the acute reference dose, when necessary. Consequently, potential confusion might occur between the “WHO classification of pesticides by hazard” and the performance of acute dietary risk assessment. For this reason, the Meeting considered that it was no longer appropriate to include this classification in future JMPR evaluations of the compound under consideration.

2.2 SETTING THE ACUTE REFERENCE DOSE ON THE BASIS OF HAEMATOLOGICAL EFFECTS

The 2001 and 2002 Joint Meetings indicated that haematological effects (e.g. methaemoglobinaemia, haemolytic anaemia) could arise from a single exposure to a chemical and hence such effects may form the basis for an acute reference dose (RfD). The 2003 Meeting set acute RfDs for famoxadone, methoxyfenozide and tebufenozide on the basis of haemolytic anaemia which occurred after repeated dosing. The mechanism by which these compounds cause haemolysis is unknown. Anaemia was accompanied, when measured, by significantly increased (but by <10%) methaemoglobinaemia. There are no data available to indicate that haemolysis caused by these compounds occurred via the formation of methaemoglobin. However, increased methaemoglobin may be a marker of oxidative stress to the erythrocyte, which is a cause of haemolysis.

The Meeting reviewed three compounds, tebufenozide, methoxyfenozide and famoxadone all with low acute oral toxicity (LD₅₀ of >5000 mg/kg in rats). In dogs given a single dose of tebufenozide, no haematological effects were observed at 89 mg/kg bw, the highest dose tested. However, haematological effects occurred in dogs after repeated doses of 5 mg/kg bw per day for 2 weeks. Methoxyfenozide caused minimal haematological effects at a dose of about 200 mg/kg bw per day for 2 weeks, with a clear NOAEL of about 20 mg/kg bw per day. Famoxadone caused mild haematological effects after 30 days (but not after 16 days) of treatment with about 60 mg/kg bw per day.

Together, these data suggest that haematotoxicity would not necessarily be expected to occur after a single dose of these compounds. Therefore, the Meeting recognizes that the setting of acute RfDs for these three compounds is based on conservative assumptions and that refinements of the approach taken by the 2003 Meeting may be possible in the future.

For such refinements, general guidance or a framework on how to perform single dose studies to address endpoints such as methaemoglobinaemia, haematotoxicity and other acute alerts would be useful. Therefore, the 2003 JMPR recommended that WHO establishes a Working Group including scientists who have helped develop the concepts of the acute RfD at JMPR. The Working Group should develop further guidance on how to interpret existing databases, including single-dose studies

and early data from repeated-dose studies, and how to perform single-dose studies in relation to establishing an acute RfD. This guidance will to be submitted for consideration by the 2004 JMPR.

2.3 REVIEW OF PROVISION OF SCIENTIFIC ADVICE

In 2001, the Codex Alimentarius Commission requested that FAO and WHO review the status and procedures of the expert bodies, such as JMPR, and develop recommendations on additional ways to improve the quality, quantity and timeliness of scientific advice to the Commission. The evaluation of Codex Alimentarius, conducted in 2002 considered this to be a matter of urgency. FAO and WHO have initiated a full review of the provision of scientific advice to Codex and Member States via expert committees and ad hoc consultations. This review will take into account ongoing activities to improve working procedures. The evaluation of the JMPR, conducted in 2001, will prove to be an important source of information in this regard. The overall review will be performed through a consultative process that started with an FAO/WHO Planning Meeting in May 2003. A Joint Workshop will be held in January 2004. This Workshop will be preceded by an electronic forum debate on key issues identified by the Planning Meeting. An independent expert consultation will be held in mid 2004 to agree upon recommendations for consideration by FAO and WHO.

2.4 PROJECT TO UPDATE THE PRINCIPLES AND METHODS FOR THE RISK ASSESSMENT OF CHEMICALS IN FOOD

The Meeting recognized the importance of this Project, particularly in view of the evolution of the risk analysis paradigm and the processes used by the JMPR. The Meeting strongly urged the timely completion of this Project and recommended that the Project:

- give clear general principles for risk assessment procedures;
- include guidance for special toxicological considerations, such as the acute RfD;
- give general guidance for analytical methods, including fitness for purpose, sampling, and quality assurance;
- give clear guidance for exposure assessment, including assessment of acute exposures,
- include clear description, with uncertainties, of the process by which maximum residue limits (MRLs) are recommended;
- for residues of pesticides and veterinary drugs, where harmonization of certain risk assessment approaches may not be possible, give clear, transparent justifications for the differences.

2.5 SELECTIVE SURVEYS TO PROVIDE RESIDUE DATA FOR ESTIMATING MAXIMUM RESIDUE LEVELS FOR SPICES

In response to the request of the 34th Session of the CCPR, the 2002 JMPR considered the options for estimating maximum residue levels for spices based on monitoring data (JMPR Report 2002 section 2.7.) and provided guidance on the format for reporting such data. As the 35th Session of the CCPR decided to elaborate MRLs based on monitoring data (Paras 187-200, ALINORM 03/24A, 2003), the present Meeting gave further consideration to possible options for estimating maximum residue levels where sufficient monitoring data are not available and prepared guidelines for conducting selective surveys to generate pesticide residue data reflecting the field and post-harvest application of pesticides.

The information presented to the CCPR or the JMPR indicated that registered or permitted uses of pesticides on specific spices may not be generally available, and farmers may use any pesticides available on the market to protect their spices that they found effective to control pests and diseases on vegetables. In addition, the spices may be indirectly exposed to pesticides which are applied to the main crops.

Post-harvest treatment is usually made on a spice sourced from several fields. The crops on the fields may have been exposed to different pesticides, which may increase the number of pesticide residues derived from pre-harvest applications.

In view of the current practice in growing spice-producing plants it may be necessary to estimate maximum residue levels for pesticides based on general agricultural practice but without established GAP. Therefore information on existing national MRLs for spices, together with registered or authorized uses of pesticides on main crops of fields where spices are grown is important for a comprehensive evaluation of the residue data. National data requirements and methods of evaluation should be included in the data submission where available.

Spices are usually difficult substrates for the determination of trace organic contaminants. Reliable identification of pesticide residues and their quantitative determination in spice samples of unknown origin can be a very laborious and complicated task especially where access to GC-MS and LC-MS-MS techniques is limited. The analysts should, therefore, have as much information as possible on the actual or possible use of pesticides on the spices to be analysed.

In a selective field survey samples are taken from fields where the crop is grown, treated directly or indirectly with pesticides, and harvested according to the local agricultural practice. The essential feature of the selective field survey is that all pesticide applications, the growth stage of the crop and post-harvest treatment of spices are recorded, and the records are attached to the sampling report. Therefore the laboratory can look for all pesticides applied, in addition to organochlorine pesticides which may be taken up from soil.

Since the uses of pesticides are known, the selective survey is a better alternative than monitoring of pesticide residues in samples of unknown origin in cases where there are not enough residue data available from previous work.

Guidelines for conducting selective surveys

- A successful survey requires full co-operation with the growers who should understand that it is conducted for promoting their production and that the correct information is essential for success.
- Sites for survey should be selected to represent the growing conditions of the particular spice. The more information and residue data provided the more realistic the maximum residue level that can be estimated.
- The minimum number of fields surveyed and samples collected depends on the diversity of the growing conditions. As an initial step, the Meeting considered that a minimum of 10 reliable residue results representing the typical growing or processing conditions with supplementary information are required for each spice-pesticide combination.
- In the case of post-harvest application the minimum of 10 samples should be taken from lots treated independently, preferably at different processing plants.

The following details should be reported.

- Person and organization responsible for organizing, supervising and reporting on the selective field survey
- Commodity description with Codex code number if available or classification by the CCPR; (Para 199, ALINORM 03/24A, 2003)

- The typical agricultural practice concerning the use of pesticides, and if available, the registered or permitted uses of pesticides on the plant producing the spice (dosage, number and method of applications, timing of application and growth stage of plant)
- Where the plant is grown between rows of a major crop, the registered or permitted uses of pesticides on the major crop
- Description of growing conditions of the plant producing the spice (e.g. main or intermediate crop), the growth stage at harvest, date of harvest and harvested part of the plant
- The date and method of application, and dosage of pesticides actually applied, for treatments
 - carried out on the fields where the samples are taken directly from the fields, or
 - details of post-harvest application together with information on pre-harvest treatments where available
- Description of the processing of the spice and its storage conditions
- Storage conditions of samples until analysis
- Portion of sample analysed
- Performance parameters of the method (LOQ, mean recovery and its CV at various fortification levels), methods of detection and confirmation of residues
- Residues of ai and metabolites (mg/kg) found in the samples.

Results should be tabulated as shown below.

Crop/spice

Pesticide application			Date of		Analysis			
ai ¹	kg ai/ha kg ai/hl	Date(s)	Harvest	Sampling	Date	Residues mg/kg		Method

¹ indicate whether the application was direct or indirect.

Since the estimation of maximum residue levels based on monitoring and survey data is a new approach it may be necessary to revise the requirements for residue data and reported information, taking into account the experience gained with the evaluation of the submissions.

2.6 EXPRESSION OF MRLS FOR FAT-SOLUBLE PESTICIDES IN MILK AND MILK PRODUCTS

At the 35th (2003) Session of the CCPR, concern was expressed at the very low MRLs proposed for some fat-soluble pesticides (e.g. diphenylamine, chlorpropham) in milk. The JMPR was requested to take into account the LOQs achievable in practice. The specific issue of diphenylamine is considered separately in this Report.

The fat content of milk varies widely. In addition, there are many milk products with varying fat contents and it would be difficult to propose separate MRLs for each of them. It was therefore originally decided to estimate MRLs for fat-soluble compounds in milk and milk products on a fat basis, i.e. on the residue levels expressed as if wholly contained in the fat. This simple system was satisfactory for very fat-soluble persistent organochlorine pesticides because it allowed the MRLs for milk to be extrapolated to all milk products, irrespective of fat content.

Currently the JMPR follows the Codex convention of expressing the MRLs for fat-soluble compounds in milks on a calculated whole-product basis, assuming all milks to contain 4% fat (FAO/WHO, 2000)¹. The residue concentration is calculated for the whole product on the basis of the concentration measured in the fat. The MRL would be 1/25th of the residue concentration estimated for the milk fat. For a milk product with a fat content below 2%, the MRL is half that specified for milk. Fat-soluble pesticides to which these general provisions apply are indicated by the letter “F” in conjunction with the MRL specified for milk. MRLs for pesticides which are of low solubility in fat are estimated on a whole milk basis and do not have the suffix “F”.

However, many pesticides are of intermediate fat-solubility and, even though regarded as fat-soluble, may be distributed between the fat and aqueous phases of the milk. For example, if the ratio of the residue concentration between the fat and aqueous phases is 15:1 in milk with 4% fat, the ratio of the total residue in the two phases is about 2:3, meaning that most of the residue remains in the aqueous phase. To comply with the Codex convention, MRLs for such less fat-soluble pesticides have the same basis as those for water-soluble pesticides and do not have the suffix “F”.

The Meeting recognized that the current methods for deriving and expressing MRLs for milk may appear to be complex and cause problems for the CCPR and enforcement authorities. An example of such a problem was the decision of the 1995 CCPR to delete the suffix “F” from MRLs set at the LOQ (ALINORM 95/24A, paragraph 180). Contrary to the intention of the JMPR in recommending such MRLs, the CCPR decision implied that analysis for compliance testing must be conducted on whole milk and that the same MRL value is then applied to both milk and milk products.

The JMPR decides whether or not an MRL for a fat-soluble compound in milk should have the suffix “F” by considering the following characteristics of the compound(s) that are covered by the definition of the residue: (i) the log P_{ow} , (ii) the solubility in fatty animal tissues, and (iii) the distribution between the fat and non-fat fractions of the milk, where available.

The rationale for recommending an MRL for a fat-soluble pesticide with the suffix “F” is illustrated with fenvalerate/esfenvalerate as an example.

The log P_{ow} of 6.2 and the animal metabolism studies indicated that fenvalerate/esfenvalerate should be described as soluble in body fat, and almost all the residue was found to partition into the fat of milk. The JMPR therefore concluded that fenvalerate/esfenvalerate residues should be described as fat-soluble and recommended an MRL in milk of 0.1 mg/kg F.

¹ FAO/WHO 2000: Codex Alimentarius Volume 2B, Pesticide Residues in Food – Maximum residue limits. Joint FAO/WHO Food Standards Programme, page 4. Rome, 2000.

The rationale for recommending an MRL for a fat-soluble pesticide without the suffix “F” can be illustrated by using spinosad as an example.

The log P_{ow} values of 4 and 4.5 for spinosyns A and D, together with the animal metabolism studies, indicated that spinosad was soluble in body fat. However spinosad residues were incompletely partitioned into the fat of milk. In a study of the treatment of dairy cows, the ratio of the residue level in cream to that in milk was 4.2 (mean of 119 observations). In a dairy cow feeding study, residue levels in cream were 3-5 times that in the milk. The JMPR concluded that spinosad should be described as fat-soluble for the purpose of measuring residues in meat but that it should not be treated as fat-soluble for the measurement of residues in milk, and therefore noted that the residue is fat-soluble but residues in milk should be measured on the whole milk. The MRL recommended for cattle milk was 1 mg/kg (without the suffix “F”).

The Meeting drew attention to the requirements for testing compliance with MRLs. Where the suffix “F” is appended, the separated and extracted milk fat is analysed; where there is no suffix, the whole milk is analysed. For the determination of recoveries, milk fat or whole milk is fortified, depending on the presence or absence of the suffix “F”.

To apply an MRL for milk which has the suffix “F” to milk products, the MRL for milk is multiplied by 25 and the resultant value applies to the fat extracted from the milk product. The residue in the milk fat is determined and neither the MRL nor the analytical result is adjusted for the fat content of the milk product. To apply an MRL for milk which does *not* have the suffix “F” to milk products, the MRL is used without change and the whole product is analysed to determine compliance with the MRL. The two procedures are not influenced by whether the MRL is at the LOQ or at some higher value.

2.7 REFINEMENT OF THE ESTIMATIONS OF MAXIMUM RESIDUE LEVELS FOR PROCESSED COMMODITIES

During recent years, many relevant processing studies have been provided to the JMPR. These are normally conducted according to national authority requirements and simulate commercial practices. Whenever possible, a processing factor (PF) is calculated and residues in the processed commodity estimated by multiplying the estimates in the raw commodity by the PF.

The JMPR has been working to increase the transparency of the evaluation process, improve the quality of the estimations and harmonize the procedures at international level. The Meeting agreed to outline the procedures for estimating maximum residue levels, STMR-Ps and HR-Ps for processed commodities which have been applied previously and/or refined at this Meeting.

Maximum residue levels. Until now, a maximum residue level in a processed commodity was derived by applying the calculated processing factor to the maximum residue level estimated for the raw commodity, and the resulting number was rounded up to the closest value from the scale of numerical values adopted by the JMPR in 2001¹. The maximum residue level in the raw commodity is, however, already a rounded-up level.

The procedure of rounding up residue values twice to achieve an estimate is not scientifically justified, and the Meeting agreed that the maximum residue level in processed commodities should be derived directly from the highest residue found in the supervised trial.

¹ Pesticide residues – Submission and evaluation of pesticide residues data for the estimation of maximum residue levels in food and feed, FAO Plant Production and Protection Paper 170, p.64

Maximum residue levels will only be estimated for processed commodities in which the residue is concentrated during the processing procedure (PF >1) and for which there is an existing Codex commodity code. When the PF is <1, the MRL in the raw commodity applies also to the processed commodity (Maximum limits for processed or ready-to-eat foods and feed, ALINORM 03/24A, 2003). Estimates of STMR-Ps and HR-Ps will be made whenever necessary, regardless of whether the PF is higher or lower than 1.

Processing factor. The processing factor is defined as the ratio of the residue found in the processed commodity to the residue in the raw commodity before processing. In many cases, the processed commodity does not have quantifiable residues (<LOQ), and the calculated processing factor will be below a certain value (PF <0.01, for example). Although the real processing factor cannot be calculated, the Meeting generally estimates the residue in the processed commodity from the limiting value (PF = 0.01). In cases where residues are not detected in the raw commodity, a processing factor cannot be calculated and estimates in processed commodities cannot be made.

HR-P and STMR-P estimates. An HR-P will only be estimated when it is needed for the calculation of an International Estimated Short-Term Intake (IESTI), that is for commodities covered by Case 1 or Case 2 as defined in Section 3 of this Report.

HR-Ps and/or STMR-Ps for commodities for human consumption will be estimated regardless of the availability of consumption data.

2.8 DEVELOPMENT OF AUTOMATED SPREADSHEET APPLICATIONS FOR THE CALCULATION OF DIETARY INTAKE

The Meeting agreed to adopt automated spreadsheet applications for the calculation of dietary intake in order to harmonize and facilitate the process. The spreadsheet applications were constructed by RIVM/SIR¹, The Netherlands, in co-operation with WHO/GEMS/Food and incorporated all available consumption data² in Excel spreadsheets. The data were linked as closely as possible to the Codex Commodities for which MRLs, HR(-P)s and STMR(-P)s have been estimated. The spreadsheets are used to calculate IEDIs and IESTIs using the formulae described in Section 3 of this Report. To use the spreadsheets, estimates made by the JMPR of ADIs, acute RfDs, STMR(-P)s, HR(-P)s, and when necessary MRLs, are entered according to the instructions attached to the templates. Calculations and the generation of a final table are then performed automatically. The present Meeting used the spreadsheet applications for the first time and welcomed the resulting reduction of the workload.

The spreadsheet applications are available on the internet at the address http://www.who.int/foodsafety/publication/chem/regional_diets and will be updated when necessary.

2.9 IMPROVING ESTIMATES OF DIETARY INTAKE

The Meeting considered the areas where the estimations of dietary intake could be improved. It was concluded that the calculations are greatly simplified by the automated spreadsheet applications

¹ National Institute for Public Health and the Environment (RIVM); Centre for Substances and Integrated Risk Assessment (SIR)

² *Long-term intake:* WHO 1998. GEMS/Food Regional Diets. Regional per capita consumption of raw and semi-processed agricultural commodities. Food Safety Unit. WHO/FSF/FOS/98.3, Rev. 1 (revised September 2003), Geneva: *Acute intake:* http://www.who.int/foodsafety/chem/acute_data. Dataset 1 (large portion sizes), GEMS/Food, revised January 1, 2003. Dataset 2 (body weights), GEMS/Food, revised January 1, 2003. Dataset 3 (unit weights), GEMS/Food, revised February 5, 2003

elaborated by RIVM/SIR¹, The Netherlands, in co-operation with WHO/GEMS/Food. However the calculated values cannot be better than the data-base or estimated factors used. For many Codex commodities for which maximum residue levels, STMR(-P)s and HR(-P)s are estimated, no dietary intake is available. Consequently, immediate refinements could be achieved by:

- improving the accuracy of consumption figures for long-term exposure by introducing the proposed 13 sub-regional diets which have been discussed in recent years by the CCPR and JMPR instead of the currently used five regional diets;
- the increased availability of large portion sizes and unit weights for the calculation of short-term exposure, especially those from developing countries.

Further improvement could be obtained by:

- evaluation of the studies submitted to the JMPR in the last decade representing typical commercial processing to investigate whether it would be possible to derive default processing factors and/or extrapolate processing data;
- refinement of generic and commodity-specific variability factors as used in the short-term intake calculations;
- elaboration of procedures for probabilistic modelling at the international level.

The last two points are discussed further below.

The 35th Session of the CCPR (ALINORM 03/24A, paras 20-31) discussed the paper “Discussion paper on the proposals for improvement methodology for point estimates” [of acute intake of pesticide residues] (CX/PR 03/3). The Report of the Session (para 28) states “The Chair summarized the discussion that: (1) the possibility of accepting limited exceedance should not be considered at present time; (2) the possibility of using a tiered approach could be considered in the future; and (3) JMPR should be asked to mention the probabilistic aspects in the point estimates, when the results exceed the acute RfD.”

The Committee also requested the JMPR to consider this paper especially in relation to the use of probabilistic aspects of point estimates.

The Committee also agreed to establish a Working Group to prepare a paper on the possible adoption of probabilistic methodology for the purpose of setting Codex MRLs. This should include worked examples of probabilistic calculations for some compounds, using supervised trials data, where the IESTI exceeds the acute RfD. The Working Group should also discuss and propose parameters to be used in probabilistic calculations at the international level, and the paper should be considered by the next Session of the Committee.

In response, the Meeting agreed in principle to adopt a tiered (i.e. sequential) approach to estimating short-term dietary intake, in which the second tier could be probabilistic modelling. However it also recognized the lack of consumption data and the lack of an available model validated at the international level, which hamper the development of such a second tier. It observed that a possible solution would be to ask the country from which the large portion as used in the JMPR point estimate came, to provide the second tier. However, this would necessitate international consensus on the parameters used in the probabilistic model. The Meeting therefore welcomed the initiative of the CCPR in deciding to establish a Working Group on this subject. The Meeting noted that a

¹ National Institute for Public Health and the Environment (RIVM); Centre for Substances and Integrated Risk Assessment (SIR)

probabilistic model useful for JMPR purposes is under development in The Netherlands (RIKILT, Institute of Food Safety) and agreed that it would consider this model when available.

The Meeting took note of the IUPAC report on short-term dietary risk assessment¹ and on the basis of the evidence presented there agreed to use in future a new default variability factor of 3 in the calculation of residue levels in high-residue units used in point estimates of short-term intake. See also Item 2.10.

In the situation that the IESTI exceeds the acute RfD, the Meeting agreed to indicate in the section on Dietary Risk Assessment ways in which those parameters used in the dietary risk assessments which are based on conservative assumptions might be refined.

2.10 IESTI CALCULATION: REFINING THE VARIABILITY FACTOR FOR ESTIMATION OF RESIDUE LEVELS IN HIGH-RESIDUE UNITS

Current JMPR procedures for estimating the short-term dietary intake of pesticide residues rely on the deterministic procedures proposed by the FAO/WHO Consultation in 1997².

The Consultation proposed methods for calculating short-term intake (1) where the residue in a composite sample reflects the residue level in a meal-sized portion of the commodity, and (2) where the meal-sized portion such as a single unit of fruit might have a higher residue than the composite. The concept of the variability factor was introduced to calculate the residue level in that single unit, originally with the conservative assumption that all of the residue might be in one unit of the composite sample. For fruit such as apples the variability factor was 10 because 10 apples were expected in a typical composite sample.

The 1999 JMPR³ summarized the methods for calculating the short-term intake of residues and reported the results of such calculations for the first time. The 1999 Meeting, taking into account the available data, used a variability factor of 7 for most items (>25 g and <250 g), a value of 5 for large items (>250 g) and a value of 10 for granular soil treatments and leafy vegetables.

The 2002 JMPR, on the basis of new data, concluded that a variability factor of 3 would be suitable for residues in head lettuce and head cabbage.

At the 35th Session of the CCPR (Paras 20-31, ALINORM 03/24A, 2003) the delegation of The Netherlands introduced a discussion paper on improved methodology for point estimates of dietary exposure in relation to setting MRLs. An unpublished IUPAC report on short-term dietary risk assessment had been used in the preparation of the paper. The CCPR agreed to establish a Working Group to prepare a paper considering the adoption of probabilistic methodology for the purpose of setting Codex MRLs. The same Session also requested the JMPR to consider possible improvements in the point estimates.

¹ Hamilton D, Ambrus A, Dieterle R, Felsot A, Harris C, Petersen B, Racke K, Wong S, Gonzalez R, Tanaka K, Earl M, Roberts G and Bhula, R. 2003. Pesticide residues in food – acute dietary exposure. Submitted for publication.

² WHO, Food consumption and exposure assessment of chemicals. *Report of a FAO/WHO Consultation, Geneva, Switzerland, 10-14 Feb, 1997*. Document WHO/FSF/FOS/97.5 (1997)

³ FAO. Dietary risk assessment for pesticide residues in food, in *Pesticide residues in food – Report 1999*. FAO *Plant Production and Protection Paper* 153:21-25 (1999).

The IUPAC report¹, now submitted for publication, summarized and analysed the available data on residue level variability from unit to unit for a number of pesticides over a range of crops (apples, carrots, celery, grapes, kiwifruit, lettuce and potatoes).

In cases where the number of unit analyses was large enough to provide 95% assurance that at least one value exceeded the 97.5th percentile, the average variability factor (97.5th percentile value of residue ÷ mean) was 2.7 (range 1.5-7.2) for supervised trials involving approximately 8000 unit analyses. The average variability factor was 3.0 (range 2.4-3.5) for market-place monitoring data involving almost 3000 unit analyses. Most of the estimated variability factors were in the 2.0-3.0 range for the 30 sets of data representing trials and market-place monitoring.

The variability factor did not generally seem to be dependent on the pesticide or the crop. However in one trial with a post-harvest application of a mixture of 3 compounds on apples there appeared to be a separation of the compounds during the post-treatment drainage of the fruit, with one of the compounds producing substantially higher residues in fruit at the bottom of the stack. Variability factors for the three compounds were 7.2, 2.8 and 2.5. In this instance the variability factor was dependent on the pesticide in combination with the method of treatment.

The Meeting agreed to adopt a default variability factor of 3 for the estimation of residue levels in high-residue units in the IESTI calculations where unit weights exceed 25 g. A variability factor is not used in IESTI calculations where unit weights are below 25 g.

The current practice will continue of using specific unit variability factors in preference to the default value where the supporting data are available, valid and sufficient.

2.11 REVISED DATA REQUIREMENTS FOR STUDIES OF ENVIRONMENTAL FATE

The 2003 CCPR considered a proposal to reduce the range of environmental fate studies to be reviewed by the JMPR (CX/PR 03/18, Agenda Item 18). The Committee agreed that the JMPR "... should proceed with the consideration of environmental fate but should focus on those aspects that were most relevant to MRL setting" and that the current data requirements should be revised accordingly (ALINORM 03/24A, para 212). The matter was also referred to the Codex Alimentarius Commission (CAC). The CAC concurred with the CCPR recommendation. (CAC, July 2003, Rome).

The current aspects of the environmental fate of residues required for elucidation, as outlined in the *FAO manual on the submission and evaluation of pesticide residues data for the estimation of maximum residue levels in food and feed*, Food and Agriculture Organization of the United Nations, Rome, 2002, Second edition, are as follows.

- Physical and chemical properties
- Metabolism and degradation in soil
- Persistence in soil under aerobic and anaerobic conditions
- Mobility of the parent compound and its transformation products in soil
- Adsorption by various soil types
- Hydrolysis rate and products
- Photolysis on soil and plant surfaces
- Crop uptake and bioavailability of parent compound and its major degradation products
- Residues in rotational crops
- Soil dissipation
- Residue degradation and disposition in water-sediment systems

¹ Hamilton D, Ambrus A, Dieterle R, Felsot A, Harris C, Petersen B, Racke K, Wong S, Gonzalez R, Tanaka K, Earl M, Roberts G and Bhula, R. 2003. Pesticide residues in food – acute dietary exposure. Submitted for publication.

The Meeting reviewed the various types of environmental fate studies as related to the process of estimating residues in commodities and concluded that some of the studies do not assist significantly in defining the residue of concern or estimating residue levels. The recommendations of the Meeting for future submissions of data on environmental fate are summarized in the Table below. It should be noted that the studies required are in some cases dependent upon the use pattern (soil, foliar, seed treatment) and that paddy rice presents a unique situation.

The Meeting adopted these revised criteria for its considerations during the 2003 Meeting and will use them in future deliberations. The Meeting proposed to incorporate these changes into the next revision of the FAO Manual.

Requirements for submission of data on environmental fate for the JMPR.

Type of study	Type of use and requirement (yes/no/conditional)						Comments
	Foliar	Soil	Plants of root, tuber, bulb, or peanut (at/after pegging)	Seed dressing (including seed potato)	Herbicide (for weeds in crop)	Paddy rice	
Physical and chemical properties	Conditional	Conditional	Conditional	Conditional	Conditional	Conditional	Only to the extent not provided for the technical material, e.g. hydrolysis and photolysis.
Degradation in soil (aerobic)	No	Yes	Yes	Yes	Yes	No	May be part of confined rotational crop.
Degradation in soil (anaerobic)	No	No	No	No	No	No	
Persistence in soil	No	No	No	No	No	No	
Mobility/leaching in soil	No	No	No	No	No	No	
Adsorption by soil types	No	No	No	No	No	No	
Hydrolysis rate and products	Yes	Yes	Yes	Yes	Yes	Yes	Hydrolysis in sterile aqueous buffers. Abiotic epimerization should be provided as appropriate (e.g. pyrethroids)
Photolysis-plant surface	Conditional	No	See foliar	No	No	See foliar	Plant metabolism may suffice. Needed for special cases (e.g., abamectin)
Photolysis-natural pond water	No	No	No	No	No	Conditional	Plant metabolism may be adequate for rice. Useful for GAP involving application to water surface.
Crop uptake and bioavailability (see rotational crops)	No	No	No	No	No	No	

Type of study	Type of use and requirement (yes/no/conditional)						Comments
	Foliar	Soil	Plants of root, tuber, bulb, or peanut (at/after pegging)	Seed dressing (including seed potato)	Herbicide (for weeds in crop)	Paddy rice	
Rotational crops-confined	Yes	Yes	Yes	Yes	Yes	No	Not required where no crop rotation (e.g. orchard crops). Soil and crop should be analysed for radiolabelled residues.
Rotational crops-field	Conditional	Conditional	Conditional	Conditional	Conditional	No	Requirement conditional on results of confined rotational crop study.
Residue degradation in water-sediment systems	No	No	No	No	No	Conditional	Metabolism study for paddy rice may be adequate. In other cases, metabolism/degradation needed, e.g. application to pond water.

2.12 PILOT PROJECT ON WORKSHARING

The revised proposal for the FAO/WHO pilot project on worksharing for the JMPR was presented according to the recommendation of the OECD Working Group on Pesticides (WPG) Registration Steering Group (RSG) meeting in March 2003. The proposal was originally presented at the November 2002 RSG meeting with the intention of parallel review by the OECD countries and the JMPR.

The pilot project proposal was revised to facilitate the use of national and other international evaluations of pesticide residues and toxicology by the JMPR. The worksharing process will be used only for new compounds in the pilot phase.

For residue reviews, worksharing will include studies or information on identity, physical and chemical properties, metabolism, environmental fate in soil and water-sediment systems (see Section 2.11 analytical methods (specialized methods used in the analysis of samples and enforcement methods), stability of pesticide residues in stored analytical samples, extraction efficiency of residue analytical methods (using radiolabelled compounds), stability during cold storage (for diverse crop samples, and for animal tissues, milk, and eggs when MRLs are needed for animal commodities) definition of the residue and fate of residues during processing (if appropriate to the crops treated).

For toxicology reviews, all data evaluations that can be released by national governments will be considered in the worksharing process. The process will include comparison of similarities and differences between decisions on selection of endpoints, acceptability of studies, and degree of documentation in the study reviews.

Criteria for worksharing include the availability of the experts involved in the national and international reviews for consultation, and of complete toxicology and residue chemistry study reports.

The 2003 CCPR selected trifloxystrobin as the first compound for the worksharing pilot project, as it has been evaluated in Australia, Canada, the USA and the EC and is scheduled for evaluation by the 2004 JMPR.

The CCPR and the OECD-WGP/RSG will be regularly informed of the progress of the pilot project on worksharing. The project will be evaluated in terms of the harmonization and acceleration of pesticide residue evaluation at national and international levels.

The Meeting acknowledged that at present national assessments are already being extensively used; the worksharing project intends to facilitate and formalize this practice.

2.13 IMPLEMENTATION OF THE RECOMMENDATIONS OF THE YORK WORKSHOP AND THE ZONING REPORT

The York Workshop of September 1999 on “Developing Minimum Data Requirements for Estimating MRLs and Import Tolerances” and the previous preparatory meetings in York in 1998 and 1999 aimed to facilitate international harmonization of data requirements for setting MRLs and import tolerances, which would also provide guidance to the JMPR in estimating maximum residue levels.

Four important areas were identified during the Workshop which required harmonization: (1) criteria for determining the minimum number of trials, (2) extrapolation of data on residues in one crop to support an MRL for a related crop, (3) processing studies, and d) global zoning. Among these only the zoning issue was pursued as it was considered the least harmonized among the issues mentioned.

At its 32nd Session the CCPR decided to refer the recommendations of the York Workshop to the 2002 JMPR. The JMPR had in fact already been using the recommendations of the York meeting whenever possible. However, some of the recommendations of the York report would need further information before their full utilization. For example, the number of trials was to be based on significance in the diet and in trade and on the number of zones in which the crop was grown, but the criteria for significance or insignificance in trade were not elaborated and the zones were not identified. FAO and the OECD undertook to address the impact of climatic zones on pesticide residues and produced the “Zoning Report”, which concluded that the impact of climate on the residues of some pesticides applied to certain crops is negligible, and residue data derived from similar use patterns (GAP) and growing conditions may be compared regardless of the geographical location of the trials. In 2002 the JMPR expressed the hope that the York meeting report would be finalized and would be made available for consideration by the JMPR.

The OECD Working Group on Pesticides adopted the Zoning Report and the report of the York Workshop at its meeting in November 2002 (ENV/JM/PEST/2002/15). The European Commission indicated an interest in following up the recommendations of the Zoning Report as it could facilitate the establishment of MRLs.

The Meeting reviewed the Zoning Report and the York Report and agreed to start applying their recommendations. However, practical experience would be necessary to see how the recommendations could be implemented in the work of the JMPR, e.g. a change in the data requirements to allow the global comparison of residue data might be necessary. Hence the JMPR would like to test the practical applicability of the principles with one pesticide in 2004 and requested FAO to initiate the process and to identify a compound suitable for the pilot project.

2.14 SUBMISSION OF ADDITIONAL DATA FOR EVALUATION OF PESTICIDE RESIDUES

The data and information required for JMPR evaluations are discussed in detail in the 3rd Chapter of the FAO Manual, with special sections on the reconsideration of previous recommendations (p. 32) and the evaluation of additional information (p. 45). In 2002 the Joint FAO Secretary to the JMPR issued a letter giving specific guidance for data submitters to facilitate the selection and submission of appropriate data.

The Manual emphasized that the submission of additional data and/or information should always be accompanied by a clear statement of the reason for it and for the suggestions or requests for changes.

The Meeting continues to receive supplementary data and information without an indication of the specific purpose for its provision. It is therefore re-emphasized that the submitter must explain clearly why the data or information was submitted, with reference to JMPR or CCPR Reports. This will be a pre-condition for scheduling the evaluation of the submitted material and will be used by the FAO Joint Secretary in presenting the rationale for the evaluation.

The Meeting reconfirmed that the evaluation of the results of additional metabolism studies, and of supervised trials revealing information on the proportions of the parent compound and significant metabolites can only be carried out at the time of a periodic review when all relevant information is available and taken into consideration in deciding on the definition of the residue.

The Meeting draws attention to the fact that trials conducted with analytical methods having lower LOQ values or reflecting the residues derived from new GAP, together with corresponding residue data, can be used for decreasing an existing MRL only under specific conditions. For instance if the critical GAP on which the current JMPR recommendation was based had been changed, or sufficient residue data reflecting the uses according to the current GAP in countries where the original trials were conducted are available with the more sensitive new method. Otherwise, the manufacturer or company supporting the use of the compound should keep the reports of these trials until the periodic review of the compound and then provide all relevant information for evaluation, regardless of whether it had been submitted earlier or not.

When the intention is to change a CXL the request should be addressed to the CCPR; other matters should be addressed to the FAO Joint Secretary to the JMPR.

3. DIETARY RISK ASSESSMENT FOR PESTICIDE RESIDUES IN FOOD

Assessment of risk from long-term dietary intake

Risks associated with long-term dietary intake were assessed for compounds for which MRLs were recommended and STMRs estimated at the present Meeting. Dietary intakes were calculated by multiplying the concentrations of residues (STMRs, STMR-Ps or recommended MRLs) by the average daily *per caput* consumption estimated for each commodity on the basis of the GEMS/Food diet^{1,2,3}. Theoretical maximum daily intakes (TMDIs) were calculated when only recommended or existing MRLs were available, international estimated daily intakes (IEDIs) were derived when STMR or STMR-P values could be used. Dietary intakes were estimated from combinations of recommended MRLs and STMR or STMR-P values. Codex MRLs that have been recommended by the JMPR for withdrawal were not included in the estimations.

Long-term dietary intakes are expressed as a percentage of the ADI for a 60-kg person, with the exception of the intake calculated for the Far East, in which a body weight of 55 kg is used⁴. The estimates are summarized in Table 1. Percentages up to and including 100% are rounded to one significant figure and values above 100% to two significant figures. Percentages above 100 should not necessarily be interpreted as giving rise to a health concern because of the conservative assumptions used in the assessments. The detailed calculations of long-term dietary intakes are given in Annex 3.

The dietary intake of thiophanate-methyl was considered together with carbendazim, as the compound is determined as carbendazim, which also has the lower ADI.

Malathion and phosmet were considered by the Meeting only for the assessment of the acute RfD. Risk assessments of long-term dietary intake for these compounds were considered by previous meetings (1999 for malathion and 2002 for phosmet).

The evaluation of parathion-methyl considered only nectarines, which were included with peaches in the assessment of the 2000 JMPR.

No new recommendations were made for diphenylamine, which was last evaluated by the 2001 JMPR.

Estimates for residues of carbofuran arising from the use of carbosulfan made at this Meeting do not affect the assessment conducted by the 2002 JMPR for this compound.

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 residues¹.

Table 1. Summary of long-term dietary of risk assessments conducted by the 2003 JMPR.

Compound		ADI (mg/kg bw)	Intake range (% of maximum ADI)	Type of assessment
CCPR code	Name			
0095	Acephate	0-0.01	2-20	IEDI
0072	Carbendazim	0-0.03	1-4	IEDI
0145	Carbosulfan	0-0.01	0-1	IEDI
0207	Cyprodinil	0-0.03	0-10	IEDI
0083	Dicloran	0-0.01	0-30	IEDI
0027	Dimethoate	0-0.002	10-150	IEDI
0084	Dodine	0-0.2	0-2	IEDI
0208	Famoxadone	0-0.006	1-7	IEDI
0037	Fenitrothion	0-0.005	120-640	IEDI
0048	Lindane	0-0.005	0-1	IEDI

Compound		ADI (mg/kg bw)	Intake range (% of maximum ADI)	Type of assessment
CCPR code	Name			
0100	Methamidophos	0-0.004	0-9	IEDI
0209	Methoxyfenozide	0-0.1	0-9	IEDI
0057	Paraquat	0-0.005	20-140	TMDI
0086	Pirimiphos-methyl	0-0.03	10-50	IEDI
0063	Pyrethrins	0-0.04	1	IEDI
0196	Tebufenozide	0-0.02	1-20	IEDI
0167	Terbufos	0-0.0006	10-40	TMDI
0162	Tolylfluanid	0-0.08	0-4	IEDI

Assessment of risk from short-term dietary intake

Risks associated with short-term dietary intake were assessed for compounds for which STMR and HR values were estimated at the present Meeting and for which acute reference doses (acute RfDs) had been established, in commodities for which data on consumption were available. The procedures for calculating the short-term intake were defined primarily in 1997 at an FAO/WHO Geneva Consultation², refined at the International Conference on Pesticide Residues Variability and Acute Dietary Risk Assessment sponsored by the Pesticide Safety Directorate⁵ 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, 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 www.who.int/foodsafety/chem/acute data. The documents are dated 01/01/2003 (large portions and body weights) and 05/02/2003 (unit weights).

International estimated short-term intake (IESTI)

Depending on the data on consumption, the IESTI for each commodity is calculated from the equation defined for each case, as shown below. The following definitions apply to all equations.

LP	highest large portion provided (97.5th percentile of eaters), in kg of food per day
HR	highest residue in composite sample of edible portion found in supervised trials from which the MRL or STMR was derived, in mg/kg
HR-P	highest residue in the processed commodity, in mg/kg, calculated by multiplying the HR in the raw commodity by the processing factor
bw	body weight, in kg, provided by the country for which the large portion, LP, was used
U	unit weight in edible portion, in kg, provided by the country in the region where the trials which gave the highest residue were carried out; calculated allowing for the per cent edible portion
v	variability factor
STMR	supervised trials median residue, in mg/kg
STMR-P	supervised trials median residue in processed commodity, in mg/kg

Case 1

The concentration of residue in a composite sample (raw or processed) reflects that in a meal-sized portion of the commodity (unit weight is < 25 g). This case also applies to meat, liver, kidney, edible offal and eggs, and for grains, oil seed and pulses when the estimate of the HR or HR-P was based on post-harvest use of the pesticide.

$$\text{IESTI} = \frac{\text{LP} * (\text{HR or HR-P})}{\text{Bw}}$$

Case 2

The meal-sized portion, such as a single piece of fruit or vegetable, might have a higher residue than the composite (unit weight of the whole portion is > 25 g). A default variability factor of 3 is applied in the equations (see Section 2.10). When sufficient data are available on residues in single units to calculate a more realistic variability factor for a commodity, the calculated value replaces the default value.

When data are available on residues in a single unit allowing estimation of the highest residue in a single unit, this value should be used in the first term in the numerator of the equation for case 2a, with no variability factor. The HR value derived from data on composite samples should be used in the second term. For case 2b, the estimated highest residue in a single unit should be used in the equation with no variability factor.

Case 2a

The unit weight of the whole portion is lower than that of the large portion, LP.

$$\text{IESTI} = \frac{\text{U} * (\text{HR or HR-P}) * v + (\text{LP-U}) * (\text{HR or HR-P})}{\text{bw}}$$

Case 2b

The unit weight of the whole portion is higher than that of the large portion, LP.

$$\text{IESTI} = \frac{\text{LP} * (\text{HR or HR-P}) * v}{\text{bw}}$$

Case 3

When a processed commodity is bulked or blended, the STMR-P value represents the probable highest residue. This case also applies to milk, and to grains, oil seed and pulses when the estimate of the STMR or STMR-P was based on pre-harvest use of the pesticide.

$$\text{IESTI} = \frac{\text{LP} * \text{STMR-P}}{\text{bw}}$$

A risk assessment for short-term dietary intake was conducted for each commodity–compound combination by assessing the IESTI as a percentage of the acute RfD. When the maximum residue level was estimated for a Codex commodity group (e.g. citrus fruits), intakes were calculated for individual commodities within the group. The selected commodities should include the one(s) that would lead to the highest intake.

The Meeting concluded that acute RfDs might be necessary for pirimiphos-methyl, carbendazim and thiophanate-methyl, but these have not yet been established. The Meeting

recommended that these compounds should be evaluated for the establishment of acute RfDs in the near future.

Acute RfDs were established for pyraclostrobin, terbufos and paraquat, but short-term intakes were not calculated as information on STMRs and HRs was not available for these compounds.

On the basis of data received by the present Meeting, the establishment of an acute RfD for cyprodinil was considered to be unnecessary. The 1998 JMPR concluded that an acute RfD was unnecessary for dicloran. The intake of these compounds was therefore not estimated.

The short-term intakes as percentages of the acute RfDs for the general population and for children are summarized in Table 2. They are rounded to one significant figure for values up to and including 100%, to two significant figures for values above 100%. Percentages above 100 should not necessarily be interpreted as giving rise to a health concern because of the conservative assumptions used in the assessments. The detailed calculations of short-term dietary intakes are given in Annex 4.

Table 2. Summary of short-term dietary risk assessments conducted by the 2003 JMPR.

Compound		Acute RfD (mg/kg bw)	Commodity	Percentage of acute RfD	
CCPR code	Name			General population	Children ≤6 years
0095	Acephate	0.003	Apple	260	630
			Beans, except broad bean	60	130
			Broccoli	100	190
			Cauliflower	140	210
			Mandarin	140	400
			Nectarine	80	170
			Peach	100	170
			Pear	140	340
			Peppers, Chili	60	110
			Peppers, Sweet	200	220
			Other commodities	0-50	0-20
0145	Carbosulfan	0.02	All commodities	0-2	0-4
0096	Carbofuran ¹	0.009	Potato, Maize	0-20	0-50
0027	Dimethoate	0.02	Cabbages	320	760
			Lettuce, Head	130	200
			Peppers, Sweet	90	140
			Other commodities	0-90	1-90
0084	Dodine	0.2	All commodities	6-30	20-80
0208	Famoxadone	0.6	All commodities	0-3	0-8
0037	Fenitrothion	0.04	Maize	80	160
			Rice, husked	120	240
			Rice, polished	150	240
			Other commodities	1-30	2-80
0048	Lindane	0.06	All commodities	0	0
0049	Malathion	2	All commodities	0-2	0-7
0049	Methamidophos	0.01	Apple	60	140
			Broccoli	60	110
			Cabbages	120	290
			Cauliflower	80	120
			Peppers, Sweet	140	150
			Tomato	150	410
			Other commodities	0-80	0-90
			0209	Methoxyfenozide	0.9
			Other commodities	0-10	0-30
0059	Parathion-methyl	0.03	Nectarine	9	20
0103	Phosmet	0.2	Apple	90	230
			Pear	60	150
			Other commodities	4-40	10-100

Compound		Acute RfD (mg/kg bw)	Commodity	Percentage of acute RfD	
CCPR code	Name			General population	Children ≤6 years
0063	Pyrethrins	0.2	All commodities	0-2	0-5
0196	Tebufenozide	0.9	All commodities	0-10	0-40
0162	Tolylfluanid	0.5	Lettuce, Head	20	40

¹ from the use of carbosulfan

Refinement of the short-term dietary risk assessment

In view of the default variability factor of 3 which the Meeting agreed to use for the calculation of Case 2 IESTIs (Section 2.10), the Meeting revised all the assessments conducted since 1999 for commodity-compound combinations for which the acute RfD had been exceeded. The results of this process are shown in Table 3. They are rounded to one significant figure for values up to and including 100%, to two significant figures for values above 100% and to 3 significant figures for values above 1000%. Percentages above 100 should not necessarily be interpreted as giving rise to a health concern because of the conservative assumptions used in the assessments. The detailed calculations of short-term dietary intake are given in Annex 4.

Table 3. Summary of short-term dietary of risk assessments conducted by the 2003 Jmpr for compounds considered previously, using a variability factor of 3.

Compound		Acute RfD (mg/kg bw)	Year of assessment	Commodity	Percentage of acute RfD	
CCPR code	Name				General population	Children ≤6 years
0008	Carbaryl	0.2	2002	Apricot, Peach, Plums	30-60	80-100
				Cherries	50	130
				Grapes	460	1210
				Nectarine	50	110
0015	Chloromequat	0.05	2000	Pear	170	400
0201	Chlorpropham	0.03	2001	Potato	1080	2680
				Potato, cooked	360	890
				Potato, cooked and peeled	9	20
0135	Deltamethrin	0.05	2002	Chinese cabbage, Spinach	30-50	60-80
0106	Ethephon	0.05	2002	Cantaloupe, Sweet peppers, Pineapple, Tomato	20-40	50-90
0085	Fenamiphos	0.003	2002	Carrot	40	90
				Grapes	60	160
				Peppers, Sweet	100	110
				Pineapple	80	190
				Tomato	110	310
0094	Methomyl	0.02	2001	Apple	200	500
				Broccoli	490	920
				Brussels sprouts	180	350
				Cabbages, Head	550	1300
				Cauliflower	410	1030
				Grapes	480	1020
				Lettuce, Head	1230	1850
				Lettuce, Leaf	300	750
				Spinach	2600	8010
				Sweet corn	70	210
				Oranges, Tomato, Watermelon	<100	40-90
0126	Oxamyl	0.009	2002	Apple	330	830
				Cucumber	80	170
				Grapefruit	510	790
				Lemon	90	330

Compound		Acute RfD (mg/kg bw)	Year of assessment	Commodity	Percentage of acute RfD	
CCPR code	Name				General population	Children ≤6 years
				Mandarin	280	840
				Melons, except Watermelons	110	320
				Oranges, Sweet, Sour	260	1050
				Peppers, Sweet	310	450
				Tomato	110	300
0058	Parathion	0.01	2000	Apple	40	90

¹ WHO (1997) Guidelines for predicting dietary intake of pesticide residues. 2nd revised edition, GEMS/Food Document WHO/FSF/FOS/97.7, Geneva

² WHO (1997) Food consumption and exposure assessment of chemicals. Report of a FAO/WHO Consultation. Geneva, Switzerland, 10-14 February 1997, Geneva

³ WHO (1998). GEMS/FOOD Regional Diets. Food Safety Issues. WHO/FSF/98.3. Geneva

⁴ Codex Alimentarius Commission, 1997, CX/PR 98/5

⁵ Pesticide Safety Directorate 1998. Pesticide Residues Variability and Acute Dietary Risk Assessment. York

4. EVALUATION OF DATA FOR ACCEPTABLE DAILY INTAKE (ADI) FOR HUMANS, MAXIMUM RESIDUE LEVELS AND SUPERVISED TRIALS MEDIAN RESIDUES (STMRS)

4.1 ACEPHATE (095)

RESIDUE AND ANALYTICAL ASPECTS

Acephate has been evaluated several times, first in 1976 and most recently in 1996. It was listed under the Periodic Review Programme by the 28th Session of the CCPR for residue review by the 2003 JMPR (ALINORM 97/24). The 2002 JMPR established an ADI and acute RfD for acephate of 0-0.01 mg/kg bw and 0.05 mg/kg bw respectively. The present Meeting received information on the metabolism and environmental fate of acephate, methods of residue analysis, freezer storage stability, national registered use patterns, supervised residue trials and national MRLs.

Some information on GAP, national MRLs and residue data was reported by the governments of Australia, Germany and The Netherlands.

Acephate is a broad-spectrum organophosphorus insecticide with uses on many crops.

The following abbreviations are used for the metabolites discussed below.

DMPT: *O,S*-dimethyl *O*-hydrogen phosphorothioate

SMPT: *S*-methyl *O*-hydrogen acetylphosphoramidothioate

OMAPAA: methyl hydrogen acetylphosphoramidate

SMPAA: *S*-methyl *O*-hydrogen phosphoramidothioate

Animal metabolism

Studies on lactating goats, quail and laying hens were reported to the present Meeting.

In the three goat studies when [*S*-methyl-¹⁴C]acephate either alone or in combination with [*S*-methyl-¹⁴C]methamidophos and/or with [carbonyl-¹⁴C]acephate was used, most of the ¹⁴C in the tissues was incorporated into natural products: proteins and amino acids in liver, kidney, muscle and milk, lipids in fat and milk, and lactose in milk. Acephate constituted a maximum of 47% of the ¹⁴C in the milk. 18-20 h after the last dose of [*S*-methyl-¹⁴C]acephate or [carbonyl-¹⁴C]acephate, the parent compound accounted for 4.2-4.8%, 14-26% and 22-26% of the ¹⁴C in the liver, kidney and muscle respectively but was not detected in the fat.

Only traces of acephate were detected in the tissues of quail 3 days after dosing with [*S*-methyl-¹⁴C]acephate, which is consistent with other observations that the metabolism of acephate is rapid. Acephate was a major component of the residue in egg whites and yolks, muscle and fat (maximum of 64% of the radiolabel in muscle, 62% in egg whites, 33% in yolks and 26% in the fat from laying hens dosed with [*S*-methyl-¹⁴C]- and [carbonyl-¹⁴C]acephate. Incorporation into lipids and proteins accounted for most of the ¹⁴C in yolk, liver and fat.

The metabolism of acephate proceeds by the hydrolysis of the ester/thioester and amide moieties to form SMPT, OMAPAA and methamidophos. Liberated carbon fragments enter the metabolic pool and are incorporated into natural products, principally proteins and lipids and, in the case of milk, lactose.

Plant metabolism

Studies on bean, cabbage and tomato seedlings, and on lettuce, cotton and bean plants were reported.

Acephate was the major component of the extracted ^{14}C residue in bean, cabbage and tomato seedlings treated by either foliar application or stem injection with [*S*-methyl- ^{14}C]acephate. Small amounts of methamidophos were also detected. Residues of acephate are translocated and the pesticide is considered to be systemic.

20 days after the third foliar application to lettuce of [*S*-methyl- ^{14}C]acephate and [carbonyl- ^{14}C]acephate, the parent compound was the main identified component (45-53%) of the extracted ^{14}C residue, and the metabolites were methamidophos (11%), SMPT (11-15%) and a metabolite tentatively identified as OMAPAA (29%). Similar results were obtained with beans harvested 14 days after three foliar applications of acephate with the same labels: acephate accounted for 62-74% of the ^{14}C in the forage and 14-15% in the beans, and the metabolites were methamidophos (7.3-7.7% of the TRR), SMPT (6.5-14%) and OMAPAA (23-57%). Most of the remaining ^{14}C was distributed in natural products (starch, protein, pectin, hemicellulose, cellulose).

In cotton harvested 21 days after three foliar applications of the same labels as above, ^{14}C residues in the trash were predominantly acephate (40-41%) with smaller amounts of SMPT (17-29%) and OMAPAA (1-27%). Methamidophos was only a minor metabolite (<2% of the TRR). In contrast, acephate represented a relatively small fraction of the ^{14}C in cotton seed meal and hulls (0.8-7.3%). OMAPAA (1-24% in hulls, 1-22% in meal) was the main metabolite with smaller amounts of SMPT (1-4.2%). Most of the ^{14}C in cotton seed was incorporated into natural products.

In plants, acephate is metabolized by ester/thioester and amide hydrolysis reactions to form methamidophos, SMPT and OMAPAA as the main metabolites. Further metabolism results in the incorporation of acephate-derived fragments into natural plant products.

Environmental fate in soil

Information was provided on the soil adsorption of acephate and on its behaviour or fate during soil and solution photolysis, aerobic and anaerobic degradation in soil, column leaching of aged residues and field dissipation.

Acephate does not undergo significant direct photolysis on soil surfaces. In aqueous solution it is stable to hydrolysis except at high pH. At pH 9 about 40% of the initial ^{14}C was present as acephate after 23 days.

The aerobic soil degradation of acephate was rapid with half-lives of ≤ 7 days. The main route of degradation appears to be microbial metabolism as only minimal degradation occurred in sterile soils and the degradation rate generally increased with both soil organic matter and moisture contents. The major degradation products were methamidophos, OMAPAA, DMPT, SMPT and SMPAA.

In field dissipation, the residues of acephate did not move down the soil profile and dissipation was rapid with half-lives of less than 3 days for both acephate and methamidophos.

In summary, acephate is not significantly degraded by hydrolysis, except in waters having high pH values. Photochemical transformation is expected to be a minor route of degradation. Degradation in field and in aquatic environments is rapid and acephate is not expected to persist in the environment.

Analytical methods

Samples in the field trials were analysed for acephate and methamidophos by solvent extraction (ethyl acetate or in the case of oily crops and fats acetonitrile/hexane), clean-up by solvent partition and/or silica column or gel permeation chromatography followed by GLC measurement with an FPD (phosphorus mode), NPD (nitrogen mode), thermionic or ion-selective MS detection. LOQs of 0.01-0.02 mg/kg for acephate and 0.01 mg/kg for methamidophos were reported for numerous commodities.

Stability of pesticide residues in stored analytical samples

The available data indicate that the combined residues of acephate and methamidophos are stable during frozen storage at -20°C in or on eggs for 6 months; cattle meat and milk for 7 months, or cattle kidney for 6 months; goat liver for 3 months; apple for 16 months; apple sauce and juice for 55 days; pinto beans for 15 months; snap beans for 15 months; Brussels sprouts for 9 months; celery for 12 months; maize grain and silage for 7 months; maize meal, flour and presscake for 2 months; cotton seed for 48 days; Bermuda grass forage and hay for 2 months; pasture grass for 9 months; lettuce for 17 months; pigeon peas for 14 months; bell peppers for 13 months; rice grain and straw for 17 months, and spearmint fresh and spent hay for 2 months.

Field-incurred residues were stable in tomato juice and purée and canned tomatoes when stored at ambient temperature (not specified) for up to 3 months.

Definition of the residue

A main metabolite of acephate in or on crops is methamidophos, which is a pesticide in its own right with its own MRLs. Analytical methods used for acephate can distinguish between acephate and methamidophos (i.e. they are not common moiety methods). Residues of methamidophos arising from the use of acephate must be reconciled with an MRL for compliance purposes. This could be achieved either by defining the residue of acephate as the sum of acephate and methamidophos or by establishing specific methamidophos MRLs for methamidophos residues arising from the use of acephate. In national systems the definition of the residue for acephate is generally acephate *per se*, and methamidophos residues resulting from the use of acephate are accounted for by separate MRLs.

For the estimation of dietary intake it is necessary to account for the residues of both acephate and methamidophos, and their relative toxicity must be taken into account. A conservative approach is to sum the residues after scaling the methamidophos residues for “potency” based on the ratio of the acephate to methamidophos maximum ADIs for STMR estimates and acute RfDs for HR estimates. The ratios are based on mass and do not require correction for molecular weight.

For acephate STMR estimation, residue = acephate + (2.5 x methamidophos)

For acephate HR estimation, residue = acephate + (5 x methamidophos)

The FAO Manual (page 51) states that “preferably no compound, metabolite or analyte should appear in more than one residue definition”. The Meeting agreed that the acephate residue should be defined as acephate.

The log P_{ow} for acephate is -0.9 and this together with the animal metabolism and feeding studies indicates that acephate should not be classified as fat-soluble.

Definition of acephate residue

for compliance with MRLs: acephate

for estimation of dietary intake: acephate and methamidophos

The definitions apply to both plant and animal commodities.

Supervised trials

When evaluation of the supervised trial data leads to an estimated maximum residue level for acephate, it is also necessary to ensure that residues of methamidophos arising from the use of acephate are covered by a maximum residue level for methamidophos. As methamidophos is also under periodic review by the current Meeting residues of methamidophos arising from the use of acephate will be considered together with those from uses of methamidophos *per se* in the methamidophos sections of the report and the evaluations.

Supervised trials were reported on alfalfa, apples, artichokes, beans, broccoli, Brussels sprouts, cabbage, cauliflower, citrus fruits (grapefruit, lemons, oranges, mandarins), cotton, cucumbers, egg plants, hops, leeks, lettuce, peaches, pears, peppers, plums, potatoes, soya beans, sugar beet and tomatoes.

No information on trials or GAP was reported for tree tomatoes (current CXL 0.5 mg/kg) and the Meeting recommended withdrawal of the CXL.

As acephate residues in crops decrease relatively slowly the number of applications has a significant influence on the final residue. To account for the influence of multiple sprays, the Meeting decided that when an upper limit on the number of sprays was not specified by GAP, 2-3 applications would be the minimum number acceptable for estimating a maximum residue level.

In some cases untreated control samples contained residues of acephate and methamidophos. Trials were considered acceptable providing the residues in control samples were less than 10% of the residues in the treated crop.

Citrus fruits

Trials on citrus fruits were conducted in Argentina (no GAP), Brazil (GAP 0.039 kg ai/ha, PHI 21 days), Greece (no GAP), Japan (GAP 0.5-2.5 kg ai/ha, 0.03-0.06 kg ai/ha, PHI 30 days), New Zealand (GAP 0.078 kg ai/ha, PHI 14 days), South Africa (no GAP) and the USA (GAP 0.56-0.84 kg ai/ha to non-bearing trees).

Data were reported from supervised trials on grapefruit, lemons, mandarins, Natsudaidai and oranges, but only those on mandarins and Natsudaidai were conducted according to GAP.

In two trials in Japan on Natsudaidai residues of acephate were 0.1 and 3.0 mg/kg (0.01 and 0.33 mg/kg for methamidophos). The Meeting decided that this was not sufficient to estimate a maximum residue level. Fourteen trials in Japan on mandarins that approximated Japanese GAP showed acephate residues of 0.38, 0.4, 0.49, 0.68, 0.78, 0.85, 0.88, 0.98, 1.7, 1.7, 1.8, 1.8, 2.6 and 5.2 mg/kg, and methamidophos residues of 0.02, 0.03, 0.04, 0.05, 0.06, 0.08, 0.08, 0.09, 0.09, 0.1, 0.14, 0.15, 0.25 and 0.26 mg/kg. In a single trial in New Zealand on mandarins conducted according to GAP in that country the residue of acephate was 3.3 mg/kg and of methamidophos 0.29 mg/kg.

The residues of acephate and methamidophos, combined as explained above, for the purpose of estimating the STMR were 0.43, 0.48, 0.64, 0.78, 0.91, 1.1, 1.1, 1.2, 1.9, 2.1, 2.1, 2.2, 3.2 and 5.9 mg/kg on a whole fruit basis. The HR for dietary intake purposes is estimated to be 6.5 mg/kg.

The Meeting estimated a maximum residue level, STMR and HR for acephate in mandarins of 7, 1.15 and 6.5 mg/kg, all based on whole fruit as insufficient information was available to estimate residues in the edible portion.

Methamidophos residues in mandarins (0.02, 0.03, 0.04, 0.05, 0.06, 0.08, 0.08, 0.09, 0.09, 0.13, 0.14, 0.15, 0.25 and 0.26 mg/kg) are considered in the appraisal of methamidophos for the estimation of maximum residue levels.

Pome fruits

Trials on apples were conducted in Denmark (no GAP), France (GAP 0.06 kg ai/hl, PHI 21 days), Germany (no GAP), Greece (GAP 0.075 kg ai/hl, PHI 15 days), Italy (GAP 0.034-0.064 kg ai/hl, PHI 30 days), The Netherlands (no GAP), Spain (GAP apples 1.1 kg ai/ha, 0.075 kg ai/hl, PHI 14 days, pome fruit 0.038-0.11 kg ai/hl, PHI 21 days), Switzerland (no GAP), the USA (no GAP) and Yugoslavia (no GAP). Trials in The Netherlands and Germany were evaluated according to GAP in France.

In two trials in France which approximated French GAP residues of acephate were 3.7 and 4.2 mg/kg (methamidophos 0.22 and 0.28 mg/kg), and in two trials in The Netherlands and three in Germany, all matching French GAP, residues of acephate were 0.65, 1.5, 2.8, 3.2 and 3.6 mg/kg (methamidophos 0.04, 0.06, 0.13, 0.14 and 0.16 mg/kg). One trial in Italy (0.56 mg/kg, methamidophos <0.1 mg/kg) and two in Greece (0.35, 0.39 mg/kg, methamidophos 0.03, 0.04 mg/kg) complied with the GAP of the respective countries.

The Meeting considered that the residues of acephate on apples were all from the same population and that the data should be combined for estimating a maximum residue level and STMR. The residues of acephate in apples from trials according to GAP (n=10) were 0.35, 0.39, 0.56, 0.65, 1.5, 2.8, 3.2, 3.6, 3.7 and 4.2 mg/kg.

Trials on pears were conducted in France (GAP 0.06 kg ai/hl, PHI 21 days), Italy (GAP 0.034-0.064 kg ai/hl, PHI 30 days), South Africa (GAP 0.038 kg ai/hl, PHI 30 days) and Spain (GAP pears 1.2 kg ai/ha, 0.075 kg ai/hl, PHI 21 days, pome fruit 0.038-0.11 kg ai/hl, PHI 21 days).

In one trial in Italy and two in Spain conducted according to the GAP of those countries acephate residues were 0.26, 0.28 and 0.55 mg/kg, with methamidophos residues of 0.03, 0.06 and <0.1 mg/kg.

The Meeting agreed to combine the data for the residues of acephate on apples and pears to estimate a maximum residue level and STMR. The residues from trials according to GAP (n=13) were 0.26, 0.28, 0.35, 0.39, 0.55, 0.56, 0.65, 1.5, 2.8, 3.2, 3.6, 3.7 and 4.2 mg/kg.

The appropriately scaled and totalled residues of acephate and methamidophos for estimating the STMR (median underlined) were 0.34, 0.44, 0.45, 0.53, 0.7, 0.75, 0.81, 1.7, 3.1, 3.6, 4.1, 4.3 and 4.8 mg/kg. The HR is estimated to be 5.4 mg/kg.

The Meeting estimated a maximum residue level, STMR and HR for acephate in pome fruits of 7, 0.81 and 5.4 mg/kg.

Methamidophos residues in apples and pears from the use of acephate (n=13) were <0.1, <0.1, 0.03, 0.03, 0.04, 0.04, 0.06, 0.06, 0.13, 0.14, 0.16, 0.22 and 0.28 mg/kg and are further considered in the methamidophos section of the report.

Stone fruits

Trials on peaches were conducted in France (GAP 0.06 kg ai/hl, PHI 21 days), Greece (GAP 0.038-0.075 kg ai/hl, PHI 15 days), Italy (GAP 0.034-0.064 kg ai/hl, PHI 21 days) and Spain (GAP peaches 2.8 kg ai/ha, 0.075 kg ai/hl, PHI 21 days, stone fruit 0.038-0.11 kg ai/hl, PHI 21 days).

In one trial in Italy and one in Spain conducted approximately according to Spanish GAP residues were <0.02 and 0.1 mg/kg (methamidophos 0.02 and 0.03 mg/kg).

Two peach trials each in Greece, Spain and France, conducting according to GAP in Greece, gave acephate residues of 0.46, 0.46, 0.63, 1.0, 1.4 and 1.4 mg/kg (methamidophos residues 0.09, 0.1, 0.16, 0.22, 0.28 and 0.35 mg/kg).

The appropriately adjusted and totalled residues of acephate and methamidophos for estimating the STMR (median underlined) were 0.69, 0.71, 1.0, 1.7, 2.0 and 2.3 mg/kg. The HR is 3.2 mg/kg.

The Meeting considered that the residues of acephate and methamidophos in peaches and nectarines treated at the same rate would be similar and noted that GAP in Greece was for stone fruit which includes both peaches and nectarines. The Meeting estimated maximum residue level, STMR and HR values of 2, 1.35 and 3.2 mg/kg respectively for acephate in peaches and nectarines.

Residues of methamidophos in peaches from the use of acephate were 0.09, 0.1, 0.16, 0.22, 0.28 and 0.35 mg/kg. These residues are considered in the appraisal of methamidophos for the estimation of maximum residue levels.

Trials on plums were conducted in France (no GAP), Germany (no GAP), Italy (GAP 0.034-0.064 kg ai/hl, PHI 21 days), South Africa (GAP 0.038 kg ai/hl, PHI 28 days) and the UK (no GAP).

In a single trial in South Africa conducted according to South African GAP for plums residues were 0.08 mg/kg (acephate) and <0.02 mg/kg (methamidophos).

The Meeting considered that a single trial on plums was inadequate to estimate a maximum residue level.

Leeks. Trials on leeks were conducted in France (no GAP), Germany (no GAP) and The Netherlands (no GAP). As no GAP was available the trials were not evaluated further.

Brassica vegetables

Trials on broccoli were reported from Australia (GAP 0.78-0.98 kg ai/ha, 0.075-0.098 kg ai/hl, PHI 14 days), Brazil (GAP 0.075 kg ai/hl, PHI 14 days), Canada (no GAP but cauliflower 0.56-0.83 kg ai/ha, PHI 28 days), France (no GAP), Japan (GAP 0.075-0.5 kg ai/ha, PHI 14 days), Spain (GAP 1.1 kg ai/ha, 0.11 kg ai/hl, PHI 14 days) and the USA (no GAP but cauliflower 0.56-1.3 kg ai/ha, PHI 14 days).

A single trial on broccoli in Australia complied with Australian GAP and showed a residue of 0.12 mg/kg (methamidophos 0.08 mg/kg). One trial in Brazil matched the GAP of that country, with an acephate residue of 0.2 mg/kg. Two trials in France and two in Spain assessed against the GAP of Spain showed residues of 0.05, 0.30, 0.34 and 1.2 mg/kg (methamidophos 0.03, 0.09, 0.10 and 0.33 mg/kg).

Trials on cauliflower were reported from Australia (GAP 0.78-0.98 kg ai/ha, 0.075-0.098 kg ai/hl, PHI 3 days), Brazil (GAP 0.075 kg ai/hl, PHI 14 days), France (no GAP), Germany (no GAP),

Italy (GAP 0.034-0.064 kg ai/hl, PHI 21 days) and The Netherlands (GAP 0.75 kg ai/ha, PHI 14 days).

One trial conducted according to GAP for cauliflower was reported from Australia (1.4 mg/kg acephate, 0.20 mg/kg methamidophos), and one from Brazil (0.1 mg/kg acephate) matched the GAP of that country.

In eight trials in The Netherlands conducted according to GAP acephate residues were <0.01, 0.02, 0.03, 0.06, 0.07, 0.08, 0.1, and 0.11 mg/kg, with methamidophos residues <0.01 (5), 0.01 (2) and 0.03 mg/kg.

Because acephate is a systemic pesticide the Meeting decided that the residue data for broccoli and cauliflower could be used as mutual support for the estimation of a maximum residue level for flowerhead brassicas. The results of the trials on broccoli and cauliflower in rank order (n=16) were <0.01, 0.02, 0.03, 0.05, 0.06, 0.07, 0.08, 0.1, 0.1, 0.11, 0.12, 0.2, 0.3, 0.34, 1.2 and 1.4 mg/kg (methamidophos <0.01(5), 0.01(2), 0.03(2), 0.08, 0.09, 0.10, 0.2 and 0.33 mg/kg).

The calculated total residues of acephate and methamidophos for estimating the STMR (median underlined) were <0.05, <0.06, <0.09, <0.1, 0.11, 0.13, 0.13, 0.19, 0.32, 0.53, 0.59, 1.9, 1.9 and 2.0 mg/kg. The HR is 2.85 mg/kg. The Meeting estimated a maximum residue level, STMR and HR of 2, 0.16 and 2.85 mg/kg respectively for flowerhead brassicas.

Residues of methamidophos in broccoli and cauliflower arising from the use of acephate (n=14) were <0.01 (5), 0.01 (2), 0.03 (2), 0.08, 0.09, 0.10, 0.2 and 0.33 mg/kg. They are considered in the appraisal of methamidophos for the estimation of a maximum residue level.

Trials on Brussels sprouts were reported from Australia (GAP 0.75-0.98 kg ai/ha, 0.075-0.098 kg ai/hl, PHI 3 days), Belgium (no GAP), Germany (no GAP), The Netherlands (GAP 0.75 kg ai/ha, PHI 28 days), South Africa (no GAP), the UK (no GAP) and the USA (GAP 0.56-1.3 kg ai/ha, maximum 2.2 kg ai/ha/season, PHI 14 days).

Two trials on Brussels sprouts in Australia matched GAP with residues of 1.5 and 12 mg/kg (methamidophos 0.11 and 1.0 mg/kg).

Trials on head cabbage were reported from Australia (GAP 0.78-0.98 kg ai/ha, 0.075-0.098 kg ai/hl, PHI 3 days), Brazil (GAP 0.075 kg ai/hl, PHI 14 days), Canada (GAP 0.56-0.83 kg ai/ha, PHI 28 days), France (GAP 0.075 kg ai/hl, PHI 7 days), Germany (no GAP), Japan (GAP 0.3-1 kg ai/ha, 0.03-0.05 kg ai/hl, PHI 7 days), The Netherlands (GAP 0.75 kg ai/ha, PHI 14 days), South Africa (GAP 0.23-0.38 kg ai/ha, PHI 3 days), the UK (no GAP) and the USA (no GAP).

One trial according to GAP for cabbage was conducted in Australia (22 and 1.5 mg/kg for acephate and methamidophos respectively). In two trials in France complying with GAP residues of acephate were 0.06 and 0.87 mg/kg (methamidophos <0.01 and 0.09 mg/kg).

The Meeting considered the number of trials on Brussels sprouts and cabbage that complied with GAP were inadequate for estimating a maximum residue level and recommended withdrawal of the existing CXL of 2 mg/kg for head cabbage.

Cucumbers. Trials were reported from France (no GAP), Italy (GAP 0.034-0.064 kg ai/hl, PHI 21 days), Puerto Rico (no GAP), Spain (GAP 1.7 kg ai/ha, 0.038-0.11, PHI 21 days) and the USA (no GAP).

Acephate residues in 2 indoor trials in Italy matching the GAP (\pm 30%) of Spain were 0.14 and 0.31 mg/kg (methamidophos <0.05 and 0.07 mg/kg). One field trial in Spain (acephate 1.9 mg/kg,

methamidophos 0.19 mg/kg) also matched GAP in that country. The Meeting considered the number of trials inadequate to estimate a maximum residue level for cucumber.

Egg plant. Trials were reported from France (no GAP), Italy (GAP 0.034-0.064 kg ai/hl, PHI 21 days) and Spain (GAP 0.038-0.11 kg ai/hl, PHI 14 days).

Acephate residues in 3 trials in France and Spain matching the GAP ($\pm 30\%$) of Spain were 0.09, 0.22 and 0.51 mg/kg (methamidophos 0.01, 0.05 and 0.07 mg/kg). The Meeting considered the number of trials inadequate to estimate a maximum residue level for egg plant.

Tomatoes. Trials were reported from Australia (GAP 0.75-0.98 kg ai/ha, 0.075-0.098 kg ai/hl, PHI 3 days), Brazil (GAP 0.075 kg ai/hl, PHI 7 days), Canada (seedling drench), France (GAP 0.075 kg ai/hl, PHI 3 days), Italy (GAP 0.034-0.064 kg ai/hl, PHI 21 days), Japan (GAP 0.5-1.0 kg ai/ha, 0.025-0.05 kg ai/hl, PHI 1 day), Spain (GAP 0.038-0.11 kg ai/hl, PHI 14 days) and the USA (no GAP).

Acephate is registered in Spain for use on tomatoes at 0.11 kg ai/hl with harvest permitted 14 days after the last application. In three trials in Spain matching GAP acephate residues were 0.05, 0.08 and 0.18 mg/kg (0.03, 0.05 and 0.11 mg/kg for methamidophos); in one trial in France and two in Italy also matching Spanish GAP $\pm 30\%$ residues were 0.08, 0.14 and 0.33 mg/kg (methamidophos 0.03, 0.05 and 0.15 mg/kg), in a single trial in Brazil according to GAP <0.05 mg/kg and in a single trial in Australia also according to GAP 1.8 mg/kg (0.5 mg/kg methamidophos). The Meeting considered that the trials in Brazil and Australia were in different residue populations from those in France, Italy and Spain and should not be combined to estimate a maximum residue level. Residues of acephate in tomatoes in rank order (n=6) were 0.05, 0.08, 0.08, 0.14, 0.18 and 0.33 mg/kg. The Meeting considered the database to be insufficient to estimate a maximum residue level for tomatoes and recommended withdrawal of the existing CXL of 1 mg/kg.

Peppers. Trials were reported from Canada (GAP sweet peppers, 0.83 kg ai/ha, PHI 7 days), France (no GAP), Italy (GAP 0.034-0.064 kg ai/hl, PHI 21 days), Spain (GAP 2.25 kg ai/ha, 0.038-0.11 kg ai/hl, PHI 14 days) and the USA (GAP bell peppers 0.28-1.3 kg ai/ha, maximum 2.2 kg ai/ha/season, PHI 7 days; non-bell, 0.56 kg ai/ha, maximum 1.1 kg ai/ha/season, PHI 7 days).

In one trial in Canada on sweet peppers according to Canadian GAP acephate residues were 3.7 mg/kg (methamidophos 1.6 mg/kg). Acephate residues in two trials in Italy and one in Spain (indoor crop) approximating the GAP of Spain were 0.84, 1.1 and 2.9 mg/kg (methamidophos 0.25, 0.25 and 0.29 mg/kg), in three trials in Spain approximating the GAP of Italy 0.03, 1.5 and 2.2 mg/kg (0.05, 0.24 and 0.34 mg/kg for methamidophos) in crops grown indoors, and in two trials in France (one indoor) according to GAP in Italy 0.34 mg/kg indoor (0.22 mg/kg methamidophos) and 1.0 mg/kg in the field (0.35 mg/kg methamidophos).

Residues of acephate in indoor-grown sweet peppers (n=5) were 0.03, 0.34, 1.5, 2.2 and 2.9 mg/kg (methamidophos 0.05, 0.22, 0.24, 0.25 and 0.34 mg/kg), and in field-grown (n=4) 0.84, 1.0, 1.1 and 3.7 mg/kg (methamidophos 0.25, 0.29, 0.35 and 1.6 mg/kg).

The Meeting considered the residues in indoor and field sweet peppers could be combined for the purposes of estimating a maximum residue level. Residues in sweet peppers in rank order, median underlined, (n=9) were 0.03, 0.34, 0.84, 1.0, 1.1, 1.5, 2.2, 2.9 and 3.7 mg/kg. The appropriately scaled and totalled residues of acephate and methamidophos for estimating the STMR (median underlined) were 0.16, 0.89, 1.6, 1.7, 1.9, 2.1, 3.1, 3.5 and 7.7 mg/kg. The HR is 11.7 mg/kg. The Meeting estimated a maximum residue level, STMR and HR for acephate in peppers of 5 mg/kg, 1.9 mg/kg and 11.7 mg/kg respectively.

Methamidophos residues were 0.05, 0.22, 0.24, 0.25, 0.25, 0.29, 0.34, 0.35 and 1.6 mg/kg and are considered in the appraisal of methamidophos for the estimation of maximum residue levels.

Lettuce. Trials were reported from Belgium (no GAP), Canada (GAP head lettuce, 0.56-0.83 kg ai/ha, PHI 7 days), France (GAP 0.075 kg ai/hl, PHI 14 days) and Germany (no GAP).

In one trial in Canada and two in France approximating national GAP acephate residues in head lettuce were 0.28, 0.67 and 1.1 mg/kg respectively (methamidophos 0.03, 0.06 and 0.09 mg/kg). The Meeting considered the number of trials inadequate to estimate a maximum residue level and recommended withdrawal of the existing CXL of 5 mg/kg for head lettuce.

Beans. Field trials on common beans (snap, green and French) were reported from Canada (no GAP), France (no GAP), Germany (no GAP), Italy (GAP green beans 0.034-0.064 kg ai/hl, PHI 21 days), Spain (GAP 1.1 kg ai/ha, 0.11 kg ai/hl, maximum 2 sprays, PHI 14 days) and the USA (GAP 0.28-1.3 kg ai/ha, maximum 2.2 kg ai/ha/season, PHI 14 days).

Acephate residues in green (French) beans in 2 trials in Italy (0.92 and 0.96 mg/kg) and five in Spain (0.06, 0.07, 0.72, 1.2 and 2.9 mg/kg) approximating the GAP of Spain were 0.06, 0.07, 0.72, 0.92, 0.96, 1.2 and 2.9 mg/kg (methamidophos 0.01, 0.04, 0.15, 0.19, 0.34, 0.45 and 0.54 mg/kg).

Acephate residues in green (snap) beans in a single trial in the USA approximating US GAP were 0.39 mg/kg (methamidophos 0.15 mg/kg).

Residues of acephate in green beans in rank order (n=8) were 0.06, 0.07, 0.39, 0.72, 0.92, 0.96, 1.2 and 2.9 mg/kg. The appropriately scaled and totalled residues of acephate and methamidophos for estimating the STMR (median underlined) were 0.1, 0.11, 0.77, 1.3, 1.4, 1.8, 2.1 and 4.3 mg/kg. The calculated HR is 5.6 mg/kg. The Meeting estimated a maximum residue level, STMR and HR for acephate in beans, except broad bean and soya bean, of 5 mg/kg, 1.35 mg/kg and 5.6 mg/kg respectively.

Residues of methamidophos in beans in rank order, median underlined, (n=8) were 0.01, 0.04, 0.15, 0.15, 0.19, 0.34, 0.45 and 0.54 mg/kg. These residues are considered in the appraisal of methamidophos for the estimation of maximum residue levels.

Beans (dry). Field trials were reported from the USA on dry beans, including lima beans, red kidney beans and Navy beans but none of these were conducted according to GAP and the trials were not considered further.

Soya beans. Field trials were reported from the USA and assessed against the GAP of Mexico (0.5-1.1 kg ai/ha, PHI 14 days). Acephate residues in seven trials approximating GAP were <0.02, <0.02, 0.03, 0.03, 0.03, 0.14 and 0.17 mg/kg (methamidophos <0.01, <0.01, <0.01, <0.01, 0.02, 0.06 and 0.06 mg/kg).

Residues of acephate and methamidophos adjusted and totalled for estimating the STMR and HR (median underlined) were 0.045, 0.045, 0.055, 0.055, 0.08, 0.29 and 0.32 mg/kg. The HR is 0.47 mg/kg. The Meeting estimated a maximum residue level, STMR and HR for acephate in soya bean (dry) of 0.3 mg/kg, 0.055 mg/kg and 0.47 mg/kg respectively. The maximum residue level is recommended to replace the existing CXL of 0.5 mg/kg for soya bean (dry).

Residues of methamidophos in soya beans in rank order, median underlined, (n=7) were <0.01, <0.01, <0.01, <0.01, 0.02, 0.06 and 0.06 mg/kg. These residues are considered in the appraisal of methamidophos for the estimation of maximum residue levels.

Potatoes. Field trials were reported from Canada (GAP 0.56-0.83 kg ai/ha, PHI 21 days), France (no GAP), Italy (GAP 0.34-0.63 kg ai/ha, PHI 21 days), the UK (no GAP) and the USA (no GAP).

In one trial in France approximating the GAP of Italy acephate residues in potatoes were <0.02 mg/kg (methamidophos <0.01 mg/kg). The Meeting considered that one trial was inadequate to

estimate a maximum residue level for potatoes and recommended the withdrawal of the existing CXL (0.5 mg/kg).

Sugar beet. Field trials were reported from France (GAP 0.5 kg ai/ha, PHI 21 days), Italy (GAP 0.34-0.63 kg ai/ha, PHI 21 days) and the UK (no GAP). As none of the trials matched GAP they were not evaluated further. The Meeting recommended the withdrawal of the existing CXLs for sugar beet (0.1 mg/kg) and sugar beet leaves or tops (10 mg/kg).

Globe artichokes. Trials conducted in France (GAP 0.075 kg ai/hl, PHI 14 days) and Italy (GAP 0.034-0.064 kg ai/hl, PHI 21 days) were reported.

In three French trials approximating French GAP acephate residues were 0.54, 1.3 and 1.6 mg/kg (methamidophos 0.08, 0.12 and 0.13 mg/kg), and in four trials according to GAP in Italy 0.08, 0.08, 0.08 and <0.1 mg/kg (methamidophos 0.02, 0.02, 0.04 and 0.08 mg/kg).

The Meeting decided that the residues in the trials in France and Italy were from different populations and should not be combined to estimate a maximum residue level, HR or STMR. The Meeting considered the number of trials in France inadequate for the purpose and decided to use the trials in Italy to estimate a maximum residue level. Residues of acephate and methamidophos, adjusted and totalled for estimating the STMR and HR (median underlined) were 0.13, 0.13, 0.18 and 0.3 mg/kg. The HR is 0.5 mg/kg.

The Meeting estimated a maximum residue level, STMR and HR for acephate in globe artichokes of 0.3 mg/kg, 0.155 mg/kg and 0.5 mg/kg.

The residues of methamidophos were 0.02, 0.02, 0.04 and 0.08 mg/kg. These residues are considered in the appraisal of methamidophos for the estimation of maximum residue levels.

Alfalfa. Trials in the USA (no GAP) were reported. As none of the trials matched GAP they were not evaluated further. The Meeting recommended the withdrawal of the existing CXL of 10 mg/kg for alfalfa forage (green).

Hops. Trials conducted in France (no GAP), Germany (no GAP), the UK (no GAP) and the USA (no GAP) were reported. As none of the trials matched GAP they were not evaluated further.

Processing

The Meeting received reports of processing studies for acephate in citrus fruits (oranges, lemons and grapefruit), apples, tomatoes, beans, potatoes and soya beans, investigating the effects of washing and further processing on incurred residues of acephate and methamidophos in a range of processed fractions.

No data were provided on the processing of mandarins. In the three citrus studies from field trials in the USA the data were sufficient for the Meeting to derive mean citrus processing factors of 0.34 (juice) and 0.61 (dry pulp) for acephate and 0.4 (juice) and 1.66 (dry pulp) for methamidophos.

Processing factors for apple juice, sauce, and wet pomace were derived from two field trials in the USA where initial acephate residues in the fruit were 0.46-1.0 mg/kg. For juice, processing factors were 1.0 for acephate and for methamidophos, and for wet pomace 0.98 and 1.35 respectively. The Meeting noted that washing did not significantly reduce residues of either compound in fruit treated 118-day before harvest and that residues of acephate in apple sauce were about half those in the raw fruit.

Studies on the effects of washing, cooking and/or canning on residues of acephate and methamidophos in common beans in the USA and France were evaluated, and the Meeting noted a

slight reduction in residues in washed beans. Cooking resulted in a reduction of acephate (mean processing factor of 0.5) and methamidophos (mean processing factor of 0.83).

The results of processing trials in the USA in 1978 with the production of soya bean meal, hulls and crude oil were reported in summary form. Residues in the crude oil were below the reported limits of quantification except in one analysis, where acephate residues (0.03 mg/kg) were half those measured in the fresh beans. Processing factors estimated by the Meeting for acephate were 0.69 for meal, 7.15 for hulls, and <0.425 for crude oil, and for methamidophos 2.0, 4.5 and <0.5 respectively.

The Meeting noted that in a study on globe artichokes reported in summary, there was a significant reduction in residues in cooked artichokes.

Farm animal dietary burdens

The Meeting estimated the farm animal dietary burdens of acephate residues using the diets in Appendix IX of the FAO Manual. The calculation from the maximum residue levels and STMRs in the feed provides the dietary burdens suitable for estimating maximum residue levels and STMRs respectively in animal commodities. In the case of acephate, the animal diet consists of commodities that are blended and the dietary burden is therefore calculated only from STMRs. This results in the same dietary burden for both maximum residue level and STMR estimation in animal commodities. The dry matter (DM) content is taken as 100% where maximum residue levels and STMRs are already expressed on the dry weight. The figures in parentheses are for methamidophos.

Commodity	STMR	Group	% DM	STMR ÷ DM	% in chosen diets			Residue, mg/kg		
					Beef	Dairy	Poultry	Beef	Dairy	Poultry
Wet apple pomace	2.2×0.98 = 2.15 (0.06×1.35 = 0.081)	AB	40	5.39 (0.2025)	40	20		2.15 (0.081)	1.075 (0.0405)	
Soya bean seed	0.03 (0.01)	VD	89	0.0337 (0.0112)	15	15	20	0.0051 (0.0017)	0.0051 (0.0017)	0.0067 (0.0022)
Soya bean meal	0.03×0.69 = 0.021 (0.01×2 = 0.02)	AL	92	0.022 (0.022)						
Soya bean hulls	0.03×7.15 = 0.2145 (0.01×4.5 = 0.045)	AL	90	0.238 (0.05)						
TOTAL					55	35	20	2.2 (0.083)	1.1 (0.0422)	0.0067 (0.0022)

The acephate and (methamidophos) dietary burdens for animal commodity maximum residue level and STMR estimation (residue levels in animal feeds expressed on a dry weight basis) are beef cattle 2.2 (0.083) ppm, dairy cattle 1.1 (0.0422) ppm and poultry 0.0067 (0.0022) ppm.

Farm animal feeding studies

The Meeting received information on residues in animal tissues and milk when dairy cows were dosed after the morning milking by capsule with mixtures of acephate and methamidophos in a ratio of 5:1, specifically chosen to reflect typical ratios observed in crop field trials, for 30 days, equivalent to 3:0.6, 10:2 and 30:6 ppm in the diet. Residues in the milk reached a plateau within 7 days and were always higher in the evening sample. Average residues of the parent compound in morning and evening milk collected from day 7 through to day 30 for the 10:2 ppm dose group were 0.062 and 0.19 mg/kg respectively, and returned to below the LOQ within two days of the end of dosing. Tissue residues in single animals slaughtered after 21 days of dosing were <0.02 (<0.01) mg/kg in liver, 0.03 (<0.01) mg/kg in heart, 0.03 (<0.01) mg/kg in kidney, 0.03 (<0.01) mg/kg in muscle and <0.02 (<0.01) mg/kg in fat for the 3:0.6 ppm dose group, and respectively <0.02 (<0.01) mg/kg, 0.10 (0.01) mg/kg, 0.21 (0.01) mg/kg, 0.08 (<0.01) mg/kg and 0.03 (<0.01) mg/kg for the 10:2 ppm dose group, and 0.08 (<0.01) mg/kg, 0.32 (0.06) mg/kg, 0.57 (0.05) mg/kg, 0.28 (0.04) mg/kg and 0.13 (0.02)

mg/kg for the 30:6 ppm dose group. Within 6 days of dosing ceasing, residues in the tissues were all below the LOQ.

In another study with dairy cows the dose was split into two and administered after the morning and after the evening milking. The capsules contained mixtures of acephate and methamidophos in a ratio of 5:1 at rates nominally equivalent to 15:3, 30:6 and 60:12 ppm in the diet. Residues in the milk reached a plateau by day 4 at 0.15 (0.01), 0.33 (0.02) and 0.85 (0.06) mg/kg for the three groups. The residues in the milk were below the LOQ within two days of the end of dosing for the 15:3 and 30:6 ppm groups and 0.07 (<0.01) mg/kg for the 60:12 ppm group. Maximum residues in the tissues in three animals slaughtered after 28 days were 0.02 (<0.01) mg/kg in the liver, 0.11 (0.01) mg/kg in the heart, 0.26 (0.02) mg/kg in the kidney, 0.12 (<0.01) mg/kg in muscle and 0.10 (<0.01) mg/kg in fat for the 15:3 ppm group, 0.04 (<0.01) mg/kg, 0.16 (0.02) mg/kg, 0.40 (0.04) mg/kg, 0.21 (0.01) mg/kg and 0.15 (<0.01) mg/kg for the 30:6 ppm group, and 0.15 (0.02) mg/kg, 0.40 (0.04) mg/kg, 0.85 (0.07) mg/kg and 0.40 (0.03) mg/kg, 0.40 (<0.01) mg/kg respectively for the 60:12 ppm group. 3 days after dosing ceased, residues in all tissues were below the LOQ in all groups.

The Meeting also received information on residues in the tissues of pigs fed a ration containing acephate and methamidophos for 30 days at rates of 3:0.6, 10:2 and 30:6 ppm in the diet. Maximum residues at 3:0.6 ppm were <0.02 (<0.01) mg/kg in the liver, 0.05 (<0.01) mg/kg in the heart, 0.04 (<0.01) mg/kg in the kidney, 0.05 (<0.01) mg/kg in muscle, <0.02 (<0.01) mg/kg in fat and 0.04 (<0.01) mg/kg in brain. Residues in all tissues were below the LOQ within a day of end of dosing.

In a trial on laying hens fed a diet containing acephate at 3 ppm for up to 92 days, residues were below the LOQ in the tissues and eggs. At higher feeding levels, maximum acephate and (methamidophos) residues in eggs were 0.09 (0.006) mg/kg from a 10 ppm feeding level and 0.19 (0.016) mg/kg at 30 ppm, and in tissues were below the LOQ in fat, kidney and liver, and 0.01 (0.008) mg/kg and 0.12 (0.046) mg/kg in muscle from the 10 and 30 ppm groups respectively.

Similar results were obtained when quail were fed diets incorporating acephate at 10 and 30 ppm for up to 148 days. Maximum residues in the eggs were 0.19 (0.007) mg/kg and 0.34 (0.014) mg/kg in the 10 and 30 ppm groups respectively. In liver and kidney they were below the LOQ, in fat 0.06 (0.014) and 0.04 (<0.001) mg/kg, and in muscle 0.01 (<0.001) and 0.04 (<0.001) mg/kg at the two feeding levels.

Maximum residue levels in animal commodities

The maximum/STMR dietary burdens for beef and dairy cattle are 2.2 (0.083) and 1.1 (0.042) mg/kg respectively, so the levels of residues in tissues and milk can be obtained by extrapolation from the highest residues in tissues at the 3 ppm feeding level and the mean residue in milk at the 15 ppm level (in the second study where cows were dosed in the morning and evening). The maximum acephate and (methamidophos) residues expected are <0.02 (<0.01) mg/kg in liver, 0.022 (<0.01) mg/kg in fat, 0.022 (<0.01) mg/kg in muscle and 0.022 (<0.01) mg/kg in kidney, and the mean residue in milk is 0.011 (0.00014) mg/kg. As the dietary burden for STMR estimation is the same as for maximum residue level estimation the STMRs and HRs can be calculated from the above values. Essentially no residues of methamidophos are expected in tissues or milk so the STMRs and HRs for dietary intake estimation are the estimated acephate residues.

Dietary burden (ppm) ¹ Feeding level [ppm] ²		Acephate, methamidophos residues, mg/kg ³				
		Milk Mean	Fat High	Muscle High	Liver High	Kidney High
MRL/STMR beef	(2.2, 0.083) [3, 0.6]		<i>(0.022, <0.01)</i> 0.03, <0.01	<i>(0.022, <0.01)</i> 0.03, <0.01	<i>(<0.02, <0.01)</i> <0.02, <0.01	<i>(0.022, <0.01)</i> 0.03, <0.01
MRL/STMR dairy	(1.1, 0.042) [15, 3]	<i>(0.011, 0.00014)</i> 0.15, 0.01				

¹ Values in parentheses are estimated dietary burdens

² Values in square brackets are actual feeding levels in the feeding studies

³ Residue values in parentheses in italics are extrapolated from the residues and feeding levels in the feeding studies to the dietary burdens. High is the highest individual tissue residue, and mean the mean milk residue in the relevant feeding group.

The maximum dietary burden for pigs is 0.008 (0.003) ppm, based on the feeding of soya beans at 25% of the total diet. The residues of both acephate and methamidophos in all tissues are expected to be <0.01 mg/kg at this level.

The Meeting estimated maximum residue levels for meat (from mammals other than marine mammals) 0.05 mg/kg, edible offal (mammalian) 0.05 mg/kg, and milks 0.02 mg/kg. The estimates are recommended to replace the existing CXLs of 0.1 mg/kg for cattle fat and meat, pig fat and meat and milks.

The maximum dietary burden for poultry is 0.0067 (0.0022) ppm. The levels of acephate and methamidophos residues in all tissues and eggs are expected to be <0.01 mg/kg at this level.

The Meeting estimated maximum residue levels for poultry meat 0.01 (*) mg/kg, poultry offal 0.01 (*) mg/kg and eggs 0.01 (*) mg/kg. As no residues are expected at the maximum feeding level for poultry, the STMRs for poultry meat, edible offal and eggs are zero.

DIETARY RISK ASSESSMENT

The Meeting considered how best to approach the dietary risk assessment of mixed residues of acephate and methamidophos and decided that an appropriately conservative approach would be to calculate the sum of the acephate and methamidophos residues after scaling the methamidophos residues to account for the difference in toxicity. The relevant factors for chronic and short-term intake were derived from the ratios of the acephate and methamidophos maximum ADI and acute RfD values and are 2.5 and 5 respectively. Dietary intake estimates for the combined adjusted residues were compared with the acephate maximum ADI and acute RfD.

Long-term intake

The evaluation of acephate has resulted in estimates of maximum residue levels and STMRs for raw and processed commodities. Consumption data were available for 22 raw or processed food commodities and were used in the dietary intake calculation. The results are shown in Annex 3.

The International Estimated Daily Intakes for the 5 GEMS/Food regional diets, based on estimated STMRs were in the range 2-20% of the maximum ADI of 0.01 mg/kg bw (Annex 3). The Meeting concluded that the long-term intake of residues of acephate 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 acephate (including any contribution from the presence of methamidophos residues) was calculated for the raw or processed food commodities

for which HRs were estimated and for which consumption data were available. Where group maximum residue levels were estimated the IESTI was calculated for all commodities within the group for which consumption data were available. The results are shown in Annex 4.

The IESTI varied from 0 to 260% of the acute RfD (0.05 mg/kg bw) for the general population, and from 0 to 630% for children aged 6 years or less. The short-term intakes from pome fruit, mandarins, cauliflower and sweet peppers were 140-260% of the acute RfD for the general population, and from pome fruit, mandarins, peaches, nectarines, beans, broccoli, cauliflower and peppers 190-630% for children. The information provided to the Meeting precluded a conclusion that the acute dietary intake from these commodities would be below the acute RfD.

The Meeting concluded that the short-term intake of residues of acephate from uses that have been considered by the JMPR is unlikely to present a public health concern, with the exception of those from pome fruit, mandarins, peaches, nectarines, beans except broad beans and soya beans, broccoli, cauliflower and peppers.

4.2 CARBENDAZIM (072)/THIOPHANATE-METHYL (077)

RESIDUES AND ANALYTICAL ASPECTS

Carbendazim and its related compounds benomyl and thiophanate-methyl were evaluated by the 1998 JMPR under the CCPR Periodic Review Programme. The Meeting recommended MRLs (expressed as carbendazim) for barley, barley straw and fodder, cucumber, gherkin, pome fruits, rape seed and tomato on the basis of carbendazim residue data; for beans (dry), garden peas (succulent seeds), grapes, pome fruits and wheat on the basis of thiophanate-methyl residue data; for banana, Brussels sprouts, carrot, cattle meat, chicken fat, edible offal (mammalian), eggs, milks, oranges, peach, pineapple, plums (including prunes), pome fruit, poultry meat, rice, rice straw and fodder and wheat straw and fodder on the basis of benomyl residue data.

The 1998 JMPR recommended the withdrawal of numerous MRLs, including those for apricot, asparagus, avocado, berries and other small fruits, broad bean (green pods and immature seeds), celery, cherries, coffee beans, common bean (pods and immature seeds), egg plant, hops, head lettuce, mango, melons, mushrooms, nectarine, bulb onion, peanut, peanut fodder, peppers, potato, sugar beet, sugar beet leaves or tops, tree nuts and winter squash.

The present Meeting received information on GAP and national MRLs for carbendazim and thiophanate-methyl from the governments of Germany and The Netherlands. The thiophanate-methyl manufacturer reported US GAP (with labels), analytical methods, information on the stability of residues in stored analytical samples and new US supervised residue trials on cherries, summer squash, snap beans, soya beans, sugar beet and peanuts. The government of Thailand provided information on carbendazim use patterns and reported supervised trials on asparagus, mangoes and peppers. Information on GAP, national MRLs and residues of carbendazim from post-harvest trials on mangoes was reported by the government of Australia.

Analytical methods

The Meeting received descriptions and validation data for analytical methods for thiophanate-methyl and carbendazim. The methods rely on HPLC with UV detection and LC/MS/MS, and achieve LOQs of 0.01-0.05 mg/kg in crops.

Stability of pesticide residues in stored analytical samples

The Meeting received information on the stability of thiophanate-methyl and carbendazim residues in various crops (fruits, fruiting vegetables, leafy vegetables, roots, pulses, and cereal grains). The residues were generally stable for the duration of the tests.

Definition of the residue

The 1998 JMPR defined the residues (for compliance with MRLs and dietary intake calculations) arising from the use of

- benomyl as “sum of benomyl and carbendazim, expressed as carbendazim”
- carbendazim as “carbendazim”
- thiophanate-methyl as “sum of thiophanate-methyl and carbendazim, expressed as carbendazim”.

At the 34th Session of the CCPR (2002), the Committee agreed to change the definition of the residue to “sum of benomyl, carbendazim and thiophanate-methyl, expressed as carbendazim”.

All the following residues are expressed as carbendazim.

Results of supervised trials on crops

Cherries. Thiophanate-methyl is registered in the USA for use on cherries 1-3 times at a rate of 0.78-1.2 kg ai/ha with a 1-day PHI. In eight trials in four states in 1996, with five applications at 1.2 kg ai/ha and 0.08-0.13 kg ai/hl for ground and 1.5-2.5 kg ai/hl for aerial application and harvest at one day, the residues (sum of thiophanate-methyl and carbendazim, expressed as carbendazim) were 0.38, 0.53, 0.60, 0.81, 1.5, 2.4, 2.7 and 9.1 mg/kg.

The Meeting estimated a maximum residue level of 10 mg/kg, an STMR of 1.16 mg/kg and an HR of 9.1 mg/kg for carbendazim residues in cherries.

Mangoes. Carbendazim is registered in Thailand for foliar use on mangoes several times at a rate of 1.5 kg ai/ha and a spray concentration of 0.03 kg ai/hl with a PHI of 7 days. In 5 trials conducted in 2001 and 2002 in Thailand in accordance with GAP (6 x 1.5 kg ai/ha, 0.03 kg ai/hl, PHI 6-7 days), the residues were 0.70, 0.71, 0.72, 0.72 and 1.1 mg/kg in fruits without stones. The results could not be evaluated because the ratio of the weight of skin and flesh to whole fruit was not reported.

Post-harvest dipping of mangoes in carbendazim is registered in Australia with a dip concentration of 0.05 kg ai/hl. Harvested fruit were dipped at a concentration of 0.05 kg ai/hl. The dip temperature was 52°C and the fruit were dipped for 5 minutes before removal and air-drying. Whole fruits were weighed and the stones then separated from skin and pulp. The peels, pulp and stones were weighed separately and their weight percentages calculated. Residues in whole fruit were 1.2, 1.3, 1.6, 1.9, 3.0 and 3.1 mg/kg and in the pulp (edible portion) 0.21, 0.29, 0.4, 0.5 and 1.7 mg/kg.

The Meeting estimated a maximum residue level of 5 mg/kg, an STMR of 0.4 mg/kg and an HR of 1.7 mg/kg for residues in mango.

Summer squash. Thiophanate-methyl is registered in the USA for use on summer squash several times at a rate of 0.2-0.39 kg ai/ha (PHI not stated). In ten trials in eight states in 1991, with eight applications at 0.38-0.40 kg ai/ha and harvest at one day, the residues (sum of thiophanate-methyl and carbendazim, expressed as carbendazim) were <0.08, <0.08, 0.08, 0.08, 0.09, 0.10, 0.12, 0.12, 0.14 and 0.32 mg/kg.

The Meeting estimated a maximum residue level of 0.5 mg/kg, an STMR of 0.095 mg/kg and an HR of 0.32 mg/kg for residues in summer squash.

Chili peppers. Carbendazim is registered in Thailand for use on vegetables at a rate of 0.25-0.50 kg ai/ha with a PHI of 5 days. In 5 trials conducted on chili peppers in 2000-2002 in Thailand in accordance with GAP (4 x 0.5 kg ai/ha, PHI 5 days), the residues were 0.55, 0.63, 0.78, 0.87 and 0.98 mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg, an STMR of 0.78 mg/kg and an HR of 0.98 mg/kg for residues in chili peppers.

Common bean (pods and/or immature seeds). Thiophanate-methyl is registered in the USA for use on beans 1-2 times at a rate of 0.78-1.6 kg ai/ha with a PHI of 14 days for snap beans and 28 days for lima beans. In eleven trials in nine states in 1990, with two applications at 1.6 kg ai/ha and harvest at 14 days, the residues (sum of thiophanate-methyl and carbendazim, expressed as carbendazim) were <0.08 (6), 0.09, 0.14, 0.16, 0.22 and 0.45 mg/kg.

The Meeting estimated a maximum residue level of 0.5 mg/kg, an STMR of 0.08 mg/kg and an HR of 0.45 mg/kg for residues in common bean (pods and/or immature seeds).

Soya bean (dry). Thiophanate-methyl is registered in the USA for use on soya beans twice at a rate of 0.39-0.78 kg ai/ha (PHI not stated). The second application must be not later than 14 days when beans become visible in the pod. In twelve trials in twelve states in 1990, with three applications at 0.64-0.85 kg ai/ha and harvest at 14 days, the residues (sum of thiophanate-methyl and carbendazim, expressed as carbendazim) were <0.08 (10), 0.25 and 0.31 mg/kg.

The Meeting estimated a maximum residue level of 0.5 mg/kg and an STMR 0.08 mg/kg for residues in soya bean (dry).

Sugar beet. Thiophanate-methyl is registered in the USA for use on sugar beet several times at a rate of 0.39-0.78 kg ai/ha with a PHI of 21 days. In eleven trials in seven states in 1997, with seed treatment and three foliar applications at 0.78-0.81 kg ai/ha and harvest at 21 days, the residues (sum of thiophanate-methyl and carbendazim, expressed as carbendazim) were <0.08 (11) mg/kg.

The Meeting estimated a maximum residue level of 0.1* mg/kg, an STMR of 0.08 mg/kg and an HR of 0.08 mg/kg for sugar beet.

Asparagus. Carbendazim is registered in Thailand for use on asparagus at a rate of 0.38 kg ai/ha with a PHI of 5 days. In 4 trials conducted in 1995-2001 in Thailand in accordance with GAP (4-5 x 0.38 kg ai/ha, PHI 5 days), the residues were <0.01, 0.05, 0.08 and 0.09 mg/kg.

The Meeting estimated a maximum residue level of 0.2 mg/kg, an STMR of 0.065 mg/kg and an HR of 0.09 mg/kg for residues of carbendazim in asparagus.

Peanuts. Thiophanate-methyl is registered in the USA for use on peanuts several times at a rate of 0.39 kg ai/ha with a PHI of 14 days. Ten trials with six applications at 0.39 kg ai/ha were carried out in five states in 1991. Peanuts were harvested according to normal commercial practices: the plants were inverted at a 14-day PHI, the remaining crops were allowed to dry for 0-7 days in the field, then separate in-shell nut and hay samples were taken. The concentrations of residues (sum of thiophanate-methyl and carbendazim, expressed as carbendazim) in the kernels were <0.08 (10) mg/kg.

The Meeting estimated a maximum residue level of 0.1* mg/kg and an STMR of 0.08 mg/kg for residues in peanut.

Soya bean fodder. The residues (sum of thiophanate-methyl and carbendazim, expressed as carbendazim) in soya bean hay in the US trials on soya beans described above were <0.3, <0.3, 0.88, 0.95, 2.1, 2.6, 3.3, 3.8, 4.4, 4.8, 5.3 and 9.5 mg/kg.

The Meeting noted a label restriction against feeding (“*Do not graze or feed treated vines or hay to livestock*”) and did not estimate a maximum residue level. The previous recommendation (withdrawal of the Codex MRL) was confirmed.

Snap bean vines. Thiophanate-methyl is registered in the USA for use on beans once or twice at a rate of 0.78-1.6 kg ai/ha with a PHI of 14 days for snap beans. In eleven trials in nine states in 1990, with two applications at 1.6 kg ai/ha and harvest at 14 days, the residues (sum of thiophanate-methyl and carbendazim, expressed as carbendazim) in vines were <0.08, 0.62, 0.65, 2.0, 2.6, 2.7, 3.2, 4.0, 7.3, 8.1 and 11 mg/kg.

The Meeting noted that snap bean forage or fodder is not mentioned as a feed item in the FAO Manual (Appendix IX) and did not estimate a maximum residue level.

Peanut fodder. The residues (sum of thiophanate-methyl and carbendazim, expressed as carbendazim) in peanut hay in the US peanut trials described above were <0.8 (6), 0.91, 1.1, 1.6 and 2.1 mg/kg (fresh weight).

Allowing for the standard 85% dry matter content of peanut hay (*FAO Manual*, p. 148), the Meeting estimated a maximum residue level and an STMR (dry weight) for residues in peanut fodder of 3 and 0.94 mg/kg.

Sugar beet leaves or tops. The residues (sum of thiophanate-methyl and carbendazim, expressed as carbendazim) in the leaves and tops from the US trials on sugar beet described above were 0.13, 0.16, 0.22, 0.24, 0.31, 0.33, 0.52, 0.69, 0.72, 0.84 and 2.2 mg/kg (fresh weight).

Allowing for the standard 23% dry matter in sugar beet tops (*FAO Manual*, p. 147), the Meeting estimated a maximum residue level and an STMR (dry weight) of 10 and 1.4 mg/kg for residues in sugar beet leaves or tops.

Dietary burdens in farm animals

The 1998 JMPR estimated dietary burdens (calculated as benomyl) of 17, 18 and 2 mg/kg for dairy cattle, beef cattle and poultry respectively, based on residues in the feed items wet citrus pulp, wet tomato pomace, raisin culls and raisin waste (JMPR residue evaluation 1998, p. 159).

The current Meeting estimated the dietary burden of carbendazim/thiophanate-methyl residues (expressed as carbendazim) in farm animals on the basis of the diets listed in Appendix IX of the FAO Manual. Calculation from MRLs and HRs provides the levels in feed for estimating MRLs for animal commodities, while calculation from STMRs in feed is suitable for estimating STMRs for animal commodities. The dry matter is taken as 100% when MRLs and STMRs are already expressed on the dry weight. In addition to the new residue data for sugar beet leaves or tops and peanut hay the Meeting took into consideration the feed items for which maximum residue levels and STMRs were estimated by the 1998 JMPR.

Maximum dietary burden

Commodity	Codex commodity group	Residue (mg/kg)	Basis	% Dry matter	Residue, on dry wt (mg/kg)	Chosen diets, %			Residue contribution (mg/kg)		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
Apple pomace, wet ¹	AB	1.3	Est. ²	40	3.25						
Barley	GC	0.5	MRL ³	88	0.568						

Commodity	Codex commodity group	Residue (mg/kg)	Basis	% Dry matter	Residue, on dry wt (mg/kg)	Chosen diets, %			Residue contribution (mg/kg)		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
Barley straw and fodder, dry	AS	2	MRL ³	89	2.25						
Citrus pulp, dry ⁴	AB	8.6	Max. res ²	91	9.4	20	20		1.88	1.88	
Peanut fodder	AL	3	MRL	100	3	25	50		0.75	1.5	
Rice, husked	GC	2	MRL ³	88	2.27	25	10	60	0.568	0.226	1.362
Rice straw and fodder, dry	AS	15	MRL ³	90	16.7	10	10		1.67	1.67	
Sugar beet leaves or tops	AV	10	MRL	100	10	20	10		2.0	1.0	
Wheat	GC	0.05*	MRL ³	89	0.056						
Wheat straw and fodder, dry	AS	1	MRL ³	88	1.14						
TOTAL						100	100	60	6.9	6.3	1.4

¹ estimated by 1998 JMPR (residue evaluation p. 159): 2 mg/kg as benomyl, equivalent to 1.3 mg/kg as carbendazim

² maximum residue estimated by 1998 JMPR (residue evaluation p. 159)

³ recommendation by 1998 JMPR

⁴ estimated by 1998 JMPR (residue evaluation p. 159): 2 mg/kg as benomyl, equivalent to 8.6 mg/kg as carbendazim

STMR dietary burden

Commodity	Codex commodity group	Residue (mg/kg)	Basis	% Dry matter	Residue, on dry wt (mg/kg)	Chosen diets, %			Residue contribution (mg/kg)		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
Apple pomace, wet ¹	AB	0.6	STMR	40	1.5						
Barley	GC	0.05	STMR ²	88	0.057			75			0.0428
Barley straw and fodder, dry	AS	0.345	STMR ²	89	0.388						
Citrus pulp ³	AB	1.408	STMR	91	1.547	20	20		0.309	0.309	
Peanut fodder	AL	0.94	STMR	100	0.94	25	50		0.235	0.47	
Rice, husked	GC	0.05	STMR ²	88	0.057	25	10		0.01425	0.0057	
Rice straw and fodder, dry	AS	2.5	STMR ²	90	2.78	10	10		0.278	0.278	
Sugar beet leaves and tops	AV	1.4	STMR	100	1.4	20	10		0.28	0.14	
Wheat	GC	0.03	STMR ²	89	0.034						

Commodity	Codex commodity group	Residue (mg/kg)	Basis	% Dry matter	Residue, on dry wt (mg/kg)	Chosen diets, %			Residue contribution (mg/kg)		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
Wheat straw and fodder, dry	AS	0.1	STMR ²	88	0.114						
TOTAL						100	100	75	1.1	1.2	0.04

¹ basis: STMR for benomyl in pome fruit estimated by 1998 JMPR: 0.6 mg/kg expressed as carbendazim

² estimated by 1998 JMPR

³ basis: STMR for benomyl in oranges 0.325 mg/kg expressed as carbendazim estimated by 1998 JMPR. Calculation as described for MRL dietary burden in 1998 JMPR residue evaluation p. 159 (0.325 x 91/21= 1.408)

The dietary burdens on a dry weight basis for MRL and STMR estimation respectively, are 6.9 and 1.1 mg/kg for beef cattle, 6.3 and 1.2 mg/kg for dairy cattle and 1.4 and 0.04 for poultry (expressed as carbendazim) or, expressed as benomyl, 10.5 and 1.7 mg/kg for beef cattle, 9.6 and 1.8 mg/kg for dairy cattle and 2.1 and 0.06 for poultry. The new dietary burden calculation is the same order as that of the 1998 JMPR.

Because the benomyl and carbendazim feeding studies reported to the 1998 Meeting showed a “nil residue situation” in animal commodities, the 1998 JMPR recommended MRLs at the LOQ of 0.05* mg/kg and estimated STMRs of 0 for cattle meat, chicken fat, edible offal (mammalian), eggs, milks and poultry meat. The Meeting confirmed the previous recommendations.

DIETARY RISK ASSESSMENT

Long-term intake

The residues of benomyl, carbendazim and thiophanate-methyl are all expressed as carbendazim which has the lowest ADI (0-0.03 mg/kg bw/day). The International Estimated Daily Intakes (IEDI) for carbendazim, based on the STMRs estimated for 33 commodities by the 1998 and 2003 JMPRs, for the five GEMS/Food regional diets were in the range of 1-4% of the ADI (Annex 3). The Meeting concluded that the long-term intake of residues of carbendazim resulting from the uses considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The International Estimated Short Term Intake (IESTI) for carbendazim was calculated for 31 food commodities for which maximum residue levels were estimated by the JMPR in 1998 and 2003 and for which consumption data were available. These results are shown in Annex 4. The Meeting concluded that an acute RfD may be necessary, but as it has not yet been established the acute risk assessment for carbendazim could not be finalized.

4.3 CARBOSULFAN (145)/CARBOFURAN

TOXICOLOGY

Carbosulfan is a carbamate insecticide that acts by inhibiting the activity of acetylcholinesterase. It was evaluated by JMPR in 1984 and 1986. A toxicological monograph was prepared by the Joint Meeting in 1984 and a monograph addendum was prepared in 1986. In 1986, an ADI of 0–0.01 mg/kg

bw was established on the basis of a NOAEL of 1.3 mg/kg bw per day in a 2-year study in mice, a NOAEL of 1.0 mg/kg bw per day in a 2-year study in rats, and a NOAEL of 1.3 mg/kg bw per day in a 6-month study in dogs. One of the metabolites of carbosulfan is carbofuran, which is itself used as a pesticide and which was evaluated by JMPR in 1976, 1979, 1980, 1982, 1996 and 2002. The 1996 JMPR established an ADI of 0–0.002 mg/kg bw and the 2002 JMPR established an acute reference dose (RfD) of 0.009 mg/kg bw for carbofuran.

Carbosulfan was re-evaluated by the present Meeting within the periodic review programme of the Codex Committee on Pesticide Residues. The Meeting reviewed new data on carbosulfan that had not been considered previously and relevant data from the previous evaluation. Conclusions of studies evaluated for the 1984 JMPR that were not available for the present evaluation are included.

After oral administration to male and female rats, absorption of radiolabelled carbosulfan is rapid and almost complete. Elimination is also relatively rapid, with most (80–90%) of the absorbed radioactivity being excreted in the urine within 48–72 h, depending on dose. After repeated dosing of rats with carbosulfan, the rate of excretion appeared to be increased (80–87% within 24 h), which may indicate that induction of metabolism had occurred.

Carbosulfan is metabolized by hydrolysis to the 7-phenol or to carbofuran and dibutylamine, and is subsequently further metabolized via hydrolysis, oxidation and conjugation to a variety of metabolites. Metabolites of the dibutylamino moiety may enter the carbon pool and be incorporated into natural constituents of the body. No marked sex-specific differences were observed in rats with regard to the excretion pattern, tissue distribution and metabolite profile of carbosulfan.

Carbosulfan (technical material) is highly toxic when administered orally, with LD₅₀s ranging from 90–250 mg/kg bw in rats. The LD₅₀ for carbosulfan was >2000 mg/kg bw in rabbits treated dermally and the LC₅₀ was 0.61 mg/l in rats treated by inhalation.

Carbosulfan is minimally irritating to the eye, slightly irritating to the skin and is a dermal sensitizer.

In general, in short-term and long-term studies of toxicity, the most sensitive effect of the oral administration of carbosulfan was the inhibition of cholinesterase activity, accompanied at the same or higher doses by clinical signs indicative of cholinesterase inhibition (e.g. salivation, lacrimation, ataxia, tremors, anogenital staining, diarrhoea). In a study of acute oral neurotoxicity in rats, the NOAEL was 0.5 mg/kg bw, on the basis of effects on brain cholinesterase activity as measured 4 h after dosing. In a 90-day study in rats, the NOAEL was 20 ppm, equivalent to 1 mg/kg bw per day, on the basis of inhibition of brain and erythrocyte cholinesterase activity. In a second 90-day study of rats fed with carbosulfan, the NOAEL was 20 ppm, equal to 1.2 mg/kg bw per day, on the basis of clinical signs, observations in a functional observational battery (FOB) and effects on body weight, body-weight gain and food consumption at a dose of 62 mg/kg bw per day. In this study, cholinesterase activity was not determined.

In a 6-month study in dogs, the NOAEL reported was 50 ppm, equivalent to 1.3 mg/kg bw per day, on the basis of effects on blood chemistry parameters and occasional reductions in food consumption and body-weight gain.

In long-term studies in mice and rats, carbosulfan was not carcinogenic at concentrations in the diet of up to and including the highest dose tested of 2500 ppm, equal to 320 and 153 mg/kg bw per day for mouse and rat, respectively. In the study in mice, the NOAEL was 20 ppm, equal to 2.5 mg/kg bw per day, on the basis of reductions in body weight, inhibition of brain and erythrocyte cholinesterase activity and reductions in absolute and relative spleen weight. In the study in rats, the NOAEL was 20 ppm, equal to 1 mg/kg bw per day, on the basis of inhibition of brain and erythrocyte cholinesterase activity and pathological changes in the eye, i.e. focal iris atrophy, iris coloboma and absence of iris tissue. The mechanism by which these pathological changes in the eye were induced is not clear.

The genotoxic potential of carbosulfan was investigated in a wide range of tests. Primarily

negative results were obtained in a number of tests in vitro and in vivo. Positive effects were observed in a few tests, however these tests were confounded by the use of very high doses in vivo, the occurrence of marked cytotoxicity in vitro and the lack of information on the purity of the test compound. The Meeting concluded that carbosulfan is unlikely to be genotoxic.

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

In a three-generation study of reproductive toxicity, carbosulfan was administered at doses of 10, 20 and 250 ppm. No effects on mating index, gestation index and number of viable fetuses were observed. At a dose of 250 ppm, pup weight, litter size and pup survival were decreased, as were the body weights of parental males and females at this dose. In parental animals, the NOAEL was 20 ppm, equivalent to 1.3 mg/kg bw per day, on the basis of the decreases in body weight. The NOAEL for pup toxicity was 20 ppm on the basis of the reductions in litter size, pup body weight and pup body-weight gain. The NOAEL for reproductive toxicity was 250 ppm, equivalent to 17 mg/kg bw per day, the highest dose tested.

In studies of developmental toxicity in rats and rabbits, carbosulfan was not teratogenic. The NOAEL for maternal toxicity was 2 mg/kg bw per day in the study in rats, on the basis of clinical signs and reduction in body weight. The NOAEL for toxicity in offspring was 2 mg/kg bw per day, on the basis of the reduction in fetal body weight. In the study in rabbits, the NOAEL for maternal and offspring toxicity was 10 mg/kg bw per day, the highest dose tested.

When tested in hens, carbosulfan did not induce delayed polyneuropathy after a single exposure.

No new human data were available.

The Meeting concluded that the present database is sufficient to characterize the potential hazard of carbosulfan to fetuses, infants and children.

Toxicological evaluation

The Meeting established an ADI of 0–0.01 mg/kg bw per day based on a NOAEL of 1 mg/kg bw per day, on the basis of pathological changes in the eye, inhibition of brain and erythrocyte cholinesterase activity and body-weight reduction in the 2-year study in rats, with a safety factor of 100. This safety factor was used because the pathological changes in the eye could not definitely be attributed to inhibition of cholinesterase.

After considering the data available to the present Meeting, as well as the previous evaluations, the Meeting established an acute RfD of 0.02 mg/kg bw. This was based on the NOAEL of 0.5 mg/kg bw per day for inhibition of brain cholinesterase activity in a study of acute neurotoxicity in rats, and a safety factor of 25, as the relevant toxic effects of carbosulfan are dependent on the C_{\max} (Annex 5, reference 95).

A toxicological monograph was prepared.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Mouse	2-year study of toxicity and carcinogenicity ^a	Toxicity	20 ppm, equal to 2.5 mg/kg bw per day	500 ppm, equal to 62 mg/kg bw per day
		Carcinogenicity	2500 ppm, equal to 320 mg/kg bw per day ^c	

Rat	Three-generation study of reproductive toxicity ^a	Parental and offspring toxicity	20 ppm, equivalent to 1.3 mg/kg bw per day	250 ppm, equivalent to 17 mg/kg bw per day
		Reproductive toxicity	250 ppm, equivalent to 17 mg/kg bw per day ^c	—
	Study of developmental toxicity ^b	Maternal toxicity	2 mg/kg bw per day	10 mg/kg bw per day
		Embryo- and fetotoxicity	2 mg/kg bw per day	10 mg/kg bw per day
	Study of acute neurotoxicity ^b	Neurotoxicity	0.5 mg/kg bw	5 mg/kg bw
	90-day study of neurotoxicity ^a	Neurotoxicity	20 ppm, equivalent to 1 mg/kg bw per day	500 ppm, equivalent to 25 mg/kg bw per day
2-year study of toxicity and carcinogenicity ^a	Toxicity	20 ppm, equal to 1 mg/kg bw per day	500 ppm, equal to 27 mg/kg bw per day	
	Carcinogenicity	2500 ppm, equal to 153 mg/kg bw per day ^c	—	
Rabbit	Study of developmental toxicity ^b	Maternal toxicity	10 mg/kg bw per day ^c	—
		Embryo- and fetotoxicity	10 mg/kg bw per day ^c	—
Dog	6-month study of toxicity ^a	Toxicity	50 ppm, equivalent to 1.3 mg/kg bw per day	500 ppm, equivalent to 13 mg/kg bw per day

a Diet

b Gavage

c Highest dose tested

Estimate of acceptable daily intake for humans

0–0.01 mg/kg bw

Estimate of acute reference dose

0.02 mg/kg bw

Studies that would provide information useful for continued evaluation of the compound

Further observations in humans

Summary of critical end-points for carbosulfan

Absorption, distribution, excretion and metabolism in animals

Rate and extent of absorption	Rapid and extensive
Dermal absorption	No data (rabbit: reduction in brain cholinesterase activity at 50 mg/kg bw per day)
Distribution	Extensive; highest concentrations in liver, kidney, omental fat, peripheral fat

Potential for accumulation	Low
Rate and extent of excretion	Relatively rapid (80–90% within 48–72 h in rats, mainly in urine)
Metabolism in animals	Major metabolites: 3-OH-7-phenol, carbofuran, 3-OH-carbofuran, 3-keto-7-phenol, 7-phenol, dibutylamine (rat)
Toxicologically significant compounds	Carbosulfan, carbofuran
<i>Acute toxicity</i>	
Rat, LD ₅₀ , oral	90–250 mg/kg bw
Rabbit, LD ₅₀ , dermal	>2000 mg/kg bw
Rat, LC ₅₀ , inhalation	0.61 mg/l
Rabbit, skin irritation	A mild irritant
Rabbit, eye irritation	A mild irritant
Dermal sensitization	Sensitizing (Buehler)
<i>Short-term studies of toxicity</i>	
Target/critical effect	Inhibition of cholinesterase activity in brain and erythrocytes
Lowest relevant oral NOAEL	1 mg/kg bw per day (rats)
Lowest relevant dermal NOAEL	5 mg/kg bw per day (rabbits)
Lowest relevant inhalatory NOAEL	0.00065 mg/l (rats)
<i>Genotoxicity</i>	Negative in most tests; unlikely to be genotoxic
<i>Long-term studies of toxicity and carcinogenicity</i>	
Target/critical effect	Inhibition of cholinesterase activity in brain and erythrocytes, pathological changes in the eye
Lowest relevant NOAEL	1 mg/kg bw per day (rats)
Carcinogenicity	Unlikely to pose a carcinogenic risk to humans
<i>Reproductive toxicity</i>	
Reproduction target/critical effect	Reduction of pup weight, litter size and pup survival (in the presence of parental toxicity)
Lowest relevant reproductive NOAEL	1.3 mg/kg bw per day (rats)
Developmental target	Reduction in pup weight (in the presence of maternal toxicity)
	Not teratogenic
Lowest relevant developmental NOAEL	2 mg/kg bw per day (rats)
<i>Neurotoxicity/delayed neurotoxicity</i>	
Neurotoxicity	Inhibition of cholinesterase activity in brain and erythrocytes, and clinical and behavioural effects associated with cholinesterase

	inhibition
Lowest relevant oral NOAEL	0.5 mg/kg bw (rats)
Delayed neurotoxicity	Negative
<i>Medical data</i>	None

Summary	Value	Study	Safety factor
ADI	0–0.01 mg/kg bw	Rat, long-term toxicity	100
Acute RfD	0.02 mg/kg bw	Rat, acute neurotoxicity	25

RESIDUE AND ANALYTICAL ASPECTS

Carbosulfan is a broad-spectrum carbamate pesticide used to control insects, mites and nematodes by soil, foliar and seed treatment applications, mainly on potatoes, sugar beet, rice, maize and citrus. Carbofuran is the main metabolite of carbosulfan in plants and is itself a pesticide.

Carbosulfan was evaluated for residues under the Periodic Review Programme by the JMPR in 1997. The present evaluation of carbosulfan includes estimates for carbofuran resulting from the use of carbosulfan. The current definition of the carbosulfan residue for compliance with MRLs and for dietary risk assessment is “carbosulfan”.

The carbofuran residue is defined as carbofuran + 3-hydroxycarbofuran for compliance with MRLs and carbofuran + 3-hydroxycarbofuran + conjugated 3-hydroxycarbofuran for dietary risk assessment.

The Meeting received information on metabolism in hens, methods of analysis, supervised trials conducted on potatoes, sugar beet, cotton, maize and rice, residues in food in commerce, and national MRLs

Animal metabolism

One metabolism study in hens was reported. The hens were dosed with either phenyl- or dibutylamine-labelled carbosulfan for 14 days at levels corresponding to approximately 0.5, 1.5 or 5 ppm in the diet. At each treatment level, a plateau of ¹⁴C residues in eggs was reached at day 5. For both labelled compounds the yolk contained higher ¹⁴C residues than the white.

The maximum ¹⁴C residues observed in egg yolk and white were 1.87 mg/kg and 0.119 mg/kg respectively at the dose of 5 ppm, and 0.18 mg/kg and 0.014 mg/kg at 0.5 ppm. Only dibutylamine was detected in yolk at 0.023 mg/kg after 9-12 days (4.3% of the TRR). Carbosulfan was less than 0.02 mg/kg.

The highest radioactive tissue residue from both labels was observed in liver. After seven days of depuration, all radioactive tissue residues were below 0.002 mg/kg.

With the phenyl-labelled compound, the major extractable residue found in the thigh muscle at day 0 was 3-hydroxycarbofuran. The 3-hydroxy-7-phenol was the major metabolite in liver. There were no detectable residues (<0.002 mg/kg equivalents) of carbosulfan or carbofuran in any tissue analysed.

A significant amount of radioactivity was found in the fat from the dibutylamine label. High ^{14}C residues were observed in the liver (1.35 mg/kg equivalents) and fat (0.30 mg/kg equivalents). After 14 days of depuration all residues had decreased to less than 0.05 mg/kg except in fat (0.37 mg/kg) and skin.

Dibutylamine was the main metabolite in the extractable fraction of the thigh muscle (22.5 % of the TRR) and liver (39.6% of the TRR) at day 0. Essentially all the radioactive residue (>95% of the TRR) in the 14-day fat sample was isolated as fatty acid. Derivatization of this fraction with bromoacetophenone and isolation of the derivatised fatty acids indicated that the radiocarbon had been mainly incorporated into palmitic (33.3% of the TRR), oleic (37.0%), stearic (7.7%) and linoleic (6.2%) acids.

The metabolism of carbosulfan in hens begins with hydrolysis to the 7-phenol, carbofuran and dibutylamine. Further hydrolysis and oxidation give 3-hydroxycarbofuran, the 3-hydroxy-7-phenol, 3-keto-7-phenol, 3-ketocarbofuran, butylamine, substituted butanols and 5-hydroxycarbofuran. Metabolism studies in rats and goats evaluated by the 1997 JMPR show a common metabolic pathway.

Residue analysis

Analytical methods are available for the determination of carbosulfan, carbofuran, 3-hydroxycarbofuran, dibutylamine and phenolic metabolites in plant and animal products. Carbosulfan and carbofuran in vegetables are extracted with hexane/2-propanol or hexane/acetone and the partitioned extract is cleaned up on a Florisil or aminopropyl SPE cartridge. The compounds are determined by GC with NPD, GC/MS or GC/MS/MS detection. The LOQ ranges from 0.01 to 0.05 mg/kg.

In a method developed in 2000, carbosulfan and carbofuran are determined by HPLC using two post-column reactors, one with H_2SO_4 to hydrolyse carbosulfan to carbofuran and the other with *o*-phthalaldehyde + *N,N*-dimethyl-2-mercaptoethylamine to form a chromophore for fluorescence detection. The LOQ was 0.05 mg/kg.

The extraction of 3-hydroxycarbofuran in vegetables was with acid hydrolysis, and was followed by partition with dichloromethane and further clean-up on a Florisil cartridge. In another method, with an alumina clean-up, carbosulfan, carbofuran and hydroxycarbofuran were determined without acid hydrolysis.

Phenolic fractions are derivatized with pentafluorobenzyl bromide (PFBBR), and 3-hydroxy-7-phenols also by ethylation, before analysis. Dibutylamine fractions are derivatized with dansyl chloride. Both the phenolic and dibutylamine derivatives are determined by GC-MS with single ion monitoring.

Validations were provided for tobacco, potatoes, a leafy vegetable and cotton seed (LOQ 0.05 mg/kg).

Results from supervised residue trials

Potatoes. Ten trials were conducted in France with soil application of carbosulfan at the GAP rate (1.25 kg ai/ha). Residues were <0.01 (3), <0.03 (4), <0.05 and 0.02 (2) mg/kg carbosulfan. Six trials were conducted at 1.85 kg ai/ha

In 4 trials in Italy according to GAP (0.75 kg ai/ha soil treatment), carbosulfan residues were <0.05 mg/kg.

In 2 trials conducted in Japan at the GAP rate (1.8 kg ai/ha, soil treatment), residues were <0.005 mg/kg. Two other trials conducted in Japan at a higher rate gave the same results.

One trial conducted in the Philippines with foliar application at 0.3 kg/ha (GAP 0.2 kg ai/ha) gave residues of <0.05 mg/kg. One trial in Brazil according to GAP (0.24 kg ai/ha and 21 days PHI) also gave residues of <0.05 mg/kg, as did two trials at 0.48 kg ai/ha.

Sixteen trials complying with GAP using soil application gave residues of <0.005 (2), <0.01 (3), <0.03 (4), <0.05 (5) and 0.02 (2) mg/kg. Samples were also analysed for residues of carbofuran and 3-hydroxycarbofuran. No residues of 3-hydroxycarbofuran were found (<0.005, <0.01 or <0.05 mg/kg).

The Meeting estimated a maximum residue level of 0.05 mg/kg and an STMR of 0.03 mg/kg for carbosulfan in potato.

Residues of carbofuran + 3-hydroxycarbofuran were <0.005 (2), <0.01 (4), <0.05 (5), 0.02, 0.03, 0.06, 0.07 and 0.11 mg/kg.

The Meeting estimated a maximum residue level of 0.2 mg/kg, an STMR of 0.05 mg/kg and an HR of 0.11 mg/kg for carbofuran in potato.

Sugar beet. Field trials on sugar beet were reported from France (GAP 0.75-1 kg ai/ha, soil treatment), Belgium (GAP 0.75 kg ai/ha, soil treatment), Spain and Italy (0.6 kg ai/ha, soil treatment).

Thirteen trials conducted in France with soil treatment according to GAP gave carbosulfan residues of <0.05 (9), 0.06 (2), 0.15 and 0.18 mg/kg.

In two trials in Belgium according to GAP for soil treatment residues were <0.02 mg/kg. Four trials in Spain and Italy with soil application according to GAP gave residues of <0.05 mg/kg

Six trials in France, 2 in Switzerland and 1 in Hungary were conducted above the GAP rate.

Nineteen trials according to GAP with soil application gave carbosulfan residues of <0.02 (2), <0.05 (13), 0.06 (2), 0.15 and 0.18 mg/kg.

The Meeting estimated a maximum residue level of 0.3 mg/kg and an STMR of 0.05 mg/kg for carbosulfan in sugar beet.

Samples from the same trials were analysed for carbofuran and 3-hydroxycarbofuran. All residues were below the LOQ, except in one trial where the residue of 3-hydroxycarbofuran was 0.06 mg/kg. Residues of carbofuran + hydroxy-carbofuran were <0.05 (18) and 0.11 mg/kg.

The Meeting estimated a maximum residue level of 0.2 mg/kg and an STMR of 0.05 mg/kg for carbofuran in sugar beet.

Maize. Field trials with soil treatment on maize were reported from Belgium (GAP 0.6 kg ai/ha, 2 trials), France (GAP 0.5 to 0.75 kg ai/ha, 9 trials), Germany (no GAP for soil application, 3 trials) and Italy (0.5 kg ai/ha, 2 trials). In the eight trials according to GAP residues were <0.05 mg/kg. Residues in four other trials conducted at a higher rate (1.5 kg ai/ha) were at the same level. No residues of carbofuran or 3-hydroxycarbofuran were found in any of the trials (<0.05 mg/kg).

Field trials were conducted with seed treatment in the Philippines (GAP 5g ai/kg seed, 1 trial) and Brazil (GAP 0.5 to 0.7 kg ai/100 kg seed, 14 trials). Residues in grain from 9 trials according to GAP and in 6 trials at a higher rate in Brazil and the one in the Philippines below maximum GAP gave residues <0.01 or <0.05 mg/kg.

The Meeting agreed that soil application is the critical use and estimated a maximum residue level of 0.05* mg/kg and an STMR of 0 for both carbofuran and carbofuran in maize grain.

Rice. Three trials with soil application in India complying with GAP (1 kg ai/ha, 37 days PHI) gave residues of <0.01 (2) and 0.02 mg/kg carbofuran in grain. 3 other trials at a double rate gave residues of <0.01 to 0.03 mg/kg.

Of 4 trials in Korea with soil application, only one was according to GAP, giving residues of <0.02 mg/kg in husked rice.

In 8 trials in Japan with seedling treatment, 4 were according to GAP, giving carbofuran residues in husked rice of <0.005 mg/kg. Four trials conducted at half or twice the rate gave the same results.

8 trials were carried out in China (GAP 0.75 kg ai/ha, 30 days PHI, foliar application) but the PHI was \geq 69 days. The residues were <0.002 mg/kg.

In 7 trials in Brazil with seed treatment within GAP (5g ai/kg seed), no residues occurred in grain (<0.01 or <0.05 mg/kg). 11 trials at a higher rate gave the same results.

In 7 trials in China above the GAP for seed treatment residues were also <0.01 mg/kg in husked rice.

Trials using soil application according to GAP were too few to support a recommendation.

Residues from the seed treatment trials according to GAP in Brazil were <0.01 (2) and <0.05 mg/kg (5).

With the support of the trials conducted at a higher rate in Brazil, the Meeting estimated a maximum residue level of 0.05* mg/kg and an STMR of 0 for carbofuran in rice grain.

Two field trials according to GAP in Brazil gave residues of carbofuran and 3-hydroxycarbofuran of <0.01 mg/kg in grain. Residues in husked rice in 35 trials in China, Korea and Japan at a higher rate than the recommended GAP were all below the LOQs.

The residues resulting from the uses of carbofuran gave residues covered by the uses of carbofuran in husked rice.

The Meeting recommended maintaining the recommendation of the 2002 JMPR for carbofuran of 0.1 mg/kg in husked rice.

Cotton seed. Twelve trials were carried out in Greece and Spain according to GAP (0.375 kg ai/ha, 2 applications, 28 days PHI, foliar application). The residues of carbofuran, carbofuran and 3-hydroxycarbofuran were all <0.05 mg/kg.

In 5 trials in Australia according to GAP (0.5 to 1 kg ai/ha, foliar application), carbofuran residues were <0.05 (4) and 0.03 mg/kg.

In 3 trials in Brazil complying with GAP (0.12 kg ai/ha, foliar application) residues of carbofuran, carbofuran and 3-hydroxycarbofuran were all <0.01 (2) and <0.05 mg/kg.

In 2 trials carried out in Brazil using seed treatment according to GAP (7g ai/kg), residues were <0.05 (2) mg/kg.

Trials according to GAP with foliar treatment gave residues of <0.01 (2), <0.05 (17) and 0.03 mg/kg.

The Meeting estimated a maximum residue level and an STMR of 0.05 mg/kg for carbosulfan in cotton seed

Fourteen trials according to GAP gave residues of carbofuran + 3-hydroxycarbofuran of <0.01 (2) and <0.05 (12) mg/kg.

The residues resulting from the uses of carbofuran were at the same levels as those from the uses of carbosulfan in cotton seed. The Meeting confirmed the recommendation of the 2002 JMPR for carbofuran of 0.1 mg/kg in cotton seed.

Feed items

Sugar beet leaves and tops. Residues from trials according to GAP in Belgium, Spain, Italy and France were <0.02 (2) and <0.05 (17) mg/kg of carbosulfan. Trials at a double rate gave the same results.

As no residues are expected in sugar beet tops, even at higher rates, the residues, allowing for 23% dry matter (DM) (FAO Manual, 2002), would probably be below the LOQ.

The Meeting estimated a maximum residue level of 0.05* mg/kg and an STMR of 0 for carbosulfan in sugar beet leaves or tops.

Residues of carbofuran + 3-hydroxycarbofuran in the same trials were 0.05 (17), 0.10 and 0.13 mg/kg.

Allowing for 23% DM, the median and highest residues in sugar beet forage were 0.217 mg/kg and 0.56 mg/kg.

The Meeting estimated a maximum residue level of 0.7 mg/kg and an STMR of 0.217 mg/kg for carbofuran in sugar beet leaves or tops.

Maize forage (whole plant). In 2 trials in Brazil according to GAP (seed treatment) residues were <0.01 mg/kg. 13 trials conducted in Belgium, France, Germany and Italy according to GAP showed residues of <0.05 mg/kg in whole plant. In 4 trials at a higher rate the results were the same.

Residues of carbosulfan in trials according to GAP were <0.01 (2) and <0.05 (13) mg/kg.

Allowing for 40% DM, the median and the highest residue of carbosulfan in maize forage would be (<)0.13 mg/kg, but as no residues are expected in maize forage, even at higher rates, the residues allowing for 40% DM would probably be below the LOQ.

The Meeting estimated a maximum residue level of 0.05* mg/kg and an STMR of 0 for carbosulfan in maize forage on a dry weight basis.

Fifteen trials according to GAP gave residues of carbofuran + 3-hydroxycarbofuran of <0.01 (2), <0.05 (11), 0.11 and 0.14 mg/kg.

Allowing for 40% DM, the median and highest residues in maize forage were (<)0.13 mg/kg and 0.35 mg/kg respectively.

The Meeting estimated a maximum residue level of 0.5 mg/kg and an STMR of 0.13 mg/kg for carbofuran in maize forage, on a dry weight basis.

Rice straw. In 2 field trials conducted according to GAP in Brazil (seed treatment) residues were <0.01 mg/kg for carbofuran, carbofuran and 3-hydroxycarbofuran. There were too few trials according to GAP to make a recommendation.

Processing

No information was provided.

Animal feeding studies

In one feeding study evaluated by the 1997 JMPR, dairy cows were dosed at 1, 3 and 50 ppm carbofuran in the diet for 28 days. At 50 ppm residues were <0.05 mg/kg in kidney, liver and muscle, 0.012 mg/kg in milk and 0.076 mg/kg in fat. Except for one sample from 10 ppm (0.007 mg/kg of 3-hydroxycarbofuran), no residues were found from the lower feeding levels in any milk sample. No information was provided on the residues in fat at lower feeding levels.

Farm animal dietary burden

The Meeting estimated the farm animal dietary burden of carbofuran from the residues in animal feeds resulting from its use.

Maximum farm animal burden of carbofuran

Commodity	Group	Residue mg/kg	Basis	% dry matter	Residue, dry basis mg/kg	% in diet			Residue contribution mg/kg		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
Maize	GC	0.05	MRL	88	0.06			80			0.05
Maize forage	AF	0.05	MRL	40	0.13	5	50	0	0.01	0.065	0
Sugar beet	AV	0.05	MRL	23	0.22	20	10	0	0.04	0.02	0
Dry citrus	AB	0.1	MRL	91	0.11						
Potato	VR	0.05	MRL	20	0.25	75	40	0	0.19	0.10	0
Rice	GC	0.05	MRL	88	0.06						
Total									0.24	0.185	0.05

STMR farm animal burden of carbofuran

Commodity	Group	Residue mg/kg	Basis	% dry matter	Residue, dry basis mg/kg	% in diet			Residue contribution mg/kg		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
Maize	GC	0	STMR	88	0						0
Maize forage	AF	0	STMR	40	0						
Sugar beet	AV	0	STMR	23	0	20	10	0	0	0	
Dry citrus pulp	AB	0.008	STMR-P	91	0.009		20			0.002	
Potato	VR	0.03	STMR	20	0.15	75	40		0.11	0.06	0
Rice	GC	0	STMR	88	0						
STMR dietary burden									0.11	0.062	0

Residue levels in animal commodities

Cattle. No carbosulfan was detected in liver, kidney or meat of cattle at a 50 ppm feeding level which is over 200 times the estimated burden. Carbosulfan was present in fat and in milk (0.076 and 0.012 mg/kg) at this feeding level.

The Meeting agreed that it was unlikely that residues of carbosulfan would be detected in products from animals fed with commodities treated with this compound.

The Meeting estimated a maximum residue level of 0.05* mg/kg, an STMR of 0 and an HR of 0 in for carbosulfan in meat (fat) and edible offal of mammals, and a maximum residue level of 0.03* mg/kg and an STMR and HR of 0 for carbosulfan in milks.

Poultry. In a metabolism study in hens no residues of carbosulfan or the metabolites carbofuran and 3-hydroxycarbofuran were found at a feeding level of 0.5 ppm in tissues (<0.002 mg/kg). Residues in eggs were 0.18 mg/kg eq in yolks and 0.014 mg/kg in whites at a 5 ppm feeding level. In the yolk 85% of the radioactivity was due to unknown products of high molecular weight (>500). Residues of carbosulfan were <0.002 mg/kg.

The Meeting agreed that it was unlikely that residues of carbosulfan would be detected in products from animals fed with commodities treated with this compound.

The Meeting estimated a maximum residue level at the limit of quantification, 0.05* mg/kg, and an STMR and HR of 0 for carbosulfan in eggs, meat and offal of poultry

The farm animal burden estimated by the 2002 JMPR was based on a diet containing 80% of alfalfa fodder and there are few animal feed items.

The Meeting agreed to confirm the 1997 recommendations of 0.05* mg/kg for carbofuran in a range of animal commodities.

DIETARY RISK ASSESSMENT

Carbosulfan

Long-term intake

The ADI for carbosulfan is 0- 0.01 mg/kg body weight/day. International estimated daily intake (IEDI) was calculated for commodities for human consumption for which STMRs were estimated in this evaluation. The results are shown in Annex 3.

International Estimated Daily Intakes for the five GEMS/Food regional diets, based on estimated STMRs, ranged from 0 to 1% of the ADI. The Meeting concluded that the intake of residues of carbosulfan resulting from its uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The International estimated short-term intakes (IESTI) for carbosulfan were calculated for commodities for which STMR and HR values were estimated in this evaluation and for which data on consumption (large portion and unit weight) were available. The results are shown in Annex 4.

The acute RfD for carbosulfan is 0.02 mg/kg. The IESTI represented 0 to 4% of the acute RfD for children and 0 to 2% of the acute RfD for the general population. The Meeting concluded that

the short-term intake of residues of carbosulfan from uses on the commodities that have been considered by the JMPR is unlikely to present a public health concern.

Carbofuran

Long-term intake

Estimates of carbofuran residues arising from the use of carbosulfan, made at this Meeting, do not affect the assessment carried out at the 2002 JMPR for this compound.

Short-term intake

The International estimated short-term intakes (IESTI) for carbofuran were calculated for commodities for which STMR and HR values were estimated in this evaluation and for which data on consumption (large portion and unit weight) were available. The results are shown in Annex 4.

The acute RfD for carbofuran is 0.009 mg/kg. The IESTI represented 0 to 50% of the acute RfD for children and 0 to 20% of the acute RfD for the general population. The Meeting concluded that the short-term intake of residues of carbofuran from uses on the commodities that have been considered by the JMPR is unlikely to present a public health concern.

4.4 CYPRODINIL (207)

TOXICOLOGY

Cyprodinil is the ISO approved name for (4-cyclopropyl-6-methyl-pyrimidin-2-yl)-phenyl-amine. Cyprodinil is a systemic fungicide that acts by inhibiting the biosynthesis of methionine. Cyprodinil has not been evaluated previously by JMPR.

In studies of metabolism in rats, radiolabelled cyprodinil administered by gavage as a single dose of 0.5 or 100 mg/kg bw, or as repeated doses of 0.5 mg/kg bw per day for 14 days, was rapidly absorbed from the gastrointestinal tract and excreted. Approximately 75% (range 71–85%) of an orally administered dose was absorbed over 48 h. At doses of both 0.5 and 100 mg/kg bw, two plasma level maxima of radioactivity were observed at approximately 0.5–1 h and 8–12 h, probably owing to reabsorption of material excreted in the bile. Approximately 92–97% of the administered dose was eliminated within 48 h in the urine (48–68%), faeces (29–47%), and bile (accounting for up to 35.4% of the dose in cannulated rats), with elimination being almost complete by 7 days. Seven days after single or repeated oral administration at the low dose, total tissue residues accounted for 0.15–0.60% of the administered dose. Cyprodinil was primarily metabolized by hydroxylation of the phenyl and pyrimidine rings and methyl group, and excreted mainly as glucuronide or sulfate conjugates in urine, faeces and bile. Approximately 3–8% of the parent compound was detected in the faeces. Excretion, distribution and metabolite profiles were essentially independent of dose, pre-treatment and site of radiolabel, although there were some quantitative sex-dependent differences in urinary metabolites.

Cyprodinil has low toxicity when administered by the oral, dermal or inhalation routes. LD₅₀ values after oral administration were >2000 and >5000 mg/kg bw in rats and mice, respectively. The LD₅₀ in rats treated dermally was >2000 mg/kg bw. The LC₅₀ in rats treated by inhalation was >1.20 mg/l (the highest attainable concentration) after an exposure of 4 h. Clinical signs of toxicity such as piloerection, hunched posture, dyspnoea, and reduced locomotor activity were seen. Cyprodinil was not a skin or eye irritant but was a skin sensitizer.

In short-term studies in mice, rats and dogs, dosing with cyprodinil in the diet or by gavage resulted in reduced body-weight gain and reduced food consumption at higher doses. These effects were seen at doses of 6000 ppm (equal to 849 mg/kg bw per day), 1000 mg/kg bw per day, and at and above 15 000 ppm (equal to 446 mg/kg bw per day) in mice, rats and dogs, respectively. The major target organs were the liver, kidney, and thyroid in rats, and the liver in mice and dogs. Increases in liver weights were observed in mice at 6000 ppm (equal to 849 mg/kg bw per day) and in rats at or above 2000 ppm (equal to 134 mg/kg bw per day). Increases in thyroid weight were observed in rats at and above 2000 ppm (equal to 134 mg/kg bw per day). Some mild to moderate histopathological changes in the liver, such as hepatocyte hypertrophy and multifocal single cell hepatocyte necrosis, were seen in both mice and rats at and above 2000 ppm (equal to 25 mg/kg bw per day in mice and equal to 134 mg/kg bw per day). In the kidneys, adverse effects were manifested in rats as chronic tubular lesions and chronic kidney inflammation at and above 2000 ppm (equal to 134 mg/kg bw per day). The NOAEL in a 90-day study of toxicity in mice was 500 ppm (equal to 73.3 mg/kg bw per day). The NOAEL in a 28-day study in rats treated by gavage was 100 mg/kg bw per day. The NOAELs in a 90-day study of toxicity in rats was 300 ppm (equal to 19 mg/kg bw per day). The NOAELs in a 90-day and a 1-year study of toxicity in dogs were 7000 ppm (equal to 210 mg/kg bw per day) and 2500 ppm (equal to 66 mg/kg bw per day), respectively.

In studies of chronic toxicity and carcinogenicity in mice and rats, there were no treatment related neoplastic findings. In mice, a slightly increased incidence of hyperplasia in acinar cells of the exocrine pancreas in males was observed at the highest dose tested, 5000 ppm (equal to 558 mg/kg bw per day). The NOAEL for systemic toxicity in mice was 2000 ppm (equal to 196 mg/kg bw per day) based on an increase in the incidence of focal and multifocal hyperplasia of the exocrine pancreas in males, reduced body weights in males and females, increased relative kidney weights in females, and increased relative liver weights in males and females, seen at the highest dose tested. In rats, histopathological changes in the liver (spongiosis hepatitis) and increased liver weights were observed at and above 1000 ppm (equal to 35.6 mg/kg bw per day). The NOAEL for systemic toxicity in rats was 75 ppm (equal to 2.7 mg/kg bw per day), based on a dose-related increase in the incidence of spongiosis hepatitis at doses of 1000 and 2000 ppm in males. There was no evidence of significant chronic toxicity in females. Cyprodinil was not carcinogenic in mice or rats.

Cyprodinil gave negative results in a battery of studies of genotoxicity in vitro in bacteria and cultured mammalian cells, and in a mouse micronucleus test in vivo.

The Meeting concluded that cyprodinil is unlikely to be genotoxic.

In view of the lack of genotoxicity and the absence of carcinogenicity in rats and mice, the Meeting concluded that cyprodinil 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 (4000 ppm, equal to 295 mg/kg bw per day). The NOAEL for parental systemic toxicity was 1000 ppm (equal to 74 mg/kg bw per day) based on decreased body-weight gain in F₀ females at the highest dose tested, 4000 ppm (equal to 295 mg/kg bw per day). The NOAEL for offspring toxicity was 1000 ppm (equal to 74 mg/kg bw per day) based on decreased pup body weights for F₁ and F₂ pups at the highest dose tested. Cyprodinil was not teratogenic in rats and rabbits at doses of up to 1000 and 400 mg/kg bw per day in rats and rabbits, respectively. In the study of developmental toxicity in rats, lower fetal body weights and an increased incidence of delayed ossification at a dose of 1000 mg/kg bw per day were considered to be secondary to maternal toxicity. At the highest dose tested, a slight increase in the number of litters in which pups were born with an extra (13th) rib was observed in rabbits in the presence of maternal toxicity, an effect that was not considered to be toxicologically relevant.

In a study of an acute neurotoxicity in rats, doses of 600 and 2000 mg/kg bw caused reduced activity, hunched posture, piloerection, increased responsiveness to stimuli, and hypothermia; the NOAEL was 200 mg/kg bw. In a study of subchronic neurotoxicity, no signs of neurotoxicity were observed in a functional observation battery, on evaluation of motor activity, or on neuropathological examination, in rats receiving cyprodinil in the diet at concentrations of up to 8000 ppm (equal to

601 mg/kg bw per day), the highest dose tested. The NOAEL was 800 ppm (equal to 54.5 mg/kg bw per day) based on liver, kidney and thyroid histopathology, and reduced body-weight gain seen at the highest dose tested (8000 ppm, equal to 601 mg/kg bw per day).

Several soil and plant metabolites of cyprodinil were investigated in the Ames test and for acute oral toxicity at the limit dose (2000 mg/kg bw). The LD₅₀ for each of these metabolites was > 2000 mg/kg bw and no mutagenic potential was detected.

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 0-0.03 mg/kg bw based on a NOAEL of 2.7 mg/kg bw per day in a 24-month study in rats fed with cyprodinil, on the basis of liver effects (spongiosis hepatitis) seen in males at higher doses, and a 100-fold safety factor.

The Meeting concluded that the establishment of an acute RfD for cyprodinil was not necessary, on the basis of its low acute toxicity, the absence of development toxicity in rats and rabbits, the lack of neurotoxicity following single exposures, and absence of any other toxicological end-point that would be elicited by a single dose.

A toxicological monograph was prepared.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Mouse	18-month study of toxicity and carcinogenicity ^a	Toxicity	2000 ppm, equal to 196 mg/kg bw per day	5000 ppm, equal to 558 mg/kg bw per day
		Carcinogenicity	5000 ppm, equal to 558 mg/kg bw per day ^c	
Rat	2-year study of toxicity and carcinogenicity ^a	Toxicity	75 ppm, equal to 2.7 mg/kg bw per day	1000 ppm, equal to 35.6 mg/kg bw per day
		Carcinogenicity	2000 ppm, equal to 73.6 mg/kg bw per day ^c	
	Multi-generation study of reproductive toxicity ^a	Parental toxicity/offspring toxicity	1000 ppm, equal to 74.0 mg/kg bw per day	4000 ppm, equal to 295 mg/kg bw per day
	Study of developmental toxicity ^b	Maternal toxicity	200 mg/kg bw per day	1000 mg/kg bw per day
		Embryo- and fetotoxicity	200 mg/kg bw per day	1000 mg/kg bw per day
Study of acute neurotoxicity ^b	Neurotoxicity	200 mg/kg bw per day	600 mg/kg bw per day	
Rabbit	Study of developmental toxicity ^b	Maternal toxicity	150 mg/kg bw per day	400 mg/kg bw per day
		Embryo- and fetotoxicity	400 mg/kg bw per day	—
Dog	1-year study of toxicity ^a	Toxicity	2500 ppm, equal to 66.0 mg/kg bw per day	15 000 ppm, equal to 449 mg/kg bw per day

- ^a Diet
^b Gavage
^c Highest dose tested

Estimate of acceptable daily intake for humans

0–0.03 mg/kg bw

Estimate of acute reference dose

Unnecessary

Studies that would provide information useful for the continued evaluation of the compound

Further observations in humans.

Summary of critical end-points for cyprodinil

Absorption, distribution, excretion, and metabolism in mammals

Rate and extent of oral absorption	Rapid; maximum reached in blood by 0.15–1.0 h; about 71–85% absorbed after 48 h
Dermal absorption	At 6 µg/cm ² , in vivo absorption in rats was 21.7% in 0–24 h; at 870 µg/cm ² , in vivo absorption was 1.9% in 0–24 h
Distribution	Extensive; highest concentrations in liver, kidney, spleen, and blood
Potential for accumulation	No evidence of significant accumulation; about 0.2–0.6% of the total dose found in tissues after 168 h
Rate and extent of excretion	Excretion was rapid; >90% excreted in to urine (48–67%) and faeces (27–45%) within 48 h
Metabolism in animals	Very extensive; metabolic pathways include hydroxylation of the phenyl and pyrimidyl rings and conjugation with sulfate or glucuronic acid; limited cleavage of bond between phenyl and pyrimidyl rings; about 3–8% unchanged cyprodinil in faeces
Toxicologically significant compounds	Cyprodinil

Acute toxicity

Mouse, LD ₅₀ , oral	> 5000 mg/kg bw
Rat, LD ₅₀ , oral	> 2000 mg/kg bw
Rat, LD ₅₀ , dermal	> 2000 mg/kg bw
Rat, LC ₅₀ , inhalation	> 1.2 mg/l (maximum attainable concentration, 4-h exposure, nose only)
Rabbit, dermal irritation	Not an irritant

Rabbit, eye irritation	Not an irritant
Skin sensitization	Sensitizing (maximization test)
<i>Short-term studies of toxicity</i>	
Target/critical effect	Histopathological findings in liver, kidneys and thyroid
Lowest relevant oral NOAEL	19 mg/kg bw per day(90-day study in rats)
Lowest relevant dermal NOAEL	No suitable study is available
Lowest relevant inhalation NOAEL	No studies are available
<i>Genotoxicity</i>	No genotoxic potential
<i>Long-term studies of toxicity and carcinogenicity</i>	
Target/critical effect	Degenerative liver lesions (spongiosis hepatitis) in males, in rats
Lowest relevant NOAEL	2.7 mg/kg bw per day (2-year study in rats)
Carcinogenicity	No carcinogenicity in mice and rats
<i>Reproductive toxicity</i>	
Reproduction target/critical effect	Reduced pup body weight
Lowest relevant reproductive NOAEL	74 mg/kg per day (rats)
Developmental target/critical effect	No toxicologically relevant effects were observed
Lowest relevant developmental NOAEL	400 mg/kg per day (rabbits)
<i>Neurotoxicity/delayed neurotoxicity</i>	
Acute neurotoxicity	No evidence of neuropathology at doses of up to 2000 mg/kg bw in rats; NOAEL was 200 mg/kg bw based on clinical signs
90-day study of neurotoxicity	No evidence of neurotoxicity or neuropathology; NOAEL was 54.5 mg/kg bw per day based on liver, kidney and thyroid histopathology
<i>Other toxicological studies</i>	
Metabolites: study of acute toxicity	LD ₅₀ of > 2000 mg/kg bw for four metabolites ^a
Metabolite: 90-day study, in diet	NOAEL of 79.5 mg/kg bw per day for CGA 249287
Metabolites: genotoxicity	No genotoxic potential for four metabolites ^a
<i>Medical data</i>	Limited data; slight eye irritation and sensitization reported in workers

Summary**Value****Study****Safety factor**

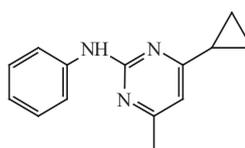
ADI	0–0.03 mg/kg bw	2-year study of toxicity and carcinogenicity	100
Acute RfD	Not allocated (unnecessary)	Not applicable	Not applicable

^a CGA 249287: (4-cyclopropyl-6-methyl-pyrimidine-2-ylamine)
 CGA 275535: 3-(4-cyclopropyl-6-methyl-pyrimidine-2-ylamino)-phenol
 NOA 422054: (4-cyclopropyl-6-hydroxymethyl-pyrimidine-2-ylamine)
 CGA 321915: 4-cyclopropyl-6-methyl-pyrimidin-2-ol

RESIDUE AND ANALYTICAL ASPECTS

Residue and analytical aspects of cyprodinil were considered for the first time by the present Meeting.

Cyprodinil, a member of the anilinopyrimidine group, is a systemic foliar and seed dressing fungicide that acts as an inhibitor of methionine biosynthesis. It has registered uses in many countries on horticultural and cereal crops.



IUPAC name: 4-cyclopropyl-6-methyl-*N*-phenylpyrimidin-2-amine
 Chemical Abstracts name: 4-cyclopropyl-6-methyl-*N*-phenyl-2-pyrimidinamine

The Meeting received information on cyprodinil 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.

Cyprodinil, labelled uniformly with ¹⁴C in the phenyl ring or at C-2 of the pyrimidine ring was used in all the metabolism studies.

Animal metabolism

The Meeting received reports of animal metabolism studies on rats, lactating goats and laying hens. The most common metabolic pathways in animals begin with hydroxylation of the methyl group or at position 5 on the pyrimidine ring or position 4 on the phenyl ring. Typically the hydroxy compounds form sulfate or glucuronic acid conjugates ready for elimination. Parent cyprodinil is a minor part of the residue and was identified in goat liver, fat and muscle and in eggs. Cleavage at the amino bridge was a minor route. The metabolism of cyprodinil in rats and farm animals is similar.

Rats. When rats were dosed orally with labelled cyprodinil, almost all (92-97%) of the radiolabel was excreted within 48 h. Most of the excretion was in the urine (48-68%) with 29-47% in the faeces. A main metabolite in faeces was identified as (6-cyclopropyl-2-phenylaminopyrimidin-4-yl)methanol. Fifteen metabolites and cyprodinil were identified in the tissues of dosed orally rats. The metabolites were mostly mono-, di- and trihydroxy compounds present as sulfate or glucuronic acid conjugates. The most common sites for hydroxylation were 4-phenyl, 5-pyrimidine and the 6-methyl group. Cleavage at the amino bridge was slight.

Goats. Lactating dairy goats were dosed orally once daily for 4 consecutive days by gelatin capsule with 0.2 mg/kg bw/day per-day of [¹⁴C-phenyl]cyprodinil or 0.19 mg/kg bw/day [2-¹⁴C-pyrimidine]cyprodinil equivalent to 8.0 and 8.9 ppm cyprodinil in the diet respectively. A parallel

high-dose study was conducted with 9.9 and 9.8 mg/kg bw/day per-day equivalent to 267 and 286 ppm cyprodinil in the diet respectively. In the low-dose goats 0.13% and 0.53% of the dose was found in the milk. In the high-dose animals ¹⁴C levels were much higher in liver and kidney (0.17-0.28 mg/kg as cyprodinil) than in muscle or fat (0.006-0.01 mg/kg). In the low-dose animals parent cyprodinil at 0.003 (1.7% of the TRR, total radioactive residue) and 0.016 mg/kg (5.8% of the TRR) was identified in liver but not in other tissues. Hydroxylated and conjugated metabolites (4-phenyl and 5-pyrimidine) were identified in the milk, kidney and liver.

Lactating dairy goats were dosed orally directly into the rumen once daily for 4 consecutive days by gelatin capsule with [¹⁴C-phenyl]cyprodinil at 4.1 mg/kg bw equivalent to 100 ppm cyprodinil in the diet. Most of the metabolites were products of hydroxylation at the 4-position on the phenyl ring, the 5-position on the pyrimidine ring and on the methyl group, which then formed glucuronic acid or sulfate conjugates. Parent cyprodinil was the major component of the residue in fat (68% of the TRR). No cyprodinil was detected in milk, but 57% of the residue in milk was accounted for by metabolite 4-(4-cyclopropyl-6-methylpyrimidine-2-ylamino)phenol and its glucuronic acid and sulfate conjugates. Metabolites identified in goat tissues and milk were mainly the same as in rat tissues.

Hens. Laying white Leghorn hens were dosed orally once daily for 4 consecutive days by gelatin capsule with 0.4 mg/kg bw of [¹⁴C-phenyl]cyprodinil or [2-¹⁴C-pyrimidine]cyprodinil, equivalent to 4.7 and 4.5 ppm cyprodinil in the diet respectively. The radiolabel was present at higher levels in the liver and kidney (0.041-0.12 mg/kg) than in other tissues or eggs (0-0.01 mg/kg). A parallel high-dose study was conducted with 19 mg/kg bw/day per-day equivalent to 215 or 226 ppm cyprodinil in the diet. Elimination of the ¹⁴C was rapid with 98% and 2% of the daily dose recovered in excreta and cage wash respectively in the first 24 h.

The ¹⁴C level in meat was too low for identification. The nature of the residue in skin and fat was also not further examined. Parent cyprodinil was not identified in liver, which had the highest level of ¹⁴C. The main identified components of the liver residue were glucuronic acid and sulfate conjugates of 4-(4-cyclopropyl-6-methylpyrimidin-2-ylamino)phenol. Cyprodinil was present at low levels in eggs (0.002 mg/kg in whites to 0.011 mg/kg in yolks, 8-12% of the TRR) from the high-dose experiment.

Plant metabolism

The Meeting received reports of plant metabolism studies on wheat, apples, peaches, tomatoes and potatoes. Cyprodinil is quite persistent and is generally the major identifiable component of the residue. It is slowly absorbed into the plant tissue where it is hydroxylated and conjugated with sugars. Cleavage of the amino bridge is a minor route. In apples much of the residue remains in the peel. Similar metabolic pathways occur in all the studied crops.

Wheat. When wheat plants were treated with [2-¹⁴C-pyrimidine]cyprodinil and [¹⁴C-phenyl]cyprodinil at the 6-8 leaf stage at 0.75 kg ai/ha and again at the panicle emergence stage at 0.5 kg ai/ha, levels of parent cyprodinil at harvest were grain 0.018 and 0.022 mg/kg, husks 0.37 and 0.44 mg/kg and straw 0.60 and 0.44 mg/kg. Cyprodinil was the major identifiable component of the residue. The pattern of extractable metabolites in wheat straw from cyprodinil with ¹⁴C in the two positions was generally similar, demonstrating that the amino bridge was usually intact. Hydrolysis experiments suggested the presence of *O*- and *N*-sugar conjugates. Sugar conjugates were identified in straw, husks and grain.

Wheat plants at the 5-leaf stage were treated once with [¹⁴C-phenyl]cyprodinil at a rate of 0.75 kg ai/ha in a greenhouse experiment which demonstrated a half-life of approximately 25 days for cyprodinil in the plant, approximately 50% loss of radiolabel in 35 days by volatility, slow but continued uptake of cyprodinil and very little translocation to new growth.

Peach. When peach trees were sprayed with either [¹⁴C-phenyl]cyprodinil or [2-¹⁴C-pyrimidine]cyprodinil and peaches were harvested 1-day after the last application cyprodinil constituted the major part of the residue. Metabolites were mainly sugar conjugates of hydroxylated cyprodinil. The presence of low levels of 4-cyclopropyl-6-methylpyrimidin-2-ylamine showed the occurrence of limited cleavage at the amino bridge.

Tomato. Greenhouse tomato plants were treated with either [¹⁴C-phenyl] or [2-¹⁴C-pyrimidine]cyprodinil and tomatoes were harvested 14 days after the second treatment. Cyprodinil was the major part of the residue (55-62%). Approximately 20% of the residue was on the surface with the remainder in the tissue. The metabolic pattern was very similar for the two labels showing that the amino bridge had remained intact. Metabolites resulted from hydroxylation at various positions and subsequent conjugation with sugars.

Potato. Greenhouse-grown potato plants were treated 3 times with foliar sprays of either [¹⁴C-phenyl] or [2-¹⁴C-pyrimidine]cyprodinil at 0.56 kg ai/ha and potato tubers were harvested 14 days after the last treatment. Cyprodinil was not identified as a residue component in the harvested tubers. Phenylguanidine was identified as a metabolite at 0.004 and 0.005 mg/kg, and other metabolites were identified in which the cyclopropyl ring was opened. The total levels of the two compounds 2-anilino-4-(3-hydroxypropyl)-6-methylpyrimidin-5-ol and 2-anilino-4-(2-hydroxypropyl)-6-methylpyrimidinamin-5-ol and their *O*-sugar conjugates were 0.015 and 0.018 mg/kg in the two experiments. Some of the ¹⁴C in potatoes (24% from the phenyl label and 13% from the pyrimidine label) was identified as being incorporated into glucose.

Apple. Golden Delicious apple trees growing in containers were sprayed 3 times with [2-¹⁴C-pyrimidine]cyprodinil at 0.050 kg ai/hl and fruit were taken at maturity, 61 days after the last treatment. Of the radiolabel in the whole fruit, 16% was identified, 39% was unextracted and 36% was unidentified and unresolved. Very little residue (<1%) remained on the surface, but most remained in the peel. Parent cyprodinil was the major identified component of the residue at 0.088 mg/kg (11% of the radiolabel). Identified metabolites were 6-cyclopropyl-2-phenylaminopyrimidin-4-ylmethanol and 4-(4-cyclopropyl-6-methylpyrimidin-2-ylamino)phenol present as sugar conjugates, and 4-cyclopropyl-6-methylpyrimidin-2-ylamine.

Environmental fate in soil

The Meeting received information on the fate of cyprodinil during aerobic degradation in a number of soils. At 20°C and moisture levels above 60% field capacity the initial half-life of parent cyprodinil ranged from 11 to 46 days. The rates of loss decreased substantially as the residues aged. Temperature and moisture levels strongly influenced the rate of disappearance with longer half-lives at lower temperatures and moisture levels.

In soil 4-cyclopropyl-6-methyl-pyrimidin-2-ylamine was an important degradation product, demonstrating that amino bridge cleavage occurred readily in soil. This compound and cyprodinil were sufficiently persistent in soil for residues still to be present in the soil at harvest of a root crop.

Hydroxylation at the 3-phenyl position of cyprodinil also produced the important soil product *N*-(3-hydroxyphenyl)-4-cyclopropyl-6-methylpyrimidin-2-ylamine. This compound has a very short half-life (less than 1 day) when it is incubated independently.

Crop rotation

The Meeting received comprehensive data from confined crop rotation studies with ¹⁴C-labelled cyprodinil and from crop rotation trials using unlabelled cyprodinil. In some trials a first crop was treated with cyprodinil while in others bare ground was directly treated with cyprodinil as an extreme case of residues in the soil from the first crop. The normal rotation in the trials was a first crop of wheat followed by a rotation root crop (e.g. sugar beet, radish, turnip), vegetable (e.g. lettuce,

mustard) or cereal (e.g. wheat, maize). The rotation crops were sown from approximately 30 days to 1 year after the last treatment of the first crop or bare ground.

Residues of cyprodinil itself at ≤ 0.06 mg/kg were detected in rotation crops where the treatment-to-sowing interval (TSI) was 1-12 months, e.g. in wheat husks (0.01 mg/kg, TSI 106 days), wheat grain (0.003 mg/kg, TSI 119 days) and radish root (0.001-0.062 mg/kg, TSI 29-366 days).

An important component of the residue at the longer intervals was identified as (2-amino-6-cyclopropylpyrimidin-4-yl)methanol. It may result from plant uptake of the soil product 4-cyclopropyl-6-methylpyrimidin-2-ylamine followed by metabolic hydroxylation of the methyl group. These two compounds were present at 1.5 and 0.5 mg/kg in wheat fodder from a wheat rotation crop sown 119 days after the cyprodinil treatment. Both compounds were at measurable levels (0.016-0.21 mg/kg) in wheat forage and fodder and radish roots from crops sown 1 year after cyprodinil application.

In the unconfined rotational crop studies with unlabelled cyprodinil, parent cyprodinil was not detected (< 0.01 mg/kg) except in wheat plants (0.01 mg/kg). 2-amino-6-cyclopropylpyrimidin-4-ylmethanol and 4-cyclopropyl-6-methylpyrimidin-2-ol were occasionally detected in the range of 0.01-0.13 mg/kg.

The unconfined rotational crop studies suggest that cyprodinil itself will very rarely occur as a residue in rotational crops and then at levels around 0.01 mg/kg.

Analytical methods

The Meeting received descriptions and validation data for analytical methods for cyprodinil and metabolite residues in crops and animal commodities. The methods rely on HPLC and GLC and generally achieve LOQs of 0.01-0.02 mg/kg in crop and animal samples.

Cyprodinil and 6-cyclopropyl-2-phenylaminopyrimidin-4-ylmethanol were taken through the procedures of the US FDA Pesticide Analytical Manual. The compounds were detected by GLC systems with NP detectors and were recovered through procedures for non-fatty foods, but not through those for fatty foods.

Extracts of washed tomato fruits from the metabolism study with [^{14}C -phenyl]cyprodinil were counted for ^{14}C and analysed for cyprodinil by HPLC method REM 141.01. The proportion of cyprodinil in the extract as measured by HPLC was 47% of the total ^{14}C (43-53%, $n = 4$). The metabolism study had found 55% of the ^{14}C in tomato fruits remaining as unchanged cyprodinil. The good agreement suggests that method REM 141.01 was quantitatively extracting the incurred residue. Aqueous methanol is used for extraction.

Stability of pesticide residues in stored analytical samples

The Meeting received information on the stability of cyprodinil, 4-cyclopropyl-6-methylpyrimidin-2-ol and 2-amino-6-cyclopropylpyrimidin-4-ylmethanol in various substrates (crops, farm animal commodities and processed commodities) at freezer temperatures for 1-2 years. Cyprodinil was generally stable for the duration of the testing, i.e. the decrease in residue level was not evident or was less than 30%. Stability in peach samples was questionable, but low and variable procedural recoveries suggested difficulties with the analyses.

2-Amino-6-cyclopropylpyrimidin-4-ylmethanol in radish roots was unstable in freezer storage. Levels dropped below 10% of their initial value within 3 months.

Definition of the residue

Parent cyprodinil is the major identifiable component of the residue when it is used on crops, and is reasonably persistent. It is a very minor residue in animal commodities where it is readily hydroxylated to derivatives that form glucuronic acid and sulfate conjugates. Parent cyprodinil was identified in the liver, fat and muscle of dosed goats and in the eggs from dosed hens.

The log P_{OW} of cyprodinil is 4.0, which suggests that it is probably fat-soluble. Cyprodinil is metabolized quickly so that it does not tend to accumulate in fat. In the dairy cow feeding study at 50 ppm feed dry weight, residues were not detected (<0.01 mg/kg) in the fat or muscle, but were just detected (0.013 mg/kg) in the liver. In the goat metabolism study, cyprodinil levels were higher in the liver than in the fat. Levels of parent cyprodinil were higher in the fat than in the muscle, so residues in the fat are appropriate for monitoring residues in meat.

The Meeting agreed to classify cyprodinil as fat-soluble.

The relevant residue for analysis and enforcement is parent cyprodinil. The same residue would be used for the estimation of dietary intake.

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

cyprodinil.

The definition applies to plant and animal commodities.

The residue is fat-soluble.

Supervised trials

The Meeting received supervised trials data for apples, pears, stone fruits, grapes, strawberries, raspberries, onions, cucumbers, egg plant, tomatoes, sweet peppers, lettuce, beans, peas, kidney beans, barley, rye, wheat, almonds and the straw and fodder of barley, rye and wheat.

In some trials residues were measured on samples taken just before the last application as well as just after it (the “zero day” residue). The former residue expressed as a percentage of the latter provides a measure of the contribution of previous applications to the final residue in use patterns involving multiple applications.

In fruits (pear, peach, plum, grapes, strawberries) the average carryover of residue was approximately 35%, which suggests that 2 applications are likely to produce a higher residue level than one application, but 3 or more applications should not produce residue levels significantly different from 2. In vegetables the carryover was lower and less consistent: peas (pods) 0%, beans, lettuce, cucumbers and peppers approximately 10% and tomatoes 36%, suggesting that the number of applications may influence the residue in tomatoes but probably not in other crops.

Residue data were evaluated only where labels (or translations of labels) describing the relevant GAP were available to the Meeting.

Apples. No labels were available for the use of cyprodinil on apples in France or Switzerland, so the residue data from those countries could not be evaluated.

GAP for apples in the USA allows 4 foliar applications of 0.26 kg ai/ha to apples until the end of flowering with 72 days PHI. Cyprodinil residues in apples from 10 US trials meeting these conditions were <0.02 (5), 0.02 (3), 0.022 and 0.024 mg/kg.

The Meeting estimated a maximum residue level and an STMR for cyprodinil in apples of 0.05 and 0.02 mg/kg respectively.

Pears. Cyprodinil may be applied to pears in Italy at 0.38 kg ai/ha and harvested 14 days after the last application. In 5 trials in Italy and one in France that matched Italian GAP cyprodinil residues in pears were 0.03, 0.05, 0.13, 0.33, 0.51 and 0.61 mg/kg.

In Spain cyprodinil may be used on pears at 0.38 kg ai/ha with harvest permitted 14 days after the last application. In 2 trials matching Spanish GAP the cyprodinil residues were 0.19 and 0.34 mg/kg.

Cyprodinil may be used at 0.26 kg ai/ha on pears in the USA with a PHI of 72 days. In 6 US trials matching GAP cyprodinil residue levels were <0.02 (4), 0.025 and 0.027 mg/kg.

The data sets from Europe and the USA appeared to be from different populations and so were not combined. The 8 residues from Europe in rank order (median underlined) were 0.03, 0.05, 0.13, 0.19, 0.33, 0.34, 0.51 and 0.61 mg/kg.

The Meeting estimated a maximum residue level and an STMR for cyprodinil in pears of 1 and 0.26 mg/kg respectively.

Stone fruits

In Italy cyprodinil may be applied to apricots at 0.38 kg ai/ha with harvest 7 days after the last application. In trials in Greece and Italy matching these conditions residue levels in apricot pulp (Greece) and whole fruit (Italy) were 0.22 and 0.03 mg/kg respectively.

The US maximum registered use for sour cherries is 0.53 kg ai/ha with a PHI of 2 days and a maximum seasonal treatment of 1.1 kg ai/ha. US trials with an application rate of 0.56 kg ai/ha (5 applications) and a PHI of 1-day did not exactly match GAP, but cyprodinil is a reasonably persistent residue so 1-day data were considered adequate. The 5 applications were excessive compared with the allowed seasonal maximum but in view of the previous information on carryover of cyprodinil residues the Meeting agreed that the conditions of the residue trials were sufficiently close to GAP to allow evaluation for cherries. The same argument applies to the US trials on peaches and plums. Residue levels in the cherries from the 11 trials were 0.40, 0.46, 0.58, 0.68, 0.78, 0.98, 1.4, 1.5, 1.5, 1.7 and 1.7 mg/kg.

In Italy cyprodinil may be applied to peaches at 0.38 kg ai/ha with a 7 days PHI. Cyprodinil residues from 2 trials in Greece and 5 trials in Italy meeting these conditions (0.30 kg ai/ha accepted as GAP, residues at 14 days higher than at 7 days in some cases) were 0.12, 0.13, 0.14, 0.20, 0.37 (pulp), 0.45, and 0.58 mg/kg. In a single trial on nectarines in Italy according to GAP the residue was 0.36 mg/kg.

French GAP allows an application rate of 0.19 kg ai/ha and a PHI of 14 days for cyprodinil use on peaches. In 2 trials where the application rate was 0.23 kg ai/ha (sufficiently close to 0.19 kg ai/ha) the residues 14 days after treatment were 0.09 and 0.1 mg/kg.

The US maximum registered use for peaches is 0.53 kg ai/ha with a PHI of 2 days and a maximum seasonal treatment of 1.1 kg ai/ha. US trials with an application rate of 0.56 kg ai/ha (5 applications) and a PHI of 1-day were accepted as valid (see discussion of cherries). Cyprodinil residues in the 13 acceptable trials were 0.26, 0.59, 0.60, 0.67, 0.68, 0.80, 0.83, 0.88, 0.92, 1.0, 1.0, 1.2 and 1.3 mg/kg.

In France cyprodinil is registered for use on plums at 0.19 kg ai/ha with a 14 days PHI. Trials at 0.23 kg ai/ha were accepted as within maximum GAP. Residue levels in plums in 4 French trials matching GAP were 0.08 and 0.14 mg/kg in the pulp and 0.06 and 0.13 mg/kg in the whole fruit. The

Meeting accepted that residue levels in the pulp were a reasonable approximation to residue levels in the whole fruit. The residue in plums from a Swiss trial matching French GAP was 0.14 mg/kg.

In Italy cyprodinil may be applied to plums at 0.38 kg ai/ha with a 7 days PHI. Cyprodinil residues from 2 trials in Italy meeting these conditions were 0.12 and 0.13 mg/kg.

The US maximum registered use for cyprodinil on plums is 0.53 kg ai/ha with a PHI of 2 days and a maximum seasonal treatment of 1.2 kg ai/ha. US trials with an application rate of 0.56 kg ai/ha (5 applications) and a PHI of 1 day were accepted as valid, as with cherries. Cyprodinil residues in the 9 acceptable trials were 0.067, 0.080, 0.10, 0.19, 0.22, 0.43, 0.50, 0.54 and 0.65 mg/kg.

No relevant GAP was available for evaluation of the plum trials in Germany and the remaining trials in Switzerland.

The Meeting, while recognizing that the residues on plums generally appeared lower than on cherries and peaches, agreed to pool the stone fruit data and estimate a group maximum residue level for stone fruits.

The combined European stone fruit residues in rank order (median underlined) were 0.03, 0.06, 0.08, 0.09, 0.10, 0.12, 0.12, 0.13, 0.13, 0.14, 0.14, 0.14, 0.14, 0.20, 0.22, 0.36, 0.37, 0.45 and 0.58 mg/kg. The combined US residues were 0.067, 0.08, 0.10, 0.19, 0.22, 0.26, 0.40, 0.43, 0.46, 0.5, 0.54, 0.58, 0.59, 0.6, 0.65, 0.67, 0.68, 0.68, 0.78, 0.8, 0.83, 0.88, 0.92, 0.98, 1.0, 1.0, 1.2, 1.3, 1.4, 1.5, 1.5, 1.7 and 1.7 mg/kg.

The two sets of data were apparently from different populations. The Meeting estimated a maximum residue level and an STMR of 2 and 0.68 mg/kg respectively for stone fruits, on the basis of the US data.

Grapes. Cyprodinil may be used on grapes in Chile at 0.38 kg ai/ha with harvest 2 days after the second application. The PHIs in the trials were 7 and 21 days, which were not sufficiently close to the recommended 2 days.

In France, cyprodinil may be used at 0.45 kg ai/ha with harvest 50 days after a single application. The trials with application rates of 0.38-0.50 kg ai/ha and PHIs of 42-89 days were accepted as complying with maximum GAP. A decline study suggested that residues were quite persistent. Residues in grapes from 16 trials were 0.02, 0.05, 0.06, 0.12, 0.16, 0.17, 0.18, 0.18, 0.24, 0.29, 0.31, 0.33, 0.36, 0.37, 0.44 and 0.78 mg/kg.

In Italy, cyprodinil may be used twice on grapes at 0.30 kg ai/ha with a 21 days PHI after the second application. In 3 trials in Italy at 0.38 kg ai/ha and 21 or 28 days PHI the residues were 0.51, 0.64 and 0.75 mg/kg.

In Spain, cyprodinil may be used twice on grapes at 0.38 kg ai/ha with a 21 days PHI after the second application. In 5 trials in Spain matching GAP the residues were 0.39, 0.54, 0.70, 1.1 and 2.1 mg/kg.

In Switzerland, a single application may be used on grapes at 0.45 kg ai/ha. The label did not specify a PHI, so it was difficult to decide which trials accorded with maximum GAP. No labels were available for GAP in South Africa or Germany.

In the USA, cyprodinil may be used on grapes at 0.53 kg ai/ha with a 7 days PHI. No more than 1.1 kg ai/ha is permitted per crop. Residue data from the trials at 0.56 kg ai/ha with a 7 days PHI but with 4 applications instead of the permitted 2 were accepted as relevant because the residue level would be mainly influenced by the last 2 applications. Cyprodinil residues in grapes from the 12 US trials were <0.02, 0.48, 0.52, 0.66, 0.82, 0.85, 0.94, 0.95, 0.96, 1.3, 1.4 and 1.8 mg/kg.

The residue data from the USA, Italy and Spain appear to be from similar populations and can be combined. Residues from the French trials (longer PHI) appear to be substantially lower and constitute a different population. The data from the USA, Italy and Spain were combined for evaluation giving residues in 20 trials in rank order (median underlined) of <0.02, 0.39, 0.48, 0.51, 0.52, 0.54, 0.64, 0.66, 0.7, 0.75, 0.82, 0.85, 0.94, 0.95, 0.96, 1.1, 1.3, 1.4, 1.8 and 2.1 mg/kg.

The Meeting estimated a maximum residue level and an STMR for cyprodinil in grapes of 3 and 0.79 mg/kg respectively.

Strawberries. In France, cyprodinil may be used on strawberries at 0.38 kg ai/ha with harvest 3 days after a single application. Trials in France (8), Germany (3) and Italy (1) were accepted as matching GAP when the application rate and PHI were correct but the number of applications was 3 and in one trial was 4. Residues on strawberries from the 12 trials were 0.10, 0.11, 0.18, 0.25, 0.27, 0.29, 0.30, 0.32, 0.33, 0.41, 0.43 and 1.2 mg/kg.

The Spanish maximum registered use for cyprodinil on strawberries is 0.38 kg ai/ha with a PHI of 7 days. In 4 trials matching GAP, residues in strawberries were 0.42, 0.75, 0.86 and 1.9 mg/kg.

Swiss registered uses allow application at 0.45 kg ai/ha with a 14 days PHI. Cyprodinil residues in 2 Swiss trials at 0.38 kg ai/ha (considered as matching GAP) were 0.12 and 0.24 mg/kg.

The US trials, with an application rate of 0.56 kg ai/ha, could not be evaluated because US GAP allows only 0.38 kg ai/ha.

In summary, cyprodinil residues from the available 18 trials in rank order (median underlined) were 0.10, 0.11, 0.12, 0.18, 0.24, 0.25, 0.27, 0.29, 0.30, 0.32, 0.33, 0.41, 0.42, 0.43, 0.75, 0.86, 1.2 and 1.9 mg/kg.

The Meeting estimated a maximum residue level and an STMR for cyprodinil in strawberries of 2 and 0.31 mg/kg respectively.

Raspberries. Swiss registered uses for cyprodinil on raspberries allow application at 0.45 kg ai/ha with a 14 days PHI. Cyprodinil residues in 4 German trials at 0.38 kg ai/ha and 13-14 days PHI, approximating Swiss GAP, produced residues of 0.23, 0.26, 0.26 and 0.38 mg/kg.

The Meeting estimated a maximum residue level and an STMR for cyprodinil in raspberries of 0.5 and 0.26 mg/kg respectively.

Onions. Supervised residue trials on onions reported from France, Germany and Italy. Swiss GAP allows application at 0.38 kg ai/ha but no PHI is specified. The Meeting agreed that data on the bulbs harvested 0-7 days after the last treatment would be accepted as equivalent to GAP data. Cyprodinil residues in bulbs from 8 trials in rank order were <0.02 (3), 0.05, 0.08, 0.09, 0.12 and 0.28 mg/kg.

The Meeting estimated a maximum residue level and an STMR for cyprodinil in bulb onions of 0.3 and 0.065 mg/kg respectively.

Cucumber and summer squash. In Spain, cyprodinil may be applied at a spray concentration of 0.038 kg ai/hl with harvest 7 days after the last of 3 applications. In 4 Spanish greenhouse trials matching GAP, residues in cucumbers were 0.05, 0.07, 0.10 and 0.12 mg/kg.

The registered use in Italy allows cyprodinil application to cucumbers at 0.30 kg ai/ha and a PHI of 7 days. In a field trial in Greece and two field trials in Spain with cyprodinil application at 0.38 kg ai/ha and 7 days PHI (conforming to Italian GAP) the residues were <0.02, 0.04 and 0.10 mg/kg. In a greenhouse trial in Greece and two greenhouse trials in Switzerland (0.38 kg ai/ha, complying with Italian GAP) the residues were 0.05, 0.09 and 0.12 mg/kg.

In summary, residues from field uses were <0.02, 0.04 and 0.10 mg/kg, and from greenhouse uses 0.05, 0.05, 0.07, 0.09, 0.10, 0.12 and 0.12 mg/kg. The Meeting agreed to combine the 10 trials for evaluation, giving <0.02, 0.04, 0.05, 0.05, 0.07, 0.09, 0.10, 0.10, 0.12 and 0.12 mg/kg.

The registered use in Italy on summer squash is the same as on cucumber. The Meeting agreed to extrapolate the cucumber values to summer squash.

The Meeting estimated a maximum residue level and an STMR for cyprodinil in cucumbers and summer squash of 0.2 and 0.08 mg/kg respectively.

Egg plant. The registered use in Italy allows cyprodinil application to egg plant at 0.30 kg ai/ha and a PHI of 7 days. In 2 Italian greenhouse trials on egg plant at 0.38 kg ai/ha and 7 days PHI the residues were 0.02 and 0.08 mg/kg.

The registered use of cyprodinil in Spain allows a spray concentration of 0.038 kg ai/hl on egg plant with a PHI of 7 days. The residues in 2 greenhouse crops with this use pattern in Spain were 0.06 and 0.10 mg/kg.

In summary the residues in egg plants were 0.02, 0.06, 0.08 and 0.10 mg/kg.

The Meeting noted that egg plant is not a major crop and agreed to estimate a maximum residue level and an STMR for cyprodinil in egg plant of 0.2 and 0.07 mg/kg respectively on the limited database.

Tomato. The registered use in Italy allows cyprodinil application to tomatoes at 0.30 kg ai/ha and a PHI of 7 days. Applications at 0.38 kg ai/ha were considered GAP. In greenhouse and tunnel trials in Greece (2), Italy (3), Spain (2), Switzerland (1) and the UK (2) complying with Italian GAP, cyprodinil residues were 0.31, 0.13, 0.12, 0.14, 0.08, 0.10, 0.12, 0.16, 0.11 and 0.08 mg/kg respectively.

The registered use of cyprodinil in Spain allows a spray concentration of 0.038 kg ai/hl with a PHI of 7 days. The residues in 2 covered crops with this use pattern in Spain were 0.13 and 0.17 mg/kg.

In Switzerland, cyprodinil may be applied to tomatoes at 0.30 kg ai/ha with harvest 3 days later. Residues in 2 glasshouse trials and one field trial in Switzerland with an application rate of 0.38 kg ai/ha were 0.16, 0.25 and 0.15 mg/kg.

The Meeting agreed to combine the data from the 15 tomato trials. The residues in rank order (median underlined) were 0.08, 0.08, 0.10, 0.11, 0.12, 0.12, 0.13, 0.13, 0.14, 0.15, 0.16, 0.16, 0.17, 0.25 and 0.31 mg/kg.

The Meeting estimated a maximum residue level and an STMR for cyprodinil in tomatoes of 0.5 and 0.13 mg/kg respectively.

Sweet peppers. The registered use in Italy allows cyprodinil application to sweet peppers at 0.30 kg ai/ha and a PHI of 7 days. Applications at 0.38 kg ai/ha were considered GAP. In a field trial (F) in Italy and a field trial and greenhouse and tunnel trials in Spain matching Italian GAP the residues were 0.02 (F), 0.05, 0.09 (F), 0.11 and 0.19 mg/kg.

The registered use of cyprodinil in Spain allows a spray concentration of 0.038 kg ai/hl with a PHI of 7 days. The residues in 3 covered crops with this use pattern in Spain were 0.12, 0.28 and 0.29 mg/kg.

The Meeting agreed to use the data from the covered crops for the evaluation, giving residues in rank order (median underlined) of 0.05, 0.11, 0.12, 0.19, 0.28 and 0.29 mg/kg.

The Meeting, noting that residues in sweet peppers were very similar to those in tomatoes from the same use pattern, estimated a maximum residue level and an STMR for cyprodinil in sweet peppers of 0.5 and 0.16 mg/kg respectively.

Lettuce. Cyprodinil is registered in France for use on lettuce in the field or glasshouse at 2 x 0.19 kg ai/ha with harvest 14 days after the second application. In 7 supervised trials in France with 3 applications of 0.23 kg ai/ha on lettuce in greenhouses and 14 days PHI, residues were 1.1, 2.7, 2.8, 2.8, 2.9, 4.1 and 6.4 mg/kg.

In Italy cyprodinil is registered for use on lettuce in the field or glasshouse at 3 x 0.26 kg ai/ha with harvest 14 days after the third application. In 3 supervised trials in greenhouses in Italy matching GAP cyprodinil residues in lettuce were 1.3, 2.0 and 2.2 mg/kg. Two field trials in Italy matching GAP produced residues of 0.06 and 0.18 mg/kg.

Cyprodinil may be used in Spain at 3 x 0.23 kg ai/ha with harvest 14 days after the third application. In 3 field trials on cos lettuce matching GAP the residues were <0.02, 1.0 and 1.1 mg/kg.

Lettuce trials in Germany and Switzerland could not be evaluated because there was no relevant label-supported GAP for German uses and the Swiss GAP did not specify a PHI.

The trials in Italy suggested that residues from glasshouse uses would be higher than from field uses and should be evaluated separately. The Meeting decided to use the greenhouse lettuce data to support the evaluation.

In summary, cyprodinil residues in lettuce from 7 greenhouse trials in France and 3 trials in Italy in rank order (median underlined) were 1.1, 1.3, 2.0, 2.2, 2.7, 2.8, 2.8, 2.9, 4.1 and 6.4 mg/kg.

The Meeting noted that the 10 trials covered 9 varieties of lettuce and decided to make recommendations for both head and leaf lettuce. The Meeting estimated maximum residue levels and STMRs of 10 and 2.75 mg/kg respectively for cyprodinil in head and leaf lettuce.

Beans. Supervised residue trials with cyprodinil on beans were evaluated against Austrian GAP for dwarf beans (0.38 kg ai/ha and 14 days PHI). Residues in pods from trials approximating this use pattern in 14 trials in France were 0.07, 0.10, 0.10, 0.11, 0.11, 0.13, 0.14, 0.14, 0.15, 0.18, 0.19, 0.20, 0.26 and 0.29 mg/kg.

In Spain cyprodinil may be sprayed on beans at a concentration of 0.038 kg ai/ha with harvest 14 days after a third application. Residues in pods from 5 trials in Spain matching this use pattern were 0.09, 0.09, 0.11, 0.12 and 0.12 mg/kg.

In summary, the residues in beans from the 19 supervised trials in rank order (median underlined) were 0.07, 0.09, 0.09, 0.10, 0.10, 0.11, 0.11, 0.11, 0.12, 0.12, 0.13, 0.14, 0.14, 0.15, 0.18, 0.19, 0.20, 0.26 and 0.29 mg/kg.

The Meeting estimated a maximum residue level and an STMR for cyprodinil in beans in pods, except broad bean and soya bean, of 0.5 and 0.12 mg/kg respectively.

Peas. No relevant information was available on labels for the evaluation of the pea data.

Barley. Cyprodinil is registered in France for use on barley as a foliar spray at 0.48 kg ai/ha, with timing specified by a growth stage instruction (use until end of earing). The instruction was interpreted as a PHI of approximately 35-50 days for the purpose of evaluating the trials. Trials in

France and Germany were considered to comply with French GAP with application rates in the range of 0.36-0.61 kg ai/ha and with PHIs of 40-50 days. Cyprodinil residues in barley grain from 41 trials meeting these conditions in rank order (median underlined) were <0.02, 0.07, 0.09, 0.11, 0.13, 0.14, 0.18, 0.22, 0.24, 0.25, 0.28, 0.31, 0.32, 0.36, 0.36, 0.40, 0.44, 0.48, 0.54, 0.55, 0.58, 0.58, 0.65, 0.67, 0.73, 0.74, 0.74, 0.75, 0.76, 0.77, 0.93, 1.1, 1.2, 1.2, 1.3, 1.3, 1.4, 1.5, 1.8, 1.9 and 2.0 mg/kg.

The Meeting estimated a maximum residue level and an STMR for cyprodinil in barley of 3 and 0.58 mg/kg respectively.

Rye. No labels were available for uses of cyprodinil on rye so the data could not be evaluated.

Wheat. Cyprodinil is registered in France for use on wheat as a foliar spray at 0.60 kg ai/ha, with timing specified by the instruction to use until the end of earing, interpreted as a PHI of approximately 45-60 days for the purpose of evaluating the trials. Trials in France, Germany, Switzerland and the UK were considered to conform to French GAP with application rates in the range of 0.45-0.75 kg ai/ha and with PHIs of 42-61 days. Cyprodinil residues in wheat grain from 29 trials meeting these conditions in rank order (median underlined) were <0.02, <0.02, 0.02, 0.02, 0.03, 0.03, 0.03, 0.04, 0.05, 0.052, 0.06, 0.06, 0.06, 0.06, 0.07, 0.07, 0.07, 0.08, 0.08, 0.10, 0.10, 0.11, 0.11, 0.13, 0.13, 0.13, 0.14, 0.16 and 0.32 mg/kg.

The Meeting estimated a maximum residue level and an STMR for cyprodinil in wheat of 0.5 and 0.07 mg/kg respectively.

Almonds and almond hulls. In the USA cyprodinil may be used on almonds in blossom at 0.53 kg ai/ha with harvest 150 days later. Cyprodinil residues were below the LOQ in almonds (<0.02 mg/kg) and almond hulls (<0.05 mg/kg) in 5 trials in the USA matching GAP conditions.

The Meeting estimated maximum residue levels and STMRs for cyprodinil in almonds of 0.02* and 0.02 mg/kg respectively, and in almond hulls of 0.05* and 0.05 mg/kg respectively.

Cereal straw and fodder. The barley trials that were evaluated for grain residues were evaluated for residues in barley straw. Residues in barley straw determined in 29 of the trials, in rank order, were 0.15, 0.15, 0.17, 0.18, 0.20, 0.22, 0.24, 0.32, 0.33, 0.33, 0.34, 0.39, 0.39, 0.40, 0.41, 0.42, 0.42, 0.45, 0.46, 0.51, 0.55, 0.61, 0.67, 0.82, 0.84, 0.87, 1.1, 1.7 and 2.5 mg/kg.

Residues in wheat straw in 29 of the wheat trials in rank order were <0.05, 0.06, 0.06, 0.088, <0.10, 0.10, 0.13, 0.19, 0.19, 0.22, 0.26, 0.28, 0.31, 0.32, 0.32, 0.39, 0.50, 0.54, 0.58, 0.65, 0.71, 0.80, 0.95, 1.0, 1.1, 1.7, 2.3, 2.5 and 5.8 mg/kg.

The Meeting decided to combine the data from barley and wheat straw to recommend an MRL for straw and fodder of cereal grains. The residues in rank order (median underlined) were <0.05, 0.06, 0.06, 0.088, <0.10, 0.10, 0.13, 0.15, 0.15, 0.17, 0.18, 0.19, 0.19, 0.20, 0.22, 0.22, 0.24, 0.26, 0.28, 0.31, 0.32, 0.32, 0.32, 0.33, 0.33, 0.34, 0.39, 0.39, 0.39, 0.40, 0.41, 0.42, 0.42, 0.45, 0.46, 0.50, 0.51, 0.54, 0.55, 0.58, 0.61, 0.65, 0.67, 0.71, 0.80, 0.82, 0.84, 0.87, 0.95, 1.0, 1.1, 1.1, 1.7, 1.7, 2.3, 2.5, 2.5 and 5.8 mg/kg.

The Meeting estimated a maximum residue level and an STMR for cyprodinil in straw and fodder (dry) of cereal grains of 10 and 0.395 mg/kg respectively.

Processing

The Meeting received information on the fate of cyprodinil residues during the brewing of beer, production of fruit juices, vinification, wheat milling and baking, drying of plums and grapes and the production of strawberry jam and tomato paste. Cyprodinil was shown to be hydrolytically stable under food processing conditions.

The processing factors (PF) shown below were calculated from the trials data. The number of trials is shown in parentheses. The factors are the mean values excluding those where residues were undetectable except for beer. Cyprodinil residues were not detected in beer in 17 trials with LOQs of 0.01, 0.005 and 0.002 mg/kg. Estimated processing factors ranged from <0.002 to <0.17 and depended on the LOQ and the residue level in the barley. The value reported (<0.01) is a best estimate.

<u>RAC</u>	<u>Processed product</u>	<u>PF</u>	<u>No.</u>
Apples	wet pomace	3.5	(7)
	juice	0.03	(2)
Barley	beer	<0.01	(17)
Grapes	juice	0.15	(22)
	wine	0.078	(46)
	raisins	2.1	(15)
Plums	dried prunes	1.7	(10)
Tomatoes	juice	0.17	(1)
	paste	0.86	(1)
Wheat	bran	3.0	(1)
	flour	0.27	(1)
	whole meal flour	0.92	(1)
	whole-grain bread	0.52	(1)

The Meeting used the processing factors to estimate maximum residue levels and STMR-Ps for processed commodities.

The processing factor for raisins (2.1) was applied to the highest residue level in grapes (2.1 mg/kg) to calculate a residue of 4.4 mg/kg. The Meeting estimated a maximum residue level of 5 mg/kg for cyprodinil in dried grapes (currants, raisins and sultanas).

The processing factor for dried prunes (1.7) was applied to the highest residue level in stone fruits (1.7 mg/kg) to calculate a residue of 2.9 mg/kg. The Meeting estimated a maximum residue level of 5 mg/kg for cyprodinil in dried prunes.

The processing factor for wheat bran (3.0) was applied to the highest residue level in wheat (0.32 mg/kg) to calculate a residue of 0.96 mg/kg. The Meeting estimated a maximum residue level of 2 mg/kg for cyprodinil in wheat bran.

The processing factors were applied to the STMRs for the raw commodities to produce the following STMR-P values: wet apple pomace 0.07 mg/kg; apple juice 0.0006 mg/kg; beer 0.0058 mg/kg; grape juice 0.12 mg/kg; wine 0.062 mg/kg; dried grapes 1.7 mg/kg; apricot juice 0.3 mg/kg; dried prunes 1.2 mg/kg; tomato juice 0.022 mg/kg; tomato paste 0.12 mg/kg; wheat bran 0.21 mg/kg; wheat flour 0.019 mg/kg; wheat wholemeal 0.064; wholemeal bread 0.036 mg/kg.

Farm animal dietary burdens

The Meeting estimated the dietary burdens of cyprodinil for livestock from the residues in animal feeds resulting from its use.

Maximum farm animal dietary burden

Commodity	group	residue mg/kg	basis	% dry matter	residue, on dry wt mg/kg	Chosen diets, %			Residue contribution, mg/kg		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
Almond hulls	AM	0.05	MRL	90	0.055						
Apple pomace, wet	AB	0.07	STMR-P	40	0.18	25			0.045		
Barley	GC	3	MRL	88	3.4	50	40	75	1.7	1.36	2.55
Straw and fodder of cereal grains	AS	10	MRL	88	11.4	25 ¹	60 ¹		2.85	6.84	
Wheat	GC	0.5	MRL	89	0.57						
Wheat bran	CM	0.21	STMR-P	88	0.24						
					TOTAL	100	100	75			
						Maximum dietary burden			4.6	8.2	2.6

¹ barley hay

STMR farm animal dietary burden

Commodity	group	residue mg/kg	basis	% dry matter	residue, on dry wt mg/kg	Chosen diets, %			Residue contribution, mg/kg		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
Almond hulls	AM	0.05	STMR	90	0.055						
Apple pomace, wet	AB	0.07	STMR-P	40	0.18	25			0.045		
Barley	GC	0.58	STMR	88	0.66	50	40	75	0.33	0.26	0.50
Straw and fodder of cereal grains	AS	0.395	STMR	88	0.45	25 ¹	60 ¹		0.11	0.27	
Wheat	GC	0.07	STMR	89	0.079						
Wheat bran	CM	0.21	STMR-P	88	0.24						
					TOTAL						
						STMR dietary burden			0.48	0.53	0.50

¹ barley hay

The cyprodinil dietary burdens for estimations of MRLs and STMRs in animal commodities (residue levels in animal feeds expressed on dry weight) are beef cattle 4.6 and 0.48 mg/kg, dairy cattle 8.2 and 0.53 mg/kg and poultry 2.6 and 0.50 mg/kg.

Farm animal feeding studies

A feeding study on lactating dairy cows was reported, which provided information on likely residues in animal tissues and milk resulting from residues in the animal diet.

Lactating Holstein cows were dosed daily by gelatin capsule with cyprodinil at the equivalent of 5, 15 and 50 ppm in the dry-weight diet for 28 consecutive days. Milk was collected throughout and a cow from each dosing group was slaughtered for tissue collection on days 28, 29 and 30. Cyprodinil residues were not detected (LOQ 0.01 mg/kg) in the milk (days 0, 1, 3, 7, 14 and 21), kidney or fat of cows from the highest dose group (50 ppm), nor in milk (day 26) or muscle from any group. Cyprodinil was present in liver (highest residue 0.013 mg/kg) from the highest dose group but not from the other groups.

Maximum residue levels in animal commodities

The Meeting noted that no cyprodinil residues (<0.01 mg/kg) were detected in milk, kidney, fat or muscle from animals dosed for 28 days at 50 ppm, which was substantially above the maximum dietary burdens for beef and dairy cattle (4.6 and 8.2 mg/kg). Cyprodinil residues were present in liver at 0.013 mg/kg in the 50 ppm dosing group, but not the 15 ppm group.

Maximum residue levels at the LOQs of suitable analytical methods would be appropriate for the animal commodities. Residue levels in tissues (except liver) and milk were essentially zero. The level of cyprodinil residues in liver was also very low but was detected at a high dose. The data for liver and kidney were used to support a maximum residue level for edible offal.

The Meeting estimated maximum residue levels of 0.01* mg/kg for cyprodinil in meat (fat) from mammals other than marine mammals and for mammalian edible offal, and a maximum residue level of 0.0004* F mg/kg for milks (equivalent to 0.01* mg/kg in the milk fat).

The Meeting estimated STMRs of 0 mg/kg for cyprodinil in muscle and fat from mammals other than marine mammals and for milks and 0.01 mg/kg for mammalian edible offal.

The Meeting noted that in the metabolism studies on laying hens cyprodinil itself was not detected in the tissues (except in kidney at 0.001 mg/kg) even at the high feeding levels of 215 and 226 ppm. Cyprodinil was detected in eggs at 0.002-0.011 mg/kg from birds dosed at the high level. The feeding levels in the metabolism study were almost 100 times the maximum dietary burden (2.6 mg/kg), so the Meeting agreed that the expected level of cyprodinil residues in poultry tissues and eggs was essentially zero.

The Meeting estimated maximum residue levels of 0.01* mg/kg and STMRs of 0 mg/kg for cyprodinil in poultry meat (fat), edible offal of poultry, and eggs, and an STMR of 0 mg/kg for cyprodinil in poultry muscle.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes of cyprodinil, based on the STMRs estimated for all commodities, for the five GEMS/Food regional diets were in the range of 0-10% of the ADI of 0.03 mg/kg bw (Annex 3). The Meeting concluded that the long-term intake of residues of cyprodinil resulting from its uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The Meeting decided that an acute RfD was unnecessary and concluded that the short-term intake of cyprodinil residues is unlikely to present a public health concern.

4.5 DICLORAN (83)

RESIDUE AND ANALYTICAL ASPECTS

Dicloran, a fungicide, was first evaluated for toxicology and residues in 1974 and subsequently in 1977. The compound was again evaluated by the Meeting in 1998 for toxicology and residues under the CCPR Periodic Review Programme. The 1998 JMPR changed the ADI from 0-0.03 to 0-0.01 mg/kg body weight and concluded that an acute RfD was unnecessary. It recommended that the definition of the residue for compliance with MRLs and for the estimation of dietary intake should be dicloran and indicated that the residue was fat-soluble. It also estimated revised

maximum residue levels for carrot and bulb onion while recommending withdrawal of the existing CXLs for grapes, head lettuce, peach, plums (including prunes), strawberry and tomato. The 33rd CCPR in 2000 decided to retain for four years the MRLs recommended for withdrawal in accordance with the procedures of the Periodic Review Programme pending the submission of additional data on these commodities.

The Meeting received information on residues in rotational crops, an analytical method, use patterns, and residue trials on nectarines, peaches, plums, grapes, strawberries, tomatoes and lettuce.

Rotational crops

When dicloran was applied to loamy sand at a rate equivalent to 3 kg ai/ha, the applied radioactivity remained mainly in the soil. Both the TRR and dicloran were significantly higher in the first growing period than the second and third in all crops. The highest residues were found in leaves or straw of lettuce, sugar beet and wheat but the TRRs decreased sharply after the first growing period. Unchanged dicloran found in plant extracts was less than 10% of the TRR in the first growing period and was at or below the limit of quantification in the second and third periods.

When dicloran was sprayed on the surface of sandy loam soil at a rate of 14.8 kg ai/ha, the average TRR in harvested crops (lettuce, turnip and wheat) was highest in the 120-day rotation and lowest in the 365-day rotation. On average, acetonitrile extracts, methylene chloride extracts and acid and alkaline extracts contained about 20%, 3% and 20% of the TRR respectively. Unextracted fractions contained about 30% of the TRR, which was found to be associated with cell wall components. Dicloran was observed in most samples on days 30, 120 and 365 at generally decreasing levels. The presence of dicloran metabolites was confirmed throughout the course of the study: 4-amino-2,6-dichlorophenol, 4-amino-2,6-dichloroacetanilide, 3,5-dichloro-4-hydroxyacetanilide, 4-amino-3,5-dichloroacetanilide, 2,6-dichloro-4-hydroxyaniline, 2,6-dichloro-4-nitrophenol, 2,6-dichlorophenol and 2,6-dichloroaniline were identified.

In a study of the uptake of dicloran from soil by rotational crops under actual field conditions dicloran was applied at a rate of 4.4 kg ai/ha and lettuce, mustard, radish, wheat and sorghum were planted 30, 120 and 360 days after the application. In most crops dicloran concentrations were below the limit of quantification (<0.05 mg/kg). The highest dicloran concentrations were found in radish roots of the 30-day rotation at 0.278 and 0.243 mg/kg.

Analytical methods

The validity of the method used for the determination of dicloran in milk, eggs and tissues from goats and hens in metabolism studies was checked. Egg white and chicken muscle samples, with and without fortification, were extracted with acetone/water (6:1), and partitioned with hexane/ethyl acetate (9:1). Milk and fat samples were extracted with acetone/water (7:1) followed by extraction of the aqueous layer with hexane and partition into acetonitrile. After a clean-up step including a solid-phase extraction on a diol column, dicloran was eluted with toluene and determined by gas chromatography with an electron capture detector. The recovery from the fortified samples ranged from 93.0 to 106.7%, showing that the method can be satisfactorily used for the determination of dicloran in these samples. However, comparison of the analytical results with those from radio-analysis indicated that while the average recoveries from egg white, chicken muscle and goat fat were above 80%, that from goat milk was 47.8%.

Residues from supervised trials

The Meeting received the results of supervised trials on nectarines, peaches, plums, strawberries and lettuce in Brazil, grapes in Brazil and Mexico and tomatoes in Italy, all conducted after the last evaluation by the 1998 JMPR. The Meeting also considered the results of supervised trials on these crops which had been evaluated by the 1998 JMPR, against GAP reported to the current Meeting.

Nectarines. Three new post-harvest trials were conducted in Brazil in 2001. The conditions (in 0.087-0.089 kg ai/hl dip) were in accordance with GAP in Chile for post-harvest application to nectarines (dip or immersion in 0.09 kg ai/hl). The residues were 2.3, 2.3 and 5.5 mg/kg.

The 1998 JMPR evaluated pre-harvest, post-harvest, and combined pre- and post-harvest trials carried out in the USA in 1968. One pre-harvest trial (PHI 1 day) did not comply with GAP in the USA which requires a PHI of 10 days. The post-harvest trials and combined pre- and post-harvest trials were not in compliance with any GAP.

One Australian post-harvest trial (0.075 kg ai/hl, SC) complied with Chilean post-harvest GAP but only the surface residue was measured and could not be used to estimate a maximum residue level.

Peaches. Two new pre-harvest supervised trials were conducted in Brazil in 2001. The conditions (0.146 kg ai/hl, 3 applications at an interval of 15 days, 1-day PHI) were in accordance with GAP in Argentina (0.15 kg ai/hl, 3 applications, 1-day PHI). The residues were 2.7 and 4.8 mg/kg.

A pre-harvest trial, and post-harvest and combined pre- and post-harvest trials conducted in the USA in 1966, 1988 and 1996 were evaluated by the 1998 JMPR. The pre-harvest trial with a PHI of 4 days was not in compliance with US GAP which requires a PHI of 10 days. Four combined trials in 1988 and 1996 with a post-harvest rate of 0.09 kg ai/hl were in accordance with post-harvest GAP in Argentina (0.09-0.11 kg ai/hl spray or immersion) and in Chile (0.09 kg ai/hl dip or immersion) but in two of these trials the last pre-harvest application was made one day before harvest while US pre-harvest GAP requires 10 days. The residues from two other trials in conformity with US GAP (pre-harvest) and Argentinean and Chilean GAP (post-harvest) were 5.3 and 5.8 mg/kg. Of two combined trials and four post-harvest trials in 1966, a post-harvest trial at an application rate of 0.15 kg ai/hl and another at 0.06 kg ai/hl approximated GAP in Argentina. The residues were 2.1 and 2.5 mg/kg.

Three Australian post-harvest trials (1973) reported only surface residues and could not be used for estimating a maximum residue level, and one pre-harvest (1964) and one post-harvest trial (1966) in Canada did not comply with any GAP.

The residues from post-harvest trials on nectarines and peaches were mutually supportive. The combined residues were 2.1, 2.3, 2.3, 2.5, 2.7, 4.8, 5.3, 5.5 and 5.8 mg/kg. The Meeting therefore estimated a maximum residue level of 7 mg/kg Po and an STMR of 2.7 mg/kg for nectarines and peaches.

Plums. Three new pre-harvest trials were carried out in Brazil in 2001. The conditions (0.146 kg ai/hl, 3 applications at an interval of 15 days, 1-day PHI) were in compliance with pre-harvest GAP in Argentina (0.15 kg ai/hl, 3 applications, 1-day PHI). The residues were <1.0, 1.1 and 1.4 mg/kg.

Four combined and one pre-harvest trial in the USA in 1986 and 1995 were not in accordance with any GAP reported to the current Meeting.

The Meeting concluded that there were too few valid trials to estimate a maximum residue level.

Grapes. Three new trials in Brazil and four in Mexico in 2001 were reported to the Meeting. Although trials were conducted in Brazil (0.256 kg ai/hl, 5 applications with an interval of 1 month, 1-day PHI), no GAP is reported for Brazil and they did not comply with GAP in Argentina (0.19 kg ai/hl, 7-day PHI).

Trials carried out in Sonora and Baja California, Mexico (2.25 kg ai/ha, 3 applications at an interval of 15 days, 1-day PHI) were in accordance with GAP in the USA (1.7-3.9 kg ai/ha for WP or 2.0 kg ai/ha for DP, 1-day PHI; applicable to grapes grown west of the Rocky Mountains only). The residues were 0.36, 0.83, 0.95 and 1.5 mg/kg.

The 1998 JMPR evaluated data from US supervised trials in California in 1967, 1984 and 1995. One trial in 1967 and two trials in 1984 with a WP application at 2.2 kg ai/ha followed by 1-3 dust applications at 2.0 kg ai/ha with 1-day PHI were comparable with US GAP (1.7-3.9 kg ai/ha for WP or 2.0 kg ai/ha for DP, 1-day PHI). The residues were 0.29, 0.62 and 6.0 mg/kg.

One US trial in 1995 with a WP application at 4.5 kg ai/ha and 3-day PHI approximated US GAP. The residue was 1.0 mg/kg

The combined residues from Mexican trials and valid US trials were 0.29, 0.36, 0.62, 0.83, 0.95, 1.0, 1.5 and 6.0 mg/kg. The Meeting estimated a maximum residue level of 7 mg/kg and an STMR of 0.89 mg/kg.

Strawberries. Three new trials were conducted in Brazil in 2001 at a rate of 0.256 kg ai/hl, with 4 (2 trials) or 11 applications (1 trial) and a PHI of 1 day. No GAP for strawberries was reported for Brazil or Argentina.

A number of trials were carried out in the USA in 1963 but no GAP for strawberries was reported for the USA.

The Meeting concluded that there were insufficient data to estimate a maximum residue level.

Tomatoes. Three new trials were conducted in Italy in 2001 at a rate of 0.095 kg ai/hl which complied with GAP in Italy (0.07-0.12 kg ai/hl). The residues at a PHI of 20 days were <0.01, 0.04 and 0.08 mg/kg.

Trials conducted in the USA in 1962 (greenhouse) and in 1963 and 1995 (field) were not in compliance with US GAP (0.84 kg ai/ha, 4 applications, PHI of 10 days). One trial in the UK in 1972 (greenhouse) reported only residues in the surface wash.

The Meeting concluded that there were too few valid trials to estimate a maximum residue level.

Lettuce. Three new pre-harvest trials were conducted in Brazil in 2001. The conditions (0.293 kg ai/hl, 2 applications at an interval of 7 days, 14-day PHI) were in accordance with pre-harvest GAP in Argentina (0.28 kg ai/hl, 10-day PHI). The residues were <0.10, 0.16 and 0.51 mg/kg.

Three field trials and one greenhouse trials were conducted in the USA in 1964 and 1972 respectively. While US GAP requires a PHI of 14 days, samples were taken only up to 4 days or at 25-26 days.

The Meeting concluded that there were too few valid trials to estimate a maximum residue level.

Processing studies

The 1998 JMPR estimated processing factors for grapes to be 1.1 to juice, 1.5 to wet pomace and 0 to sun-dried grapes, so STMR-Ps were calculated to be 0.98 mg/kg for grape juice, 1.3 mg/kg for wet pomace and 0 mg/kg for sun-dried grapes.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Dietary Intakes (IEDIs) were calculated for the five GEMS/Food regional diets using STMRs for 3 commodities estimated by the current Meeting and 2 estimated by the 1998 JMPR, and STMR-Ps for two processed commodities (Annex 3). The ADI allocated by the 1998 JMPR was 0-0.01 mg/kg bw. The calculated IEDIs were 0-30% of the maximum ADI. The Meeting concluded that the intake of residues of dicloran resulting from the uses considered by the 1998 JMPR and the current JMPR was unlikely to present a public health concern.

Short-term intake

The 1998 JMPR agreed that an acute RfD was unnecessary for dicloran. The Meeting therefore concluded that the short-term intake of dicloran residues was unlikely to present a public health concern.

4.6 DIMETHOATE (027)

TOXICOLOGY

Dimethoate is an organophosphate ester, and virtually all its toxic effects are due to the inhibition of acetylcholinesterase activity. Dimethoate was evaluated for toxicological effects by JMPR in 1963, 1965, 1967, 1984, 1987, and 1996. An ADI of 0–0.002 mg/kg bw was established in 1996 on the basis of the apparent NOAEL of 1.2 mg/kg bw per day for reproductive performance in a study of reproductive toxicity in rats and applying a safety factor of 500. Although a safety factor of 100 would normally be used in deriving an ADI from a study of this type, the Meeting was concerned about the possibility that reproductive performance might have been affected at 1.2 mg/kg bw per day in this study and therefore used a higher-than-normal safety factor. No data were available to assess whether the effects on reproductive performance were secondary to the inhibition of cholinesterase activity. The 1996 JMPR concluded that it was not appropriate to establish the ADI on the basis of results of studies of volunteers, since the crucial end-point (reproductive performance) had not been assessed in humans. The present review was undertaken to consider the need for establishing an acute RfD and to evaluate new studies submitted by the sponsor.

The LD₅₀ of dimethoate when administered orally was about 314–600 mg/kg bw in rats and 150 mg/kg bw in mice.

Acute neurotoxicity was studied in rats given dimethoate by gavage at a single dose of 0, 2, 20 or 200 mg/kg bw after preliminary studies had shown that peak effects for clinical signs occur at about 2 h post-dosing. Abnormal clinical signs and effects on functional observational battery (FOB) parameters were seen at the highest dose, mainly on the first 2 days after treatment and were reversed by day 7. The NOAEL was 2 mg/kg bw, on the basis of the absence of pupil response at 20 mg/kg bw and above. Cholinesterase activity was not analysed in this study.

In a study of acute neurotoxicity in rats given dimethoate in the diet at single doses of 0, 1, 2, 3 or 15 mg/kg bw, no clinical signs and no effects on FOB parameters were observed. A statistically significant inhibition of cholinesterase activity in erythrocytes of males (29%) and in the brain cortex of females (11%) was observed at 3 mg/kg bw and above.

In a special study designed to assess effects on cholinesterase activity, pre-weaning rats (aged 11 days) and young adult rats (aged 7–8 weeks) received dimethoate by gavage at single doses of 0, 0.1, 0.5 or 3 mg/kg bw. There was no difference in susceptibility between pre-weaning and young adult rats. A statistically significant inhibition of brain cholinesterase activity in pre-weaning rats (17–18%) and in young adult rats (12–14%) and of erythrocyte cholinesterase activity in pre-weaning and young adult female rats (26–27%) was observed at 3 mg/kg bw.

The Meeting concluded that the overall NOAEL for acute effects on cholinesterase activity was 2 mg/kg bw.

The Meeting also considered a number of studies in human volunteers which indicated that single or repeated oral doses of dimethoate of up to 0.2 mg/kg bw did not induce clinical effects nor inhibit cholinesterase activity in the blood. It was concluded that these studies were not conducted according to current standards (no details on study design, e.g. age and sex of individual volunteers, were given and no raw data were provided). Therefore, the Meeting considered that the studies in humans were only supportive for setting the acute RfD.

The Meeting also reviewed new studies that were not relevant to the establishment of an acute RfD. In a study of neurotoxicity, rats received dimethoate in the diet at concentrations of 0, 1, 50 or 125 ppm for 91–94 days. The NOAEL for systemic toxicity and neurotoxicity was 1 ppm (equal to 0.06 mg/kg bw per day), on the basis of inhibition of erythrocyte cholinesterase activity (34–49%) and small faeces at 50 ppm (equal to 3.22 mg/kg bw per day) and above.

In a special study designed to assess effects on the activity of cholinesterase, pregnant rats, pre-weaning rats and young adult rats received dimethoate by gavage at repeated doses of 0, 0.1, 0.5 or 3 mg/kg bw per day. The NOAEL was 0.1 mg/kg bw per day, on the basis of a consistent, statistically significant inhibition of brain cholinesterase activity (10–13%) in pregnant, pre-weaning and young adult rats and of erythrocyte cholinesterase activity (23%) in pre-weaning female pups at 0.5 mg/kg bw per day and above.

In a study of developmental neurotoxicity, pregnant rats received dimethoate by gavage at doses of 0, 0.1, 0.5 or 3 mg/kg bw per day from day 6 of gestation to post-natal day 10, and their offspring received the same doses by gavage from post-natal day 11 to post-natal day 21. The NOAEL for functional development of the nervous system and systemic toxicity in the offspring was 0.5 mg/kg bw per day, on the basis of developmental delay observed for some functional parameters and increased pup mortality at a dose of 3 mg/kg bw per day. The Meeting considered these effects to be of no relevance for setting the acute RfD, since they would not be expected to occur after a single exposure and concluded that the new studies supported the current ADI of 0.002 mg/kg bw.

Toxicological evaluation

After considering the previous evaluations of dimethoate and the new data submitted, the Meeting

established an acute RfD of 0.02 mg/kg bw on the basis of the overall NOAEL of 2 mg/kg bw for cholinesterase inhibition in studies in rats, and a safety factor of 100. This acute RfD was supported by the NOAEL of about 0.2 mg/kg bw per day in studies in volunteers receiving single or repeated doses, which were evaluated by the 1996 JMPR.

The Meeting recognized that it may be possible to refine this acute RfD based on further characterization of the effects caused by dimethoate.

An addendum to the toxicological monograph was prepared.

Estimate of acute reference dose

0.02 mg/kg bw

Studies that would provide information useful for continued evaluation of the compound

- Further observations in humans
- The two-generation study of reproductive toxicity (available in abbreviated form at the 2003 Meeting)

RESIDUE AND ANALYTICAL ASPECTS

Dimethoate is a systemic insecticide typically applied as an emulsifiable concentrate (EC) at a rate of 0.2-0.9 kg ai/ha. The latest evaluation of dimethoate residues was in 1998 within the CCPR Periodic Review Programme and the toxicology was reviewed in 1996 when an ADI of 0-0.002 mg/kg bw was allocated for the sum of dimethoate and omethoate expressed as dimethoate.

The 1998 JMPR recommended the definition of the residue to be dimethoate for compliance with MRLs and the sum of dimethoate and omethoate, each considered separately, for the estimation of dietary intake.

The manufacturers reported information on physical and chemical properties, plant metabolism and toxicity of metabolites, environmental fate in water-sediment systems, stability of residues in stored analytical samples, use patterns, residues resulting from supervised trials on crops, fate of residues in storage and processing, residues in food in commerce or at consumption and national MRLs. Information on national GAP was provided by the governments of Thailand, The Netherlands, Germany, Brazil, Poland and Australia.

The Meeting considered the new information and reviewed the residue data, taking into account the revised use patterns. Where sufficient residue data reflecting the changed use conditions were available new MRLs were recommended. However the previously estimated maximum residue levels were not changed if the GAP on which they depended was still in effect.

Plant metabolism

Two new plant metabolism studies with [¹⁴C]dimethoate on potatoes and wheat were evaluated.

After two spray applications of [¹⁴C]dimethoate to potatoes at a mean rate of 340 g/ha per application with 14 days between applications, significant residues were present in foliage decreasing from 12.3 mg/kg as dimethoate after the second application (day 0) to 1.3 mg/kg at day 14 and slightly increasing to 3.5 mg/kg fresh weight at day 28 as moisture loss from the crop caused concentration of the residue. ¹⁴C residues in tubers remained constant throughout the study and ranged from 0.19 to 0.30 mg dimethoate equivalent/kg.

After two spray applications of [¹⁴C]dimethoate to wheat at 710 g/ha and 420 g/ha with 41 days between applications, significant residues were present in all plant parts. Levels of radioactivity were highest in those parts of the plant directly exposed to the spray, representing up to 29.7 mg/kg dimethoate equivalents in the whole plant immediately after the first application. Concentrations of radioactivity in ears and the remainder of the plant represented 22.7 mg/kg and 16.1 mg/kg respectively, immediately after the second application. At the early harvest (day 62) the concentration of radioactivity in straw had decreased to 6.4 mg/kg dimethoate equivalents although levels in hulls represented 23.3 mg/kg. In grain, which was not directly exposed to the spray, the total radioactivity represented 2.3 mg/kg. The levels increased slightly at the normal harvest (day 73), as a result of drying of the crop, and were 4.3 mg/kg, 33.7 mg/kg and 7.8 mg/kg in grain, hulls and straw respectively.

A similar metabolic profile was found in potato and wheat plants:

- Oxidation to yield omethoate (metabolite II)
- *O*- and *N*-demethylation of omethoate to yield *O*-demethyl *N*-demethyl omethoate (XXIII)
- Hydrolysis at the amide bond to give dimethoate carboxylic acid (III) and subsequent degradation to give *O,O*-dimethyl dithiophosphoric acid (XV).
- Demethylation and rearrangement to yield *O*-demethyl dimethoate (X) or *O*-demethyl isodimethoate (XII).
- Demethylation of omethoate to give *O*-demethyl omethoate (XI) and subsequent hydrolysis of the amide bond to give *O*-demethyl omethoate carboxylic acid (XX).

No dimethoate or omethoate was detected in the edible parts of potatoes or wheat (i.e. tubers or grain) at any time, indicating that translocation of dimethoate or omethoate did not take place to a significant extent. The plant metabolites of omethoate (III, XI, XII, XX) were found to be toxicologically insignificant.

Methods of analysis

The method used for white cabbage and lettuce involves extraction with ethyl acetate and clean-up of the extract by gel permeation chromatography. Quantification of both dimethoate and omethoate was carried out by gas chromatography with a flame photometric detector in the phosphorus mode or mass selective detection. The LOQ was 0.01 mg/kg.

Whole fruit, peel and pulp except lemons of citrus fruits were analysed by extraction with acetone, followed by partitioning into dichloromethane. The extract was treated with activated charcoal and final clean-up was by column chromatography with activated silica gel. Quantification was by GC with an FPD in the phosphorus mode with an LOQ of 0.01 mg/kg.

Lemon homogenates were extracted with dichloromethane. The solvent was changed to hexane and dimethoate and omethoate were partitioned into water. The aqueous extract was analysed by LC-MS providing an LOQ of 0.01 mg/kg. This method was also applied to olives with the same LOQ. Olive oil was extracted with acetonitrile after dissolution in hexane.

Cherry homogenate was extracted into dichloromethane and, after removal of water with anhydrous sodium sulfate, cleaned up with activated charcoal. Quantification of dimethoate and omethoate was by GC with an FPD in the phosphorus mode with an LOQ of 0.01 mg/kg.

Apples, artichokes, celery, cherries, lettuce, tomatoes, wheat (grain, green plants and straw), sugar beet, (tops and roots), asparagus and melons (peel and pulp) were analysed using dichloromethane for extraction, followed by clean-up by liquid/liquid partition with hexane. Dimethoate and omethoate were partitioned into water for quantification by liquid chromatography with mass spectrometric detection (LOQ 0.01 mg/kg) for all samples. A small modification using an ENVI-Carb Bondelut cartridge pre-wetted with dichloromethane and a double aliquot of the extract (20 ml, equivalent to 2 g of sample) was validated and the limit of quantification was decreased to 0.001 mg/kg in wheat grain.

Methods were validated for the determination of dimethoate and omethoate residues in milk, eggs and animal tissues, where the LOQ was 0.001 mg/kg for milk and eggs and 0.01 mg/kg for tissues.

In a multi-residue method ethyl acetate is used to extract plant samples and extraction is followed by a GPC clean-up. Quantification is by GC with an NPD.

In the DFG S19 multi-residue method acetone was used for extraction, its volume adjusted according to the water content of the sample to achieve an acetone to water ratio of 2:1 during extraction. To separate excess water the extract was saturated with sodium chloride and partitioned with dichloromethane. The clean-up was by GPC with cyclohexane-ethyl acetate elution. Quantification of dimethoate and omethoate was by GC with an NPD.

A modified DFG S19 method used GC with an atomic emission detector for determination, with an internal standard added before extraction (2 µg aldrin dissolved in toluene). Extraction was with acetone. After saturation with sodium chloride and dilution with dichloromethane clean-up was by GPC with cyclohexane/ethyl acetate as eluent. The residue was dissolved in 200 µl toluene before analysis.

Another multi-residue method for olives, oranges, lettuce and wheat grain consisted in extraction with ethyl acetate followed by clean-up by gel permeation chromatography. Olive oil was extracted with acetonitrile after dissolution in hexane. Extracts were analysed by GC with an FPD on a DB-17 column. Quantification was by comparison with matrix-matched external standards. Confirmation was by GC with an FPD on a 30 m DB 1701 column.

Stability of residues in stored analytical samples

Dimethoate and omethoate in cherries were stable up to 6 months during storage at -18°C. The government of Australia reported stability of dimethoate and omethoate in mangoes stored for 3 months at -10°C.

Results of supervised trials on crops

The toxicological evaluation of omethoate, the major plant metabolite of dimethoate, revealed that it is about 10 times as toxic as dimethoate. Since consumers are exposed to both dimethoate and omethoate residues at the time of consumption, the difference in toxicity was taken into account (1998 JMPR residue evaluations, p. 510) by multiplying the omethoate residues by a factor of 10 for calculation of the sum of the residues. The total toxicologically significant residues, calculated in this way, were used for the estimation of dietary exposure. The present meeting followed the same practice. In the case of undetectable residues, the concentration of omethoate residues was calculated by taking into account the average ratio of dimethoate to omethoate in the edible portions of the crop at the specified pre-harvest interval. The sum (C_T) of dimethoate (C_D) and omethoate (C_O) residues reported for the specific commodities was calculated as $C_T = C_D + (10 \times C_O)$. The HRs and STMRs were estimated on the basis of the calculated C_T values.

Citrus fruits (oranges, mandarins/clementines and lemons). Dimethoate EC is registered for use on citrus in Spain, Italy, Greece, Brazil, Thailand and Morocco. The highest application rate according to GAP in southern Europe is 0.06 kg ai/ha. The application rate in Thailand is 0.3 to 0.6 kg ai/ha (0.02-0.04 kg ai/ha) and in Brazil 0.04 kg ai/ha. The PHIs are 3 days in Thailand and Brazil and 20-21 days in Spain, Italy and Greece. The number of applications is not specified in any country.

Eight supervised trials were conducted on oranges and eight on mandarins and clementines in Spain, Italy and Greece using dimethoate EC 400 g/l at application rates between 2.05 and 2.22 kg ai/ha (0.06 g ai/ha) applied three times as a foliar spray. In 1999 two lemon trials were reported from Italy and Greece where Dimethoate EC 400 g/l was applied three times at a rate of 2.08-2.16 kg ai/ha (0.06 kg ai/ha).

Dimethoate residues in whole orange fruit in southern Europe in trials complying with Greek or Spanish GAP in rank order were 0.29, 0.37, 0.41, 0.65, 0.77, 0.83, 0.85 and 1.50 mg/kg. The omethoate residues were <0.01, 0.02, 0.03 (2), 0.04 (2) and 0.05 (2) mg/kg. The residue concentrations in the orange pulp were <0.01 (2), 0.01, 0.02 (3), 0.03, 0.07 mg/kg for dimethoate and 0.002, <0.01(2), 0.01, 0.02, 0.03(2), 0.08 for omethoate. The average ratio of dimethoate to omethoate was 2.63.

Dimethoate residues in whole mandarins or clementines based on Greek or Spanish GAP in rank order were 0.35, 0.37, 0.52, 1.04, 1.17, 1.34, 1.48 and 3.10 mg/kg. The omethoate residues were 0.06, 0.08 (5) and 0.13 (2) mg/kg. The residues in the edible portions of the samples were <0.01 (2), 0.01 (2), 0.02 (3) and 0.07 mg/kg for dimethoate and <0.01, 0.02, 0.04, 0.05 (3), 0.11 and 0.13 mg/kg for omethoate. The average ratio of dimethoate to omethoate was 0.53.

Residues in whole lemon fruit at a 21-day PHI were 0.76 and 1.10 mg/kg dimethoate and 0.07 and 0.11 mg/kg omethoate. The residues in the edible portions were 0.05 and 0.19 mg/kg dimethoate and 0.05 and 0.06 mg/kg omethoate.

In supervised trials according to GAP in Brazil in 2002 dimethoate EC 400 g/l was sprayed 3 times on oranges at 0.8-1.60 kg ai/ha (0.04-0.08 kg ai/ha) with 3 days PHI. The LOQs were 0.02 mg/kg for dimethoate and 0.30 mg/kg for omethoate. The dimethoate residues in whole fruit were 0.15, 0.20 and 0.48 mg/kg. Residues of omethoate were <0.30 mg/kg in all trials.

In four supervised trials in Thailand in 2001 and 2002 dimethoate EC 400 g/l was sprayed on pomelos 4 times at 0.60 kg ai/ha (0.04 kg ai/ha). The residue results were reported only for dimethoate (LOQ 0.01 mg/kg). The trials complied with Thai GAP. The residues on whole fruit at 3 days PHI were 0.02, 0.06, 0.11 and 0.21 mg/kg.

The dimethoate residues from GAP applications in whole oranges, mandarins/clementines, lemons and pomelos were in the same range and can be combined for estimating a maximum residue level. They are in rank order 0.15, 0.2, 0.29, 0.35, 0.37 (2), 0.41, 0.48, 0.52, 0.65, 0.76, 0.77, 0.83, 0.85, 1.04, 1.1, 1.17, 1.34, 1.48, 1.50 and 3.1 mg/kg.

The dimethoate equivalents of the sum of dimethoate and omethoate residues in the citrus pulp (excluding the Brazilian trials) in rank order are 0.03, 0.049, 0.059, 0.11, 0.16, 0.20, 0.2, 0.22, 0.22, 0.32, 0.33, 0.41, 0.41, 0.45, 0.68, 0.81, 1.12, 1.37 mg/kg.

The Meeting estimated a maximum residue level of 5 mg/kg for citrus fruits, and an HR of 1.4 mg/kg and STMR of 0.27 mg/kg for the edible portion of citrus fruits. For the purpose of estimating STMR-*P*s for processed commodities, the STMRs are 0.76 mg/kg for dimethoate and 0.035 mg/kg for omethoate.

Cherries. Four residue trials were conducted in southern Europe between 1999 and 2001. Cherries were sprayed once with dimethoate EC 400 g/l at a rate between 0.74 and 0.78 kg ai/ha (0.05 kg

ai/hl). GAP in Austria, Belgium, Germany, Italy, Portugal and Spain specifies application rates between 0.02 and 0.04 kg ai/hl except in Spain (0.04-0.06 kg ai/hl) and a PHI of 20-21 days in Austria, Germany and Italy, and 14 days in Belgium, Portugal and Spain. The maximum number of applications is 3 in Germany (with 8-14 days intervals) but is not specified in other countries. Thus, the residue trials complied with GAP in Spain and represent the worst-case situation.

The residues in cherries from southern European trials, evaluated with respect to Spanish GAP, in rank order were 0.12, 0.18, 0.21 and 0.33 mg/kg dimethoate, 0.05, 0.12(2) and 0.17 mg/kg omethoate.

The dimethoate equivalents of the sum of dimethoate and omethoate residues in cherries were 0.68, 1.32, 1.53 and 1.91 mg/kg.

The Meeting recommended an MRL of 2 mg/kg, confirming the existing CXL.

Mangoes. In Australia 5 supervised trials were conducted in 2001 and 2002 on mangoes with dimethoate EC 400 g/l as 3 foliar sprays, 3 foliar sprays plus one dip application, and one dip application only. Application rates were 0.03 kg ai/hl for foliar and 0.04 kg ai/hl for dip applications. Post-harvest treatment of mango fruits by dipping in dimethoate solution for one minute is compulsory whether mangoes had previously received a dimethoate foliar application or not. The residue trials complied with GAP in Australia. The residues were determined separately as dimethoate and omethoate in the peel and pulp, then calculated as dimethoate (sum of dimethoate and omethoate) in the whole fruit, allowing for the weight of the stone. The limit of reporting was 0.02 mg/kg for both dimethoate and omethoate.

Dimethoate residues in whole mango fruit from the Australian trials at a PHI of 3 days for the pre-harvest application and 0 days for the post-harvest application in rank order were 0.18, 0.25, 0.26, 0.34 and 0.43 mg/kg for dimethoate and 0.02 (2), 0.03, 0.05 and 0.06 mg/kg for omethoate.

The average ratio of dimethoate to omethoate was 2.5. The dimethoate equivalents of the sum of dimethoate and omethoate residues in mango pulp were 0.12, 0.15, 0.36, 0.39 and 0.68 mg/kg.

The Meeting estimated a maximum residue level of 1 mg/kg Po for mango, and an HR of 0.68 mg/kg and STMR of 0.36 mg/kg for the edible portion of mangoes.

Olives. Nine trials were conducted in Spain, Italy and Greece from 1999 to 2001. Dimethoate EC 400 g/l was applied four times to olives at application rates of 0.42-0.45 kg ai/ha (0.06 kg ai/hl; water volume 700 l/ha) and 0.71-0.76 kg ai/ha (0.06 kg ai/hl; water volume 1200 l/ha). Dimethoate EC 400 g/l is registered for foliar application to olives in Greece at the rate of 0.03 kg ai/hl repeated at 20-day intervals and a PHI of 20 days for high volume sprays and 15 days for LV and ULV sprays (ULV from air only). In Italy the rate is 0.028-0.56 kg ai/hl with up to 3 applications and 28 days PHI, in Portugal 0.03-0.06 kg ai/hl with one or two sprays and 21-42 days PHI, in Spain 0.04-0.06 kg ai/hl with 60 days PHI and in Morocco 0.04-0.06 kg ai/hl. The highest GAP application rate in southern Europe is 0.06 kg ai/hl which matches the rates in the residue trials.

The dimethoate residues in olives at 28 days PHI in rank order were <0.01 (2), 0.01, 0.03, 0.04, 0.13, 0.15, 0.21 and 0.34 mg/kg. The omethoate residues were 0.06 (2), 0.07, 0.20, 0.22, 0.26, 0.33, 0.40 and 0.44 mg/kg.

The average ratio of dimethoate to omethoate was 0.4. The dimethoate equivalents of the sum of the dimethoate and omethoate residues in olives were 0.61, 0.61, 0.73, 2.01, 2.24, 2.75, 3.31, 4.01 and 4.34 mg/kg.

The Meeting estimated a maximum residue level of 0.5 mg/kg for fresh olives, and an STMR of 2.24 mg/kg and an HR of 4.3 mg/kg for the estimation of dietary intake. For the purpose of

estimating the STMR-Ps for processed commodities the STMRs are 0.04 mg/kg for dimethoate and 0.22 mg/kg for omethoate.

Cauliflower. A set of 8 trials, conducted in the UK in 1996 and 1997, was described in the 1998 JMPR evaluation. Dimethoate EC 400 g/l was sprayed at 0.4 kg ai/ha (0.067 kg ai/hl) six times per year, the last application at growth stage BBCH 43-49.

Dimethoate EC 400 g/l is registered for use on cauliflower in Denmark, Germany, The Netherlands, Poland, the UK and Spain. Rates of application range between 0.2 and 0.4 kg ai/hl with PHIs of 14-42 days and 1-6 applications. Six of the trials were evaluated against UK GAP. Dimethoate residue levels at 21 days in rank order were <0.01 (4), 0.02 and 0.11 mg/kg and the omethoate residues were <0.01 (6) mg/kg.

The average ratio of dimethoate to omethoate was 6.5. The dimethoate equivalents of the sum of dimethoate and omethoate residues were 0.025 (4), 0.035 and 0.13 mg/kg.

Noting that the critical GAP in the UK has been changed from a PHI of 7 days to 21 days, the Meeting estimated a maximum residue level of 0.2 mg/kg for cauliflower to replace the existing draft MRL of 0.5 mg/kg, and an STMR of 0.025 mg/kg and HR of 0.13 mg/kg.

Brussels sprouts. Eight trials in the UK in 1996 and 1997 were described in the 1998 JMPR evaluation. According to UK GAP dimethoate EC 400 g/l may be applied 6 times at the rate of 0.4 kg ai/ha (0.067 kg ai/hl), the last application at growth stage BBCH 43-49, with a PHI of 14 days. Dimethoate EC (400-404 g/l) is registered for use in Germany (0.24-0.36 kg ai/ha twice with a PHI of 14 days), The Netherlands (0.20 kg ai/ha, once or twice and PHI 21 days), and Spain (0.04-0.06 kg ai/hl and PHI 21 days). The GAP of the UK has the highest application rate in northern Europe and represents the worst-case situation.

The residues in Brussels sprouts at 14 days PHI in rank order were dimethoate 0.03 (2), 0.04, 0.06, 0.10 (2) and 0.11 (2) mg/kg and omethoate <0.01 (2), 0.02, 0.03 (2), 0.04, 0.07 and 0.11 mg/kg. The average ratio of dimethoate to omethoate was 2.98. The dimethoate equivalents of the sum of dimethoate and omethoate residues in Brussels sprouts were 0.064, 0.14, 0.23, 0.34, 0.36, 0.50, 0.81, 1.20 mg/kg.

Noting that the critical GAP in the UK has been changed from a PHI of 7 days to 21 days, and that the residues from other trials were <0.1 mg/kg, the Meeting estimated a maximum residue level of 0.2 mg/kg for Brussels sprouts to replace the existing draft MRL of 1 mg/kg, and an STMR of 0.35 mg/kg and HR of 1.2 mg/kg.

Head cabbages. Eight residue trials were conducted outdoors in the UK in 1996 and 1997 (evaluated by the 1998 JMPR) and one trial in Poland in 1996 (only dimethoate residues were reported). GAP was reported from Denmark, Finland, Germany, The Netherlands, Norway, Sweden, Spain and Poland but not from the UK. 0.4 kg ai/ha (0.067 kg ai/hl) was applied six times in the UK trials which were evaluated against German GAP. The residues of dimethoate at 14 days PHI in rank order were 0.01, 0.04, 0.06, 0.11, 0.34, 0.67, 0.71 and 0.99 mg/kg and of omethoate 0.01, 0.02 (2), 0.07, 0.25, 0.35, 0.46 and 0.64 mg/kg.

The average ratio of dimethoate to omethoate was 2.47. The dimethoate equivalents of the sum of dimethoate and omethoate residues in cabbage were 0.05, 0.09, 0.12, 0.39, 1.55, 1.71, 1.72 and 3.26 mg/kg.

The Meeting confirmed its previous recommendation (2 mg/kg, now a CXL) for head cabbages (excluding Savoy cabbage). The Meeting estimated an STMR of 0.97 mg/kg and an HR of 3.26 mg/kg.

Sweet peppers. Seven supervised trials were conducted in 2001 and 2002 in Australia. Dimethoate EC 400 g/l was applied by post-harvest dipping at 0.04 kg ai/hl or as a pre-harvest foliar treatment at 0.3 kg ai/ha with 7 days PHI followed by post-harvest application at 0.04 kg ai/hl. The residues were determined in the whole fruit. The limits of reporting were 0.02 mg/kg for dimethoate and 0.02-0.04 mg/kg for omethoate. The trials complied with Australian GAP.

The residues of dimethoate after foliar application at a 7-day PHI were 0.03 (2) and 0.14 mg/kg. Since the residues after foliar and post-harvest application were 0.23, 1.71 and 1.75 mg/kg, it was concluded that the contribution of foliar application to the residues after post-harvest application was negligible and residues from all post-harvest trials could be used for evaluation.

The dimethoate residues after post-harvest (with or without foliar) application were 0.23, 0.27, 1.26, 1.46, 1.5, 1.56, 1.71, 1.75, 1.8 and 2.95 mg/kg. Omethoate residues were 0.19 (2) and not detected.

The average ratio of dimethoate to omethoate was 39. The dimethoate equivalents of the sum of dimethoate and omethoate residues were 0.24, 0.28, 1.27, 1.51, 1.57, 1.72, 1.76, 2.96, 3.36 and 3.7 mg/kg.

The Meeting estimated a maximum residue level of 5 mg/kg, an STMR of 1.64 mg/kg and an HR of 3.7 mg/kg for sweet peppers. The maximum residue level is recommended to replace the existing CXL of 1 mg/kg for peppers.

Melons. Eight residue trials were conducted in Italy, Spain and Greece in 2000 and 2001. No information on GAP for dimethoate use on melons, pumpkins or watermelons was available. The Meeting could not estimate a maximum residue level, STMR or HR.

Tomatoes. Eight supervised trials in 2000 and 2001 were reported from Spain and Italy. Tomatoes were treated twice at 0.614-0.653 kg ai/ha (0.1 kg ai/hl). GAP in Germany on tomatoes in glasshouses is 0.24 to 0.48 kg ai/ha with three applications and 3 days PHI, and in Ireland 0.034 kg ai/hl by foliar application and 7 days PHI. Brazil requires 0.04 kg ai/hl foliar application and 14 days PHI. GAP in Italy is 0.028 to 0.040 kg ai/hl and 21 days PHI. The supervised trials in Italy and Spain did not comply with the corresponding GAP, and the results could not be evaluated. The Meeting recommended withdrawal of the draft MRL of 2 mg/kg.

Head lettuce. Nine residue trials were conducted in Spain, Italy and Greece in 2000 and 2001. Lettuce was sprayed outdoors once at 0.41-0.42 kg ai/ha (0.04 kg ai/hl). GAP in Spain is 0.04-0.06 kg ai/hl LV with 14 days PHI, in Greece 0.03-0.05 kg ai/hl and 20 days PHI and in Italy 0.028-0.040 kg ai/hl and 14 days PHI. The number of sprays is not specified. The trials were evaluated against GAP in Italy.

The residues of dimethoate at 14 days PHI in rank order were <0.002 (3), <0.01 (3), 0.03, 0.07 and 0.11 mg/kg and of omethoate <0.01 (5), 0.01, 0.02, 0.04 and 0.06 mg/kg.

In northern Europe residue trials on lettuce were conducted in 1996 and 1997. Lettuce was sprayed outdoors at a rate of 0.34 kg ai/ha (0.17 kg ai/hl) six times. GAP in Denmark is 0.30-0.32 kg ai/ha (number of application not specified) with a 21-day PHI, in the UK 0.34 kg ai/ha 6 times with a 14-day PHI, in Germany 0.24-0.36 kg ai/ha twice or 0.40 kg ai/ha once with a 21-day PHI, in Ireland 0.34 kg ai/ha repeated as necessary with a 7-day PHI and in The Netherlands 0.20 kg ai/ha 1 or 2 times with a 21-day PHI. Thus, the trials complied with UK GAP and represent the worst-case situation.

The residues of dimethoate at 14 days PHI in ranked order were 0.01, 0.02 (3), 0.04, 0.07 (2) and 0.11 mg/kg and of omethoate <0.01 (5), 0.02 and 0.03 (2) mg/kg.

The residues from southern and northern Europe seem to be from the same population and may be evaluated together, giving residues at 14 days in ranked order of <0.002 (3), <0.01 (3), 0.01, 0.02 (3), 0.03, 0.04, 0.07 (3) and 0.11 (2) mg/kg for dimethoate, and <0.01 (10), 0.01, 0.02 (2), 0.03 (2), 0.04 and 0.06 for omethoate.

Eleven residue trials were conducted in glasshouses in the UK in 1996 and 1998. Dimethoate EC 400 g/l was applied once at 0.34 kg ai/ha (0.17 kg ai/hl) with a PHI of 28 days. GAP for glasshouse use was reported from Ireland (0.34 kg ai/ha, repeated as necessary, 28-day PHI). The supervised trials complied with Irish GAP.

The residues in ranked order were <0.01, 0.01 (2), 0.02 (2), 0.06, 0.16, 0.17, 1.1 (2) and 2.2 mg/kg for dimethoate and <0.01 (4), 0.01, 0.03 (2), 0.04, 0.17, 0.20 and 0.29 mg/kg for omethoate.

Since the indoor use resulted in higher residues the glasshouse trials were used for estimation of a maximum residue level, an STMR and an HR.

The average ratio of dimethoate to omethoate was 11. The dimethoate equivalents of the sum of dimethoate and omethoate residues in indoor lettuce were 0.03 (4), 0.11, 0.31, 0.31, 0.41, 1.71, 2.01 and 2.70 mg/kg.

The Meeting estimated a maximum residue level of 3 mg/kg for head lettuce, recommended to replace the draft MRL of 0.5 mg/kg, and an STMR of 0.31 mg/kg and HR of 2.7 mg/kg.

Sugar beet. Eight trials were conducted in 2000 and 2001 in southern Europe (including 2 decline trials and 2 at-harvest trials in Spain, and 2 decline curve trials and 2 at harvest trials in Italy). Rates of 0.62-0.64 kg ai/ha (0.06 kg ai/hl) were applied twice with a 30-day PHI. Dimethoate EC 400 g/l is registered for use on sugar beet in many countries (Finland, Germany, Greece, Italy, The Netherlands, Poland, Spain, Sweden, the UK and Ireland), with GAP in Italy 0.02-0.04 kg ai/hl, 30 days PHI, Spain 0.04-0.06 kg ai/hl, 60 days PHI and Greece 0.03-0.05 kg ai/hl, 14 days PHI. In one trial in Spain the residue of dimethoate in sugar beet leaves or tops was 0.13 mg/kg at 14 days. The residues of dimethoate at 30 days in sugar beet leaves or tops in rank order were <0.002 (7) and <0.01 mg/kg, and of omethoate <0.01 (4), 0.02 (2), 0.03 and 0.04 mg/kg. No residues of dimethoate or omethoate (<0.01 mg/kg) were found in sugar beet root at PHIs of 30-60 days.

Six residue trials conducted in 1994 and 1995 in Germany, the UK and The Netherlands are described in the 1998 JMPR evaluations. No residues were detected in sugar beet roots. In addition, 2 new trials were conducted in 2001 in the UK and Germany. The first application was 0.08-0.09 kg ai/ha (0.02-0.09 kg ai/hl) and the second at BBCH 38-39 0.41-0.42 kg ai/ha (0.02-0.09 kg ai/hl) with PHIs of 29-30 days. Residues in roots were undetectable (<0.002 mg/kg, LOQ 0.01 mg/kg).

The results of the recent supervised trials evaluated by the present Meeting confirm the recommendations (0.05 mg/kg for root and 0.1 mg/kg for leaves or tops) made by the 1998 JMPR.

Globe artichokes. Four trials were conducted in Italy and Spain in 2000 and 2001. Dimethoate EC 400 g/l was applied three times to artichokes at 0.42-0.43 kg ai/ha (0.04 kg ai/hl) with a PHI of 28 days. The only GAP for dimethoate in Italy is 0.06 kg ai/hl and a PHI of 20 days. Thus, the residue trials approximated GAP in Italy. The residues in the trials at 28 days PHI in ranked order were <0.01, 0.02 (2) and 0.04 mg/kg for dimethoate, and <0.01 (3) and 0.02 mg/kg for omethoate.

The average ratio of dimethoate to omethoate was 5.0, on the basis of the LOD values.

The dimethoate equivalents of the sum of dimethoate and omethoate residues in artichokes were 0.1 (3) and 0.2 mg/kg.

The Meeting estimated a maximum residue of 0.05 mg/kg, an STMR of 0.1 mg/kg and an HR 0.2 mg/kg for globe artichokes.

Asparagus. Six residue trials at rates of 0.41-0.43 kg ai/h (0.04 kg ai/hl) applied twice, the second application at fern stage, were conducted in Spain and Italy in 2000, 2001 and 2002. GAP in Italy is 0.028-0.04 kg ai/hl with a PHI of 14 days and in Greece is 0.03-0.05 kg ai/hl (3 applications). The trials were evaluated against GAP in Italy.

The residues of dimethoate and omethoate were below the limit of detection (<0.002 mg/kg) except in one sample, where 0.01 mg/kg dimethoate was found.

Since the trials in compliance with US GAP evaluated by the 1998 JMPR indicated higher residues, the results of the new trials did not affect the previously estimated maximum residue level.

Celery. Four residue trials were conducted in Italy and Spain in 2000 and 2001. Celery was sprayed with dimethoate EC 400 g/l twice at 0.49-0.51 kg ai/ha (0.05 kg ai/hl). The highest GAP application rate in southern Europe is 0.04 kg ai/hl with PHI 20-21 days (Italy). Thus, the residue trials complied with GAP. The residues were <0.002, 0.07, 0.09 and 0.28 mg/kg for dimethoate, and <0.01, 0.02 and 0.04(2) mg/kg for omethoate.

The average ratio of dimethoate to omethoate was 4.42. The dimethoate equivalents of the sum of dimethoate and omethoate residues in celery were 0.03, 0.2 and 0.4 (2) mg/kg.

The Meeting estimated a maximum residue level of 0.5 mg/kg, an STMR of 0.2 mg/kg and an HR 0.4 mg/kg for celery.

Wheat grain. Eight residue trials were conducted in Italy and Spain in 2000 and 2001. Wheat was sprayed once at 0.40-0.44 kg ai/ha (0.10 kg ai/hl). GAP in Italy is 0.020-0.028 kg ai/hl, PHI 28 days and in Portugal 0.04 kg ai/hl, PHI 14 days.

Only one grain sample from day 14 was analysed. The residues in grain at 28 days were <0.001, <0.01 (4), 0.007, 0.014 and 0.024 mg/kg of dimethoate, and <0.001 (2), 0.002 (2) and <0.01 (4) mg/kg of omethoate.

Seven residue trials were conducted in Germany and the UK in 2001 and 2002. Dimethoate was applied at 0.71-0.77 kg ai/ha (0.35 kg ai/hl) at the first application and 0.35-0.39 kg ai/ha (0.18 kg ai/hl) at the second. The highest GAP application rate in northern Europe is 0.68 kg ai/ha in Germany, Ireland and the UK at the first application and 0.34 kg ai/ha at the second. The PHI in Germany is 21 days. The trials were evaluated against German GAP.

Residues in wheat grain at 28 days (2 trials at 42 days) in ranked order were <0.001 (5) and 0.001 (2) mg/kg of dimethoate, and <0.001 (5), 0.001 and 0.002 mg/kg of omethoate.

In 1998 the critical GAP was from the UK, allowing 4 applications and a PHI of 14 days. Current GAP permits one application before 31 March. The high residues in 1998 derived from the UK trials according to UK GAP at that time, should therefore be excluded from the current evaluation.

The average ratio of dimethoate to omethoate was 9.5. The dimethoate equivalents of the sum of dimethoate and omethoate residues in wheat grain were 0.021 (13), 0.029 and 0.049 mg/kg.

The Meeting estimated a maximum residue level of 0.05 mg/kg for wheat to replace the estimate of 0.2 mg/kg, an STMR of 0.021 mg/kg and an HR of 0.05 mg/kg.

Wheat straw. The residues in wheat straw from the above trials in southern Europe at a 28-day PHI were <0.01, 0.03 (2), 0.10, 0.11, 0.16, 0.37 and 0.45 mg/kg of dimethoate, and <0.01 (4), 0.01, 0.02, 0.07 and 0.08 mg/kg of omethoate.

The residues in wheat straw from northern Europe at PHI 28 days (or at earliest commercial harvest) in ranked order were <0.002 (3), <0.01 (2), 0.02, 0.05 and 0.07 mg/kg of dimethoate, and <0.002 (5), <0.01 (3) mg/kg of omethoate.

The average ratio of dimethoate to omethoate was 7.06. The adjusted sum of dimethoate and omethoate residues in wheat straw were 0.002, 0.006 (2), 0.01, 0.02, 0.05 (2) and 0.07 mg/kg (fresh weight).

Allowing for the standard 88% dry matter for wheat straw (FAO Manual, p. 149), the Meeting estimated a maximum residue level of 1 mg/kg for wheat straw to replace the draft MRL of 10 mg/kg and an STMR of 0.017 mg/kg for wheat straw.

Fate of residues during processing

Processing studies were reported on olives, cabbages and wheat. The STMR-P values of dimethoate and omethoate were calculated from their STMRs in the raw agricultural commodities and the corresponding processing factors, and then the combined STMR-P was calculated from the individual STMR-P values taking into account the multiplying factor of 10 for omethoate.

In studies on processing olives treated with dimethoate 0.39-3.01 mg/kg in the RAC yielded 0.17-1.26 mg/kg dimethoate in crude olive oil. The results are in line with the studies reported in the 1984 evaluation.

Processing studies on oranges treated with dimethoate were evaluated in 1998 (Residue Evaluations, p. 490). The estimated processing factors were used to estimate the STMR-P values from the STMRs for citrus fruits (dimethoate 0.76, omethoate 0.?? mg/kg) estimated by the present Meeting.

The estimated processing factors and STMR-Ps for orange juice, dry orange pulp, processed olive products and wheat products are summarized below.

Processed commodity	Processing factor		STMR of RAC, mg/kg		STMR-P ¹ , mg/kg
	Dimethoate	Omethoate	Dimethoate	Omethoate	
Orange juice	0.14 ²	0.21 ²	0.76	0.035	0.49
Orange pulp, dry	2.1 ²	1.7 ²	0.76	0.035	1.7 ³
Olive oil, raw	0.43	0.019	0.04	0.22	0.059
Olive oil, refined	0.016	0.019	0.04	0.22	0.042
Olive, processed	0.21	0.12	0.04	0.22	0.43
Wheat wholemeal ²	0.19	0.1	0.09	0.01	0.027
White wheat flour	0.079	0.071	0.09	0.01	0.014

¹ Based on sum of dimethoate and 10 times omethoate (except dry orange pulp)

² Based on processing factors reported by 1998 JMPR

³ Based on sum of dimethoate and omethoate

The outer leaves of cabbages contained most of the residues (0.19 mg/kg compared with 0.05 mg/kg in whole cabbage) which are removed as part of kitchen processing. Both dimethoate and omethoate were decomposed during cooking.

Residues in animal commodities

On the basis of the metabolism studies, the 1998 JMPR concluded that it was unlikely that residues would occur in animal commodities and did not calculate the animal burden. Consequently the animal burden was not calculated by the present Meeting and MRLs for animal commodities are recommended to be maintained.

DIETARY RISK ASSESSMENT

The toxicological evaluation of omethoate revealed that it is about 10 times as toxic as dimethoate. Since consumers are exposed to both dimethoate and omethoate residues present at the time of consumption, the difference in toxicity was taken into account by multiplying the omethoate residues with a factor of 10 for calculation of the sum of residues. The total toxicologically significant residues, calculated in this way, were used for the estimation of dietary exposure. The sum (C_T) of dimethoate (C_D) and omethoate (C_O) residues was calculated as $C_T = C_D + (10 \times C_O)$. The HR and STMRs were estimated from the calculated C_T values.

Long-term intake

The International Estimated Dietary Intakes (IEDIs) were calculated for the five GEMS/Food regional diets using STMRs for 12 commodities and STMR-Ps for orange juice, processed olives, virgin olive oil, wheat flour and wheat wholemeal. The IEDI was 150% of the ADI (0-0.002 mg/kg bw) for the European diet. IEDIs for the other four regional diets were in the range of 10-90% of the ADI (Annex 3).

The information provided to the JMPR precludes an estimate that the dietary intake would be below the ADI.

Short-term intake

The International Estimated Short-Term Intakes (IESTIs) were calculated for commodities for which maximum residue levels or STMR(P)s were estimated by the current Meeting. An acute reference dose of 0.02 mg/kg bw was established by the 2003 JMPR. The results are shown in Annex 4.

The IESTI represented 0-320% of the acute RfD for the general population and 1-760% of the acute RfD for children. The values 320 and 130% represent the estimated short-term intakes for head cabbages and head lettuce, head respectively for the general population. The values 760, 200 and 140% represent the estimated short-term intake for head cabbages, head lettuce and sweet peppers respectively for children. The information provided to the JMPR precludes an estimate that the dietary intakes calculated for these 3 commodities would be below the acute reference dose. The Meeting concluded that the short-term intake of residues of dimethoate and omethoate from uses of dimethoate on commodities, other than these three, that have been considered by the JMPR is unlikely to present a public health concern.

The Meeting noted that the acute RfD could be refined upon re-evaluation of the whole toxicological profile of dimethoate.

4.7 DIPHENYLAMINE (030)

RESIDUE AND ANALYTICAL ASPECTS

The CCPR at its 35th Session (Paragraph 57, ALINORM 03/24a, 2003) decided to advance the MRL for cattle milk to Step 5 and requested JMPR to clarify whether whole milk or milk fat was fortified in the recovery experiments. The Committee noted that the definition of the residue should indicate that the compound is fat-soluble.

Recovery tests were successful for both whole milk and milk fat. Analytical recoveries by the enforcement method for diphenylamine from samples fortified at 0.01 and 1.0 mg/kg were satisfactory for whole milk, skimmed milk and cream (milk fat). The results are summarized in Table 14, p. 169 of the JMPR Residue Evaluations, 2001. The 2001 JMPR recommended that diphenylamine should be described as fat-soluble.

The recommended maximum residue level for milk is 0.0004*F.

The "F" indicates that the recommended maximum residue level is calculated as 4% of the estimated concentration in milk fat (0.01 mg/kg). Milk fat is the fraction of the milk that is analysed. The asterisk indicates that the estimated concentration in milk fat is at or about the LOQ for milk fat (0.01 mg/kg). Analytical recoveries were satisfactory for diphenylamine in cream (milk fat) at 0.01 mg/kg.

4.8 DODINE (084)

RESIDUE AND ANALYTICAL ASPECTS

Dodine, 1-dodecylguanidinium acetate (dodecylguanidine monoacetate), is a fungicide and bactericide registered for foliar use on pome fruits, stone fruits including cherries, and nuts including walnuts.

Dodine is the only active substance from the guanidine family, which was first evaluated in 1974 for toxicology and residues by the JMPR and subsequently in 1976 and 1977. The latest toxicology review was in 2000. It was listed under the Periodic Review Programme at the 30th Session of the CCPR (ALINORM 99/24) for review by the 2001 JMPR but was re-scheduled for 2003.

The 2000 JMPR allocated an acceptable daily intake for humans of 0-0.1 mg/kg bw and an acute reference dose of 0.2 mg/kg bw.

The 1977 JMPR considered that a feeding study with large animals to determine whether feeding apple pomace and grape pomace would contribute residues to meat and milk was still desirable.

The manufacturer supplied information on identity, methods of analysis, use pattern, metabolism in plants and farm animals, residue trials on apples, pears, cherries, peaches and plums, storage stability in analytical samples, effects of processing on residues and fate in the environment.

In addition, information on GAP was provided by the governments of France and The Netherlands.

Dodine is currently formulated as wettable powders, suspension concentrates and wettable granules. It is a slightly yellow fine powder with low solubility in water (<1g/l) and organic solvents. Dodine is not considered fat-soluble, as its log octanol/water partition coefficient is 0.96.

Animal metabolism

The metabolism of radiolabelled dodine has been investigated in rats and a lactating goat. The metabolic pathway in both rats and goat suggests that dodine is extensively metabolized by both species by initially forming a carboxylic acid chain with the elimination of urea and a consequent series of 2-carbon degradation cycles, consistent with the beta oxidation pathway used by mammals to degrade medium to long chain fatty acids.

Rat metabolism was reviewed by the 2000 JMPR. Cumulative excretion in urine and faeces was reported as being above 90% of the dose. Absorbed dodine is extensively metabolized in rats. Four metabolites were seen in urine: hydroxydodecylguanidine, the main metabolite, urea, and two unidentified metabolites which appeared to be a mixture of carboxylic acid products arising from oxidation of the alkane side chain.

In a lactating goat dosed orally for five consecutive days with [¹⁴C]dodine at the mean equivalent dietary level of 12.8 ppm by gelatin capsule, dodine was extensively metabolized. Sixty eight per cent of the dose was excreted in urine (38%), faeces (30%) and milk (0.05%). Less than 1% of the dose remained in the tissues. Dodine was a minor component in all edible tissues and no parent compound was present in milk. In the dosed goat, ¹⁴C levels were much higher in kidney and liver (0.168 mg/kg and 0.109 mg/kg as dodine) than in muscle or fat (0.02 mg/kg-0.008 mg/kg as dodine). Hexylguanidine carboxylic acid, octylguanidine carboxylic acid and dodecylguanidine carboxylic acid were identified but none exceeded 0.001 mg/kg dodine equivalents in the foreleg muscle or 0.05 mg/kg in the liver and kidney; urea was present in all edible tissues and milk (from <0.01 mg/kg dodine equivalents in milk and muscle to <0.017 mg/kg in liver and kidney).

Plant metabolism

Plant metabolism studies on apples, strawberries and pecan trees were reported. In apples and strawberries, the parent compound was the main component of the residue; metabolism appeared to be more active in nuts with dodine and guanidine being the main residues found in kernels. In apples much of the residue remained in the peel. The metabolism of dodine was found to be essentially similar among the plants tested. Degradation of dodine in fruits is a relatively slow process, occurring by successive oxidation and hydrolysis to CO₂ and ammonia; guanidine and urea are intermediate degradation products.

After three foliar applications of [¹⁴C]dodine to field grown apple trees at a rate of 0.108 kg ai/hl each, radioactive residues at mature harvest (7 days after the third application) were mainly located in the apple peel (82.3% of the TRR). Dodine accounted for 72 to 89% of the TRR extracted from apple peel and pulp. Several minor metabolite fractions were observed, all below 0.01 mg/kg except one compound tentatively identified as guanidine, found at 0.017 mg/kg dodine equivalents.

After four foliar applications of [¹⁴C]guanidine dodine to strawberries at 3.12 kg ai/ha, radioactive residues in mature fruit harvested 14 days after the third and fourth applications represented 4.3 to 6.8 mg/kg dodine equivalents. Unchanged dodine accounted for >85% of the TRR in washed strawberries. Several metabolite fractions were observed, all below 0.01 mg/kg dodine equivalents except one at 0.05 mg/kg. No major metabolite was found, although urea and guanidine were identified as possible metabolites. In rinses (2.5% of the TRR), the parent was also the major component of the residue. No degradation product occurred at >0.01 mg/kg dodine equivalents.

After three foliar applications of [¹⁴C]dodine to pecan trees during the growing season at 0.2 kg ai/hl, a low level of the applied dodine reached the kernels. Kernels isolated from mature pecans contained 0.114 mg/kg radioactive residues, composed of guanidine (0.041 mg/kg expressed as dodine, 36% of the TRR) and dodine (0.015 mg/kg, 13.2% of the TRR). Twenty per cent of the TRR (0.023 mg/kg dodine equivalents) was associated with the free fatty acid fraction.

Most of the parent compound undergoes extensive metabolism to guanidine, followed by subsequent metabolism to $^{14}\text{CO}_2$ and NH_3 . Carbon dioxide is assimilated into the metabolic pool. The very high proportion of lipid in the kernels is consistent with incorporation of $^{14}\text{CO}_2$ into the fatty acid fraction.

Immature pecans (including shells and hulls) harvested before the second application (60 days after the first) contained 2.152 mg/kg TRR, dodine (0.976 mg/kg, 43.2% of the TRR) and guanidine (0.326 mg/kg dodine equivalents, 14.4% of the TRR) being the main compounds. Two unidentified metabolites, putative oxidation products of dodine, accounted for 0.2 mg/kg dodine equivalents (9.3% of the TRR) and 0.288 mg/kg dodine equivalents (13% of the TRR).

Environmental fate

Soil

The Meeting received information on the degradation of dodine under aerobic conditions in a number of soils, on soil photolysis and on field dissipation.

Aerobic soil degradation of dodine is rapid; the calculated half-lives ranged from 3 to 10 days in the tested soils. This degradation ultimately results in the formation of carbon dioxide without the formation of any other significant degradation products or persistent unextractable residues.

Field experiments confirmed that dodine is not a persistent compound and has a rather short half-life ranging from 6 to 18 days at four locations; it did not move down the soil profile. Dodine did not undergo significant photolysis on soil surfaces.

It is suggested that the degradation of dodine in the environment is mainly microbial.

Analytical methods

The Meeting received a description and validation of analytical method 45137 for dodine in fruit crops. The method is based on GC with mass-selective detection (MSD) and achieved an LOQ of 0.05 mg/kg in apples, plums, peaches, pears and cherries, and 0.1 mg/kg in wet apple pomace.

Dodine is extracted from the fruit by homogenization with methanol and the solution is filtered and brought to a volume. An aliquot is cleaned up by liquid-liquid partition and the dodine is derivatized by refluxing for two hours with hexafluoroacetylacetone in 1-chlorobutane. The solvent is evaporated and the samples are dissolved in cyclohexane for GC-MSD.

Wet apple pomace samples from the metabolism study with [^{14}C]dodine were extracted and analysed by method 45137 giving an average value of 2.15 mg/kg. The average value obtained by LSC after re-extraction according to the apple method was 1.95 mg/kg, which is close to method 45137.

Stability of residues in stored analytical samples

The Meeting received information on the stability of dodine in various substrates at freezer temperatures.

In the two studies conducted to examine the stability of dodine residues under deep freezer storage conditions, no significant degradation of dodine was observed, for the duration of the study, in any of the substrates analysed.

The Meeting concluded that dodine was stable up to 18 months in apple, cherry, peach, apple juice and wet apple pomace samples when stored frozen.

Definition of the residue

Dodine was the main identified component (in samples containing ≥ 0.05 mg/kg) detected in edible portions in plant metabolism studies, representing 80.6% of the extracted TRR in apple pulp, 86.5% of the extracted radioactivity of washed strawberries and 13.2% of the TRR in mature pecan kernels. No major metabolite was identified except in pecan kernels where guanidine represented 36% of the TRR but only 0.041 mg/kg.

In the metabolism study on a lactating goat dosed orally dodine represented less than 1% of the TRR in edible tissues and was not identified in milk. The major metabolites of dodine identified in tissues and milk, resulting from beta oxidation, were hexylguanidine carboxylic acid, octylguanidine carboxylic acid and dodecylguanidine carboxylic acid, each representing less than 0.05 mg/kg dodine equivalents.

The Meeting concluded that dodine residues, both for compliance with MRLs and for the estimation of dietary intakes should be defined as dodine.

The definition applies to both plant and animal commodities.

Results of supervised trials

Supervised trials with the foliar application of WP and SC formulations to apples, pears, peaches, cherries and plums were reported from Europe (Belgium and France) and the USA.

In all supervised trials reported from France on pears, residues were measured on fruit taken just before the last application as well as just after it. The first residue expressed as a percentage of the second provides an indication of the contribution of previous applications to the final residue in the case of multiple applications. The average carryover of 48% (range 16%-91%) suggests that the number of applications may have an influence on the final residue at harvest. Decline studies on both apples and pears suggest that dodine has an average half-life of about 20 days after multiple applications. It is therefore considered that 2 applications will be likely to produce a higher residue level than one application and would provide reliable information for estimating residue levels.

Trials were not reported on strawberries or grapes for which CXLs exist at 5 mg/kg for both commodities. The Meeting agreed to recommend withdrawal of these CXLs.

Apples. Field data were reported from France and the USA.

GAP for France is 0.7 kg ai/ha with a PHI of 28 days for SC formulations and allows a maximum of four applications. Seventeen supervised residue trials in France complied with the French PHI and application rate but would probably have produced lower residues than expected as the interval between the penultimate and last applications was generally longer than intended. The residues at mature harvest were 0.07, 0.12, 0.14 (2), 0.16, 0.17 (2), 0.23, 0.25, 0.31, 0.32, 0.34, 0.39, 0.49, 0.59, 0.61, 0.87.

GAP in the USA specifies foliar application of 0.75 to 2.2 kg ai/ha with a PHI of 7 days for the WP formulation, with no information on the maximum number of applications. Thirteen trials in the USA complied with US GAP; the residues were 0.88, 1.03, 1.10, 1.14, 1.32, 1.43, 1.44, 1.55, 1.73, 1.85, 2.01, 2.28 and 2.35 mg/kg.

The Meeting decided to use only the US trials in the evaluation because the two populations of results were considered to be different.

Pears. Field data were reported from Belgium, France and the USA.

GAP for France is the same as for apples. Fourteen supervised trials in France matched French GAP. The residues in rank order were 0.16, 0.18, 0.25, 0.26, 0.29, 0.31, 0.37, 0.40, 0.61, 0.54 (2), 0.6, 0.61 and 1.3 mg/kg.

GAP for Belgium is 1 kg ai/ha for SC formulations and allows three or four applications. Two Belgian trials supported the Belgian use pattern and the residues were 0.37 and 0.45 mg/kg.

GAP from the USA is for foliar application at 1.5-2.25 kg ai/ha with a PHI of 7 days for the WP formulation. Seven trials in the USA accorded with US GAP. The residues in rank order were 0.50, 1.68, 1.71, 1.74, 1.82, 1.94 and 2.43 mg/kg.

The Meeting decided to use only the US trials in the evaluation because the results from Europe and the USA were considered to be from different populations with higher residues in the US trials.

As the use patterns of dodine on pears and apples were considered similar in terms of PHIs and dose rates, the Meeting agreed to combine the results from the US trials for estimating a maximum residue level for pome fruits.

The combined residues in the 20 trials were 0.50, 0.88, 1.03, 1.10, 1.14, 1.32, 1.43, 1.44, 1.55, 1.68, 1.71, 1.73, 1.74, 1.82, 1.85, 1.94, 2.01, 2.28, 2.35 and 2.43 mg/kg.

The Meeting agreed to recommend the withdrawal of the existing separate CXLs of 5 mg/kg for apples and pears and made a new recommendation for pome fruits of 5 mg/kg, and estimated an STMR of 1.70 mg/kg and an HR of 2.43 mg/kg.

Cherries. Field trials were reported from France. Dodine is not registered in France on for use on cherries. Two of the French trials could be evaluated against Spanish GAP (0.05-0.08 kg/hl, 15 days PHI, no information on the maximum number of applications allowed) for foliar applications of the SC formulation. The results were 0.14 (2) mg/kg.

Dodine is registered in the USA at a dose rate of 0.75-1.5 kg for foliar applications but no current PHI was provided. GAP in Canada is 1.5 kg/ha by foliar application with a WP formulation and a PHI of 7 days but no information was provided on the maximum number of applications. The six US trials were evaluated against Canadian GAP. The results in rank order were 0.34, 1.08, 1.15, 1.27, 1.4 and 2.11 mg/kg.

The Meeting decided to use the results of US trials in the evaluation and agreed to recommend withdrawal of the current CXL of 2 mg/kg for cherries to be replaced by 3 mg/kg, and estimated an STMR and an HR of 1.21 mg/kg and 2.11 mg/kg respectively, both expressed on the whole fruit as no information was available on the edible portion.

Peaches and nectarines. Field trials on peaches were reported from France and the USA.

Five of the 7 supervised residue trials reported from France complied with the current French GAP of 0.9 kg ai/ha by foliar application of an SC formulation with a 60-day PHI (last treatment at the end of flowering). The results were <0.05 mg/kg in whole fruit and <0.05(2), 0.05 and 0.07 mg/kg (in pulp).

Nine supervised trials reported from the USA complied with the current US GAP of 1.5-3 kg ai/ha by foliar application with a WP formulation and a PHI of 15 days. The results in rank order were 0.46, 0.48, 0.68, 0.77, 1.27, 1.65, 1.77, 2.50 and 3.71 mg/kg.

The results from the US trials were evaluated. The Meeting confirmed the previous recommendation for an MRL of 5 mg/kg, now a CXL, and estimated an STMR of 1.27 mg/kg and an HR of 3.71 mg/kg (both expressed on whole fruit as no information was available on the edible portion).

The Meeting agreed to extrapolate the recommendations to nectarines as current GAP for peaches applies to nectarines in the USA.

Plums. Field trials were reported from the USA. Dodine is not registered for use on plums in the USA, so the trials could not be evaluated.

Processing

One processing study was reported from the USA on apples. The residue in processed fractions was determined after six foliar applications to apple trees, each at the nominal rate of 7.3 kg ai/ha. Samples taken at 7 days PHI were processed the next day into fresh unclarified juice and wet pomace using procedures closely simulating commercial practices.

Dodine in the processed fractions was determined by the current validated method and the results show that the residue concentrates in the wet pomace (processing factor of 5.11) with very little found in the juice (processing factor 0.09).

These processing factors were applied to the STMR of the raw commodity to estimate STMR-Ps of 8.69 mg/kg and 0.15 mg/kg in wet apple pomace and apple juice respectively.

Farm animal dietary burden

The Meeting estimated the dietary burden of dodine residues in farm animals on the basis of the feeding stuffs listed in appendix IX of the FAO manual.

Wet apple pomace might be used as feed for dairy and beef cattle. As this is a processed commodity the STMR-P estimated by the Meeting was used for the estimation of both the maximum and the median farm animal dietary burdens.

Farm animal dietary burden

Commodity	STMR-P (mg/kg)	Group	Dry matter %	Residue on dry basis mg/kg	Percent of diet		Residue contribution	
					Beef cattle	Dairy cattle	Beef cattle	Dairy cattle
Apple	8.69	AB	40	21.7	40	20	8.7	4.4
				Total			8.7	4.4

The dodine dietary burdens for animal commodity MRL and STMR estimations (residue levels in animal feed expressed on dry weight) are beef cattle 8.7 ppm, dairy cattle 4.4 ppm.

Farm animal feeding studies

No animal feeding study was provided. However in the metabolism study on a lactating goat dosed orally for five consecutive days with a calculated mean daily dose of 12.8 ppm and slaughtered approximately 23 h after the last dose (the plasma peak was reached 8 h after the last dose), dodine is

not considered fat-soluble. The Meeting therefore expected that on the basis of the current calculated dietary burdens, residues of dodine would be low in the edible tissues, organs and milk of beef or dairy cattle ingesting 8.7 ppm or 4.4 ppm dodine respectively.

Maximum residue levels in animal commodities

In the absence of an animal feeding study and method of analysis for dodine in animal products, the Meeting did not estimate a maximum residue level or STMR for animal products.

FURTHER WORK OR INFORMATION

Desirable

1. A method of analysis in animal products.
2. A farm animal feeding study.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes of dodine, based on the STMRs estimated by the Meeting for pome fruits (apple and pear), peach, nectarine and cherry and on STMR-P for apple juice were within the range 0-2% of the maximum ADI of 0.1 mg/kg bw (JMPR 2000) for the five GEMS/Food regional diets (Annex 3).

The Meeting concluded that the intake of residues of dodine resulting from the uses considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The International Estimated Short Term Intakes (IESTIs) for dodine were calculated for commodities for which STMRs or HRs were estimated by the current Meeting.

On the basis of the acute reference dose of 0.2 mg/kg bw allocated in 2000, the estimated intakes based on the HRs estimated by the Meeting for apple, pear, peach, nectarine and cherry were in the range 6%-30% of the acute RfD for the general population and 20%-80% of that for children up to 6 years (Annex 4).

The Meeting concluded that the short-term intake of residues of dodine resulting from the uses considered by the JMPR is unlikely to present a public health concern.

4.9 FAMOXADONE (208)

TOXICOLOGY

Famoxadone is the ISO approved common name for 5-methyl-5-(4-phenoxyphenyl)-3-phenylamino-

2,4-oxazolidinedione. It is a racemic mixture containing two enantiomers in a 50 : 50 ratio. The mechanism of antifungal action of famoxadone is inhibition of the mitochondrial respiratory chain at complex III, which results in decreased production of ATP.

Famoxadone has not been evaluated previously by JMPR. Consequently, famoxadone is being reviewed at the present Meeting in the context of the JMPR New Compounds Review Programme.

Studies in rats show that about 40% of the administered dose of radiolabelled famoxadone is absorbed and rapidly eliminated from the body in the faeces (> 75% in 24 h) and urine (about 10% in 24 h). Most of the administered dose found in the faeces is unmetabolized famoxadone. In rats, absorption from the gastrointestinal tract becomes the limiting factor for internal exposure at doses greater than about 800 mg/kg bw. It appeared that there were no important differences in metabolism between dogs and rats, within the limits imposed by the different doses used, and that there were no significant differences between male and female rats (only males having been used in the experiments with dogs). The primary metabolic pathway involved the hydroxylation of the parent molecule to the corresponding mono- and di-hydroxylated derivatives, which were only recovered from the faeces. Metabolites resulting from the cleavage of the oxazolidinedione ring moiety were recovered from the urine. A sulphate was the major urinary metabolite containing the phenoxyphenyl moiety, whereas 4-acetoxylaniline was the major urinary metabolite containing the phenylamino moiety. No parent famoxadone was detected in the urine.

Famoxadone has low acute toxicity when administered by oral, dermal, and inhalation routes. The acute LD₅₀ after oral administration is > 5000 mg/kg bw in rats and the LD₅₀ after dermal administration is > 2000 mg/kg bw in rabbits. The LC₅₀ in rats after 4 h is > 5300 mg/m³, the only concentration tested. Famoxadone produces transient mild dermal irritation and transient mild eye irritation, but does not cause skin sensitization.

In short-term studies of oral administration in rodents, dogs and non-human primates, and long-term studies of oral administration in rodents, NOAELs were based on effects on body weight and nutrition, mild haemolytic anaemia, and/or mild to moderate liver toxicity. Mild regenerative haemolytic anaemia was found in rats, mice, dogs and monkeys, as indicated by decreased erythrocyte counts, haemoglobin and/or haematocrit, increased reticulocyte counts, or other related changes in haematological parameters. Methaemoglobin was not measured. Secondary effects of anaemia were also found in the spleen (e.g. increased spleen weight, deposition of haemosiderin pigment, extra-medullary haematopoiesis), in the bone marrow (compensatory erythropoiesis), and in the liver (increased Kupffer cell pigment, increased bile pigment). In studies involving repeated dosing, anaemia was found to occur early in the study and often appeared to be compensated for later. In an experiment in which rats were fed famoxadone at a single dose level of 800 ppm, equal to 61.6 mg/kg bw per day, blood samples were taken at multiple timepoints. Mild anaemia was observed after 30 days, but not after 16 days. Famoxadone also induced hepatocellular responses that are normally considered to be adaptive (e.g. enlarged livers, increased liver weights and liver : body-weight ratios, hepatocellular hypertrophy). These adaptive responses were characterized by increased quantities of cytochrome P-450 and/or increased rates of peroxisomal β -oxidation. Hepatotoxicity, which was mild, was observed only at higher doses and was characterized by mild histopathological lesions (e.g. single cell or focal necrosis, hepatocellular degeneration, diffuse fatty change, eosinophilic foci) and marginally elevated concentrations of blood enzymes suggestive of liver damage. The NOAELs after short-term oral administration were 62.4 mg/kg bw per day in mice treated for 3 months, 13 mg/kg bw per day in rats treated for 3 months, 1.2 mg/kg bw per day in dogs treated for 1 year and 100 mg/kg bw per day in cynomolgus monkeys treated for 1 year.

Long-term studies in rats (2 years) and mice (18 months) show little evidence of irreversible organ toxicity, although chronic dietary exposure of female mice increased the incidence of generalized amyloidosis. Other effects that were observed, some of which formed the basis for the NOAEL values, were reductions in body-weight gain, hepatotoxicity and mild regenerative anaemia. The NOAELs for long-term toxicity were 700 ppm, equal to 96 mg/kg bw per day, in mice, and 200 ppm, equal to 8.4 mg/kg bw per day, in rats. Famoxadone did not demonstrate any evidence of

carcinogenic potential at doses up to the highest tested, which were 400 ppm, equal to 17 mg/kg bw per day, in rats and 7000 ppm, equal to 96 mg/kg bw per day, in mice.

Famoxadone was tested for genotoxicity in an adequate range of studies, both in vitro and in vivo. The results observed were largely negative. Although famoxadone produced a weak clastogenic effect in an in vitro study, the Meeting did not consider this to be toxicologically significant.

The Meeting concluded that famoxadone is unlikely to pose a genotoxic risk to humans. Because the results of the studies of carcinogenicity were negative, the Meeting concluded that famoxadone is unlikely to pose a carcinogenic risk to humans.

In a two-generation study of reproductive toxicity in rats, the NOAEL for adult rats and their offspring was 200 ppm, equal to 11.3 mg/kg bw per day in adults, on the basis of systemic toxicity in the parental rats and reduced body-weight gain in the offspring at a dose of 800 ppm, equal to 45 mg/kg bw per day; no other signs of reproductive toxicity were observed at this dose, the highest tested. In studies of developmental toxicity in rats and rabbits, no effects were observed in fetuses at doses of 1000 mg/kg bw per day, the highest dose tested. The results from the two studies of developmental toxicity and the study of reproductive toxicity did not demonstrate any increased susceptibility of fetuses or pups to famoxadone.

In 28-day studies of immunotoxicity in rats and mice, no evidence of immunotoxicity was found in rats receiving doses in the diet of 800 ppm, equal to 55 and 57 mg/kg bw per day in males and females respectively, or in mice receiving doses in the diet of 7000 ppm, equal to 1664 mg/kg bw per day in females, the highest doses tested. In male mice, there was a minimal but significant reduction in the primary humoral response to sheep erythrocytes at a dose of 7000 ppm; the NOAEL for this activity in male mice was thus 2000 ppm, equal to 327 mg/kg bw per day. The toxicological significance of this effect was considered to be minimal.

Clinical and microscopic evidence of lens opacities were clearly observed in female and male dogs (in both the 3-month and 1-year studies), at doses below those at which any other effects were observed in any other species. The mechanism by which these effects are induced is not understood.

Famoxadone does not appear to be neurotoxic. Some observations of minor effects made in an experiment investigating acute neurotoxicity were attributed to general malaise. Other than some clinical observations in males and females fed with the high dose of famoxadone in the 3-month study in dogs (myotonic twitching, possibly a result of high concentrations of serum potassium), no evidence for neurotoxicity was found in any other studies of toxicity, including a short-term study of neurotoxicity in rats.

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

Toxicological evaluation

An ADI of 0–0.006 mg/kg bw was established for famoxadone on the basis of the NOAEL of 1.2 mg/kg bw per day in a 1-year study in dogs treated by gavage, with a safety factor of 200; an extra safety factor was added because this study in dogs is not viewed as a long-term study. The critical effect was the occurrence of cataracts in dogs at 300 ppm, equal to 8.8 mg/kg bw per day; some of these cataracts developed late in the study, indicating that progression might have been possible, had a long-term study been conducted.

The Meeting established an acute RfD of 0.6 mg/kg bw for famoxadone on the basis of a NOAEL of 61.6 mg/kg bw per day for 16 days, the only dose tested, in a study of haematotoxicity in rats and a safety factor of 100 (see general item 2.2).

A toxicological monograph was prepared. G3

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Mouse	18-month study of toxicity and carcinogenicity ^a	Toxicity	700 ppm, equal to 96 mg/kg bw per day	2000 ppm, equal to 274 mg/kg bw per day
		Carcinogenicity	7000 ppm, equal to 887 mg/kg bw per day ^c	—
Rat	2-year study of toxicity and carcinogenicity ^a	Toxicity	200 ppm, equal to 8.4 mg/kg bw per day	400 ppm, equal to 17 mg/kg bw per day
		Carcinogenicity	400 ppm, equal to 17 mg/kg bw per day ^c	—
	Two-generation study of reproductive toxicity ^a	Parental toxicity	200 ppm, equal to 11 mg/kg bw per day	800 ppm, equal to 45 mg/kg bw per day
		Offspring toxicity	200 ppm, equal to 11 mg/kg bw per day	800 ppm, equal to 45 mg/kg bw per day
	Study of developmental toxicity ^b	Maternal toxicity	250 mg/kg bw per day	500 mg/kg bw per day
		Offspring toxicity	1000 mg/kg bw per day ^c	—
	Special study of haematotoxicity ^a	Anaemia	800 ppm, equal to 62 mg/kg bw per day for 16 days	800 ppm, equal to 62 mg/kg bw per day for 30 days
Single-dose study of neurotoxicity ^b	Neurotoxicity	2000 mg/kg bw ^c	—	
3-month study of neurotoxicity ^a	Neurotoxicity	800 ppm, equal to 47 mg/kg bw per day ^c	—	
Rabbit	Study of developmental toxicity ^b	Maternal toxicity	1000 mg/kg bw per day ^c	—
		Offspring toxicity	1000 mg/kg bw per day ^c	—
Dog	1-year study of toxicity ^a	Toxicity	40 ppm, equal to 1.2 mg/kg bw per day	300 ppm, equal to 8.8 mg/kg bw per day

^a Diet^b Gavage^c Highest dose tested*Estimate of acceptable daily intake for humans*

0–0.006 mg/kg bw

Estimate of acute reference dose

0.6 mg/kg bw

Studies that would provide information useful to the continued evaluation of the compound

- Observations in humans
- Investigation of species differences in erythrocyte sensitivity to haemolysis
- Investigation of the mechanisms by which cataracts are formed in dogs

Summary of critical end-points for famoxadone*Absorption, distribution, excretion and metabolism*

Rate and extent of oral absorption	About 40% absorbed and > 75% of the administered dose eliminated in faeces in 24 h
Dermal absorption	No study of direct dermal absorption available
Distribution	Distributed throughout the body; tissue residues generally very low; highest concentrations in liver and fat
Potential for accumulation	Low, due to rapid excretion
Rate and extent of excretion	> 75% excretion within 24 h
Metabolism in animals	Extensive
Toxicologically significant compounds (animals, plants and environment)	Parent
<i>Acute toxicity</i>	
Rat, LD ₅₀ , oral	> 5000 mg/kg bw
Rat, LD ₅₀ , dermal	No data
Rat, LC ₅₀ , inhalation	5300 mg/m ³ (4 h)
Rabbit, LD ₅₀ , dermal	> 2000 mg/kg bw
Rabbit, skin irritation	Mild irritant
Rabbit, eye irritation	Mild irritant
Skin sensitization	Not sensitizing (Magnusson and Kligman).

Short-term studies of toxicity

Target/critical effect	Body-weight gain decrement, hepatotoxicity, regenerative haemolytic anaemia and lens opacities
Lowest relevant oral NOAEL	1.2 mg/kg bw per day (1-year study in dogs)
Lowest relevant dermal NOAEL	250 mg/kg bw per day (28-day study in rats)
Lowest relevant inhalation NOAEL	No data available

Genotoxicity No genotoxic potential

Long-term toxicity and carcinogenicity

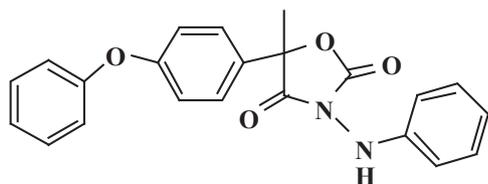
Target/critical effect	Decreased body-weight gain, hepatotoxicity and regenerative haemolytic anaemia
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Lowest relevant NOAEL	8.4 mg/kg bw per day: (2-year study in rats)
<i>Carcinogenicity</i>	No carcinogenic potential
<i>Reproductive toxicity</i>	
Reproductive target/critical effect	Reduced parental and offspring body weight, clinical signs
Lowest relevant reproductive NOAEL	11 mg/kg bw per day
Developmental target/critical effect	Not teratogenic
	Not embryotoxic or fetotoxic
Lowest relevant developmental NOAEL	> 1000 mg/kg bw per day (rats)
<i>Neurotoxicity/delayed neurotoxicity</i>	
Target/critical effect	None
Lowest relevant NOAEL	> 1000 mg/kg bw
<i>90-day study of neurotoxicity</i>	
Target/critical effect	None
Lowest relevant NOAEL	> 47 mg/kg bw per day
<i>Other toxicological studies</i>	None available
<i>Medical data</i>	None available

<i>Summary</i>	Value	Study	Safety factor
ADI	0–0.006 mg/kg bw	Dog, 1-year study, cataracts	200
Acute RfD	0.6 mg/kg bw	Rat, study of haematotoxicity in rats, haemolytic anaemia	100

RESIDUE AND ANALYTICAL ASPECTS

Famoxadone is an oxazolidinedione fungicide belonging to the quinol inhibitor family, which inhibits mitochondrial respiration of fungi. The compound was scheduled at the 33rd Session of the CCPR (ALINORM 01/24A) for evaluation by the 2003 JMPR as a new compound. Data on metabolism and environmental fate, methods of residue analysis, supervised trials on grapes, melons, cucumbers, tomatoes, potatoes, barley and wheat, a cow feeding study and the fate of residues in processing were reported. Information on GAP, national MRLs and residue data was reported by the governments of Germany, The Netherlands and Poland.



IUPAC name: 3-anilino-5-methyl-5-(4-phenoxyphenyl)-1,3-oxazolidine-2,4-dione

Chemical Abstracts name: 5-methyl-5-(4-phenoxyphenyl)-3-(phenylamino)-2,4-oxazolidinedione

Metabolism in animals

Metabolism studies were conducted with [^{14}C]famoxadone labelled in the phenoxyphenyl and the phenylamino moieties.

Rats given single or multiple oral doses of 5 and 100 mg/kg body weight of ^{14}C famoxadone excreted between 88.8 and 96% of the administered radioactivity in the faeces and from 3 to 12% in the urine, most within 24 h. Famoxadone was the major component in faeces, and the monohydroxy derivative in the phenoxyphenyl and the dihydroxy in the phenoxyphenyl and phenylamino moieties the main metabolites, each representing up to 13% of the administered dose. In urine, only hydrolytic and cleavage products were detected, including 4-aminophenyl acetate (4-acetoxyaniline), at up to 7% of the administered dose. When [^{14}C]famoxadone was given to biliary-cannulated rats in a single oral dose of 5 mg/kg bw, excretion in bile ranged from 30 to 39% and in faeces from 56 to 65% of the administered dose. Famoxadone was the only labelled component in faeces, and it was not detected in the bile. The main metabolites released in bile treated with β -glucuronidase/sulfatase were the monohydroxylated compound, the catechol 1,2 dihydroxybenzene and a hydrolysis cleavage product (α -hydroxy-4-(4-hydroxyphenoxy)- α -methylbenzeneacetic acid), none higher than 6% of the administered dose.

Lactating goats dosed orally for 7 days at the equivalent of 10 ppm in the diet excreted most of the radioactivity (>80%) in the faeces. Famoxadone was the major radioactive component in milk and tissues. Radioactive residues in milk reached a plateau at day 6–7, with up to 0.025 mg/kg ^{14}C famoxadone equivalents. On average, famoxadone was present in muscle at 0.009 mg/kg, in fat at 0.086 mg/kg, in liver at 0.025 mg/kg, in kidney at 0.011 mg/kg and in milk at 0.006 mg/kg, representing from 18.5 to 57.5% of the TRR in each matrix. Mono- and dihydroxylated metabolites were detected in either faeces or liver at up to 4.8% of the TRR. Individual components released by protease digestion and the remaining unextractable residues were <0.05 mg/kg.

Laying hens dosed for 7 consecutive days at a dietary level of 10 ppm excreted most of the radioactivity in faeces (>88%). Eggs accounted for <0.04% and tissues for <0.15% of the administered dose. Radioactive residues were equivalent to <0.01–0.067 mg/kg in the egg yolk and 0.06–0.3 mg/kg in liver. No residues (<0.01 mg/kg famoxadone equivalents) were detected in muscle, skin or egg white. Famoxadone was the major component in the excreta (up to 17.8% of the TRR), followed by the polar metabolite 5-(4-hydroxyphenyl)-5-methyloxazolidine-2,4-dione (15.4% of the TRR) The major radioactive compound in egg yolk and liver was the mono-hydroxylated compound (up to 0.08 mg/kg famoxadone equivalents). No radioactive famoxadone was detected in liver.

In summary, famoxadone accumulation in animals is low, with most of the administered radioactivity being excreted in faeces. The metabolism includes hydroxylation of the phenoxyphenyl and phenylamino rings, hydrolytic cleavage of the oxazolidinedione moiety, and cleavage of the hydrazine bond and the phenoxyphenyl ether linkage. Low levels of famoxadone or metabolites were found in goat and poultry tissues, milk and eggs.

In plants

When grape vines were treated with a simulated WG formulation of [¹⁴C]famoxadone (3 times at 0.3 kg ai/ha) most of the radioactivity was recovered from the surface of the leaves and fruits (79 to 98% of the TRR), with >95% of the residue identified as famoxadone. A minor metabolite, 1-(4-phenoxyphenyl)ethanone, was also observed (<2%). In the fruit, famoxadone residues reached a maximum of 0.03 mg/kg equivalents at day 14.

Tomato plants were treated twice with a simulated WG formulation of [¹⁴C]famoxadone at a rate of 0.63 kg ai/ha. Most of the radioactivity was extracted with acetone (about 80% of the TRR). On average, more than 90% of the residue was famoxadone and no significant metabolites were identified (<10% of the TRR). At 14 days the residue of famoxadone in tomato fruit was 0.07 mg/kg.

When potato plants were treated in a greenhouse 3 times at 0.3 kg ai/ha with a WG of [¹⁴C]famoxadone most of the applied radioactivity was recovered in the acetone wash of the foliage surface (mean of 86.5 and 61.8% at days 37 and 51). 76-95% of the residue was characterized as famoxadone. Two minor hydrolytic metabolites were observed, 1-(4-phenoxyphenyl)ethanone and α -hydroxy- α -methyl-4-phenoxybenzeneacetic acid 2-phenylhydrazide, accounting for <5% of the total radioactivity. Negligible systemic translocation of radiolabelled residues to the tubers was found (<0.01 mg/kg famoxadone equivalent).

In mature wheat plants from a field harvested 50 days after the last of 3 applications at 0.2 kg ai/ha of EC [¹⁴C]famoxadone low levels of ¹⁴C residues were detected in the grain (0.01-0.02 mg/kg equivalents). Most of the radiolabelled residues (>98%) were found in the straw (average 3.4 mg/kg). Famoxadone was the main component (average 0.36 mg/kg ¹⁴C equivalents) of the extractable residues in the foliage and mature straw. The main metabolites were monohydroxy-famoxadone (0.24 mg/kg famoxadone equivalents in straw at day 72), dihydroxy-famoxadone (0.30 mg/kg famoxadone equivalents in foliage at day 29) and a conjugation product (0.26 mg/kg famoxadone equivalents in foliage at day 29).

In summary, famoxadone was the main compound found in treated grapes, tomatoes and potatoes. Little translocation of the radioactivity to potato tubers was found and residues in wheat grain were low. Metabolism in wheat plants was significant, mainly through hydroxylation and conjugation.

Environmental fate

The degradation of famoxadone in soils under aerobic conditions showed half-lives varying from 2 days in silt loam to 11 days in sandy loam. The DT₉₀ was 134 days. Famoxadone was not detected in the unextractable residues subjected to strong acidic treatments. Approximately 79.4 to 93.3% of the parent compound remained after 90 days in sterile soil, indicating that famoxadone is degraded mainly by microbes. The major degradation product was the phenoxyphenyl-hydroxylated famoxadone (IN-KZ007), with a peak of 7 to 16% within 4 days, and the hydrolysis cleavage product α -hydroxy- α -methyl-4-phenoxybenzeneacetic acid (IN-JS940) which reached a peak of 11% of the applied radioactivity. The half-life of IN-KZ007 and IN-JS940 in soils varied from 3.2 to 15 days and 6 to 23 h respectively.

Under field conditions in the USA and Canada, unquantifiable or low residues of famoxadone were found below the 15 cm depth, showing low mobility in soil. The half-life in various soils varied from 5 to 28 days.

One rotation crop study was reported to the Meeting. Soils treated once or three times with famoxadone at 0.4 kg ai/ha were aged under greenhouse conditions for 30, 120 and 365 days before

planting different crops. Famoxadone residues were detected in lettuce, sugar beet roots, wheat forage and straw (0.02 to 0.06 mg/kg equivalents), but not in sugar beet tops or wheat grain (<0.01 mg/kg eq). Average residues in treated soils were 0.26 and 0.04 mg/kg famoxadone equivalents at days 30 and 120 respectively. No famoxadone was detected in crops or soil after 365 days. On average, crop:soil residue ratios were 0.11 in lettuce, 0.19 in sugar beet, 0.10 in wheat foliage and 0.58 in wheat straw. When these ratios were applied to an average field soil famoxadone residue of 0.09 mg/kg, found 14 days after the last of 8 applications at 0.18 kg ai/ha (twice GAP) in a supervised trial on potatoes in Italy, the calculated residues of famoxadone in lettuce, sugar beet and wheat, after application to potatoes, ranged from 0.01 mg/kg in lettuce and wheat foliage to 0.05 mg/kg in wheat straw.

In summary, famoxadone is degraded in soil by microbes, with a half-life up to 28 days in the field, mainly through hydroxylation. The compound has low mobility and low translocation to crops in soils containing aged residues.

Residue analysis

Famoxadone can be extracted from crops with acetonitrile/water. The extract is partitioned with hexane and famoxadone quantified by reversed phase HPLC with UV detection or HPLC/MS (positive thermospray). The LOQ is 0.02 mg/kg for grapes and cereal grain and 0.05 mg/kg for cereal straw and forage. Average recoveries of famoxadone at levels from 0.02 to 0.5 mg/kg ranged from 74 to 109% with a maximum RSD of 21% (3 samples at each level).

Clean-up on a Florisil/sodium sulfate SPE column can follow the extraction before quantification by column-switching HPLC on a phenyl column followed by a C-18 column, with UV detection. The LOQ is 0.02 mg/kg. Average recoveries from tomato fruit, purée and paste at 0.02 and 0.12 mg/kg ranged from 82 to 93%, with a maximum RSD (n=3) of 21%. Extraction of incurred residues from tomato samples with acetonitrile/water showed an average extraction efficiency of 110% compared with the method used in the metabolism study described above.

In another method, samples are extracted with acetone/water, the extract cleaned up on GPC and silica gel columns, and famoxadone determined by GC with an ECD. The limit of quantification is 0.05 mg/kg for raisins and tobacco, 0.02 mg/kg for grapes and cucumbers and 0.01 mg/kg for wine, potatoes and wheat grain. Average recoveries at levels from 0.01 to 0.5 mg/kg ranged from 76 to 106%, with maximum RSD of 9.5% (5 samples at each level).

Samples of milk, eggs and animal tissues can be extracted with ACN/water, partitioned with hexane, cleaned up on a Florisil SPE column and analysed by GC with an NPD. Average recoveries from beef muscle and fat, milk, poultry muscle and eggs at 0.02 and 0.5 mg/kg ranged from 85 to 107%, with an RSD of 4 to 12% (n=3 at each level).

In a method for analysing animal tissues, the sample is mixed with C-18 packing, the mixture is washed with hexane and famoxadone is eluted with acetonitrile. The eluate is filtered through a bed of basic alumina and the extract is passed through graphitized carbon followed by silica SPE columns. Famoxadone is determined by column-switching HPLC (phenyl and C-18 columns) with UV detection. The LOQ is 0.01 mg/kg for whole milk, skimmed milk, cream and whole egg and 0.05 mg/kg for bovine liver. Recoveries ranged from 70 to 105% at 0.01 to 2.0 mg/kg fortification levels. This method was proposed for regulatory use. The extraction efficiencies of this method for incurred radiolabelled famoxadone residues found in milk, liver and fat in a goat metabolism study, compared to the method used in the study (extraction with acetonitrile and clean-up by C-18 SPE) were $\geq 87.4\%$.

Stability of residues in stored analytical samples

The stability of famoxadone in grapes, potatoes, wheat forage, straw, grain and soil fortified at 1 mg/kg and stored at -20°C was determined. After 18 months, 70% (in wheat grain and straw) to 99% (in grapes) of the famoxadone remained in the samples. Famoxadone at 0.3 mg/kg was stable in tomatoes and peppers after 18 months (110 and 107% remained respectively) and in cucumbers after 10 months (102% remaining). It was also stable in tomato paste at 1 mg/kg and tomato purée (0.3 mg/kg) stored at -10°C, with 93 and 89% of the residues remaining after 18 months. Two studies on potatoes showed different results for the stability of famoxadone. In one, residues dropped to half after 3 months in samples fortified with 1 mg/kg. In the other, conducted with a supervised trial on potatoes, residues were stable up to 10.5 months at 0.3 mg/kg. The analytical recoveries in both studies were at acceptable levels.

The storage stability of famoxadone was evaluated in whole milk samples fortified with 0.1 mg/l and in muscle and liver samples containing incurred residues from a feeding trial. The average percentage of famoxadone remaining in milk after 117 days was 87%, and residues in muscle (0.072 mg/kg) did not change significantly from day 21 to day 138. In liver, residues were 0.069 ± 0.010 mg/kg at day 21 and 0.065 ± 0.023 mg/kg at day 139.

Definition of the residue

Metabolism studies showed that famoxadone was the main radiolabelled residue in vegetable crops, milk and cow tissues. In egg yolk and hen liver, a monohydroxylated metabolite was the major residue, but present at low concentration. Famoxadone concentrates in the fat of treated goats and in egg yolk. In a cow feeding study, to be described later, residues also concentrated in fat and cream. Famoxadone has a log K_{ow} of 4.65.

The Meeting agreed that the definition of the famoxadone residue for compliance with MRLs and for dietary intake estimations in plant and animal commodities should be famoxadone. The compound is fat-soluble.

Results of supervised trials

Grapes. Famoxadone can be used on grapes in Europe at a maximum application rate of 0.05 kg ai/ha (France and Greece), 0.09 kg ai/ha (Italy and Spain) or 0.144 kg ai/ha (Germany). Spain and Greece allow a maximum of 6 applications per season and the other countries a maximum of 3 applications, except Germany (8). The PHI in all countries is 28 days (40 days in Italy for formulations with fosetyl-Al).

A total of 25 trials using 10 to 12 applications, with a 7-day interval, were conducted in these countries between 1995 and 1999, at 0.05 to 0.146 kg ai/ha. The initial application was at flowering. The varieties used in the trials were mainly for the production of wine. In five decline studies residues decreased by 61.8%, on average, from day 1 to day 30 after the last application.

Residues within about 28 days PHI were 0.19 (2), 0.25, 0.24, 0.29, 0.37, 0.46, 0.48 (3), 0.50 (2), 0.54, 0.55, 0.56, 0.62, 0.66 (2), 0.74, 0.90 (2), 0.98, 1.0, 1.2 and 1.5 mg/kg.

The Meeting agreed that with applications starting at flowering it is unlikely that the first applications would influence the residue levels, and that all the trials conducted at GAP rate and PHI in Europe should be considered for the estimations.

The Meeting estimated a maximum residue level of 2 mg/kg, an STMR of 0.54 mg/kg and an HR of 1.5 mg/kg for famoxadone in grapes.

Cucumber and summer squash. The current Italian label indicates that famoxadone may be applied to cucumbers at 0.112 kg ai/ha at flowering, followed by 2 applications at the same rate (maximum of 3 applications) with a minimum 1-week interval, with a 10-day PHI. This label applies also to zucchini (summer squash) and melons. The label does not give any explicit restriction to the use under protected conditions. There is no GAP for famoxadone in Greece or Spain.

Ten trials were conducted on protected cucumbers using 5 applications at 0.065 to 0.118 kg ai/ha (1 week interval) in Italy, Greece and Spain in 2001. Decline studies showed residues decreasing by 39%, on average, from day 1 to day 7 after the last application. Residues at 7 days PHI were 0.01 (2), 0.02 (3), 0.03 (2), 0.05 (2) and 0.10 mg/kg.

The Meeting agreed that, as cucumbers under protected conditions grow quickly, it is unlikely that the higher number of applications used in the trials would influence the residue within a 10-day PHI. The Meeting also agreed to evaluate the trials conducted in Greece and Spain against Italian GAP and extrapolate the recommendations to summer squash.

The Meeting estimated a maximum residue level of 0.2 mg/kg, an STMR of 0.025 mg/kg and an HR of 0.10 mg/kg for famoxadone in cucumber and summer squash.

Melons. In Italy, famoxadone GAP for cucumbers also applies to melons. There is no GAP for famoxadone use on melons in Greece, France or Spain. Twenty trials were conducted on melons using 5 applications at about the Italian rate in Italy, Greece, France and Spain either in the glasshouse or in the field in 1991. No significant difference in residue levels was found between the glasshouse and field trials. Residues 7 days after the last application ranged from 0.02 to 0.22 mg/kg in whole fruit. Residues in pulp were <0.01 or 0.01 mg/kg from day 1 to 7, and in one sample the residue 2 h after the last application was 0.22 mg/kg.

As the trials were not according to GAP (too many applications), the Meeting agreed not to recommend an MRL of famoxadone in melons.

Tomato. Thirty-six trials were conducted in Europe on tomatoes, where maximum GAP is 0.09 kg ai/ha in France, Spain and Greece and 0.11 kg ai/ha in Italy. France and Spain allow up to 4 applications and a PHI of 3 days. Italy allows 3 applications and 10 days PHI or 6 applications of a lower rate (0.005 kg ai/ha) and 3 days PHI. Greece allows 8 applications and 3 days PHI. Trials were conducted using 5 or 7 applications at 0.07 to 0.137 kg ai/ha, with a PHI of 3 days or decline studies from 0 to 7 or 14 days.

Six trials conducted in the south of France according to French GAP gave residues at 3 days PHI of 0.03, 0.08, 0.10 (2), 0.12 and 0.15 mg/kg, and three with 7 applications complying with GAP in Greece showed residues of 0.08, 0.10 and 0.15 mg/kg.

In Greece, 3 trials according to Greek GAP (7 applications) and 4 trials according to Italian GAP (5 applications) gave residues at 3 days PHI of 0.04, 0.09, 0.10, 0.11(2), 0.15 and 0.16 mg/kg.

In Italy, eleven trials with 5 or 7 applications matching either Greek or Italian GAP gave residues at 3 days PHI of 0.02 (2), 0.03 (3), 0.04, 0.05, 0.18, 0.33, 0.74 and 1.1 mg/kg.

In Spain, 5 trials with 7 applications which matched Greek GAP and 3 trials according to Spanish GAP gave residues at 3 days PHI of 0.02, 0.04, 0.05 (2) 0.07, 0.10, 0.12 and 0.18 mg/kg. One trial conducted at 0.131-0.137 kg ai/ha gave residues of 0.20 mg/kg.

Thirty six trials conducted according to GAP in Europe gave residues, in rank order, of 0.02 (3), 0.03 (4), 0.04 (3), 0.05 (3), 0.07, 0.08 (2), 0.09, 0.10 (5), 0.11(2), 0.12 (2), 0.15 (3), 0.16, 0.18 (2), 0.20, 0.33, 0.74 and 1.1 mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg, an HR of 1.1 mg/kg and an STMR of 0.10 mg/kg for famoxadone in tomato.

Potato. Famoxadone can be applied in Europe with a 14 days PHI. The application rate is 0.09 kg ai/ha in Greece, Italy and Spain (up to 8, 6 and 4 applications respectively), 0.175 kg ai/ha in the UK and Germany (12 and 6 applications respectively) and up to 6 application at 1.15 kg ai/ha in Belgium. There is no approved GAP in Denmark or France. In 12 trials conducted in Europe at a higher rate (6 to 12 applications at 0.164 to 0.224 kg ai/ha), residues at 14 days PHI were <0.02 mg/kg.

A metabolism study on potatoes with 3 applications of 0.3 kg ai/ha showed <0.01 mg/kg famoxadone equivalents in tubers.

Data from supervised trials conducted at higher rates and from the metabolism study support the conclusion that no residues are to be expected in potato tubers after the plants are treated with famoxadone according to good agriculture practices.

The Meeting agreed to recommend an MRL of 0.02* mg/kg, and estimated an HR and an STMR of 0 mg/kg for famoxadone in potato.

Barley. The current UK label indicates that famoxadone may be applied once or twice before quarter ear emergence to barley as a foliar spray at a maximum rate of 0.150 kg ai/ha. In Belgium, only 1 application is allowed, with a 28 days PHI. Sixteen trials using two foliar applications at 0.15 or 0.20 kg ai/ha were conducted in Belgium, France, Germany and the UK. Samples were collected at maturity, 32-78 days after the last application.

Twelve trials conducted with winter barley matching the UK GAP rate gave residues of <0.02 (8), 0.04 (2), 0.08 and 0.11 mg/kg 32 to 78 days after the last application. Four trials conducted at 0.2 kg ai/ha gave residues of <0.02 to 0.18 mg/kg.

The Meeting estimated a maximum residue level of 0.2 mg/kg and an STMR of 0.02 mg/kg for famoxadone in barley.

Wheat. The current UK label indicates that famoxadone may be applied to winter wheat before flowering as a foliar spray up to 3 times at a maximum rate of 0.150 kg ai/ha, with a maximum of 0.45 kg ai/ha per season. In Belgium, GAP is one application of 0.15 kg ai/ha and 28 days PHI. Fifteen trials were conducted in Belgium, France, Germany and the UK. In 10 trials with 1 application of 0.28 kg ai/ha and 2 of 0.15 kg ai/ha, samples harvested at maturity, between 36 and 66 days after the last application, gave residues of <0.02 (9) and 0.04 mg/kg in grain. The Meeting agreed that it is unlikely that the higher rate in the first application would influence the residues in the grain at a mature stage, and evaluated these trials. In 5 trials with 3 sprays of 0.20 kg ai/ha, residues were in the same range (<0.02-0.06 mg/kg).

The Meeting estimated a maximum residue level of 0.1 mg/kg and an STMR of 0.02 mg/kg for famoxadone in wheat.

Barley straw and forage. In twelve trials within the GAP rate, residues in barley straw harvested at maturity (32-78-day PHI) were 0.16, 0.19, 0.34, 0.47, 0.85, 0.86, 0.93, 0.96, 1.4, 1.5, 2.5 and 3.8 mg/kg. Allowing for 88% DM (FAO Manual, 2002), the median and the highest residues in barley straw are 0.99 (0.895/0.88) and 4.2 mg/kg (3.8/0.88) respectively. Trials at higher rates gave residues from 0.35 to 3.9 mg/kg. Forage samples were harvested in two trials at 7, 14 and 21 days after the last application. Residues after 7 days were 1.4 and 1.8 mg/kg.

The Meeting estimated a maximum residue level of 5 mg/kg and an STMR of 0.99 mg/kg for famoxadone in barley straw.

As too few trials were conducted, the Meeting agreed not to estimate a maximum residue level for famoxadone in barley forage.

Wheat straw and forage. In ten trials within the GAP rate, residues in wheat straw harvested at maturity (34-45 days PHI) were 0.55, 1.2, 1.6, 1.7, 2.0, 2.1, 2.5, 2.7, 2.9 and 4.3 mg/kg. Allowing for 89% DM (FAO Manual, 2002), the median and the highest residues in wheat straw are 2.28 (2.05/0.89) and 4.8 mg/kg (4.3/0.89) respectively. Residues from 5 trials at a higher rate gave residues from 3.4 to 11 mg/kg. Wheat forage samples were harvested in two trials at 0, 7, 14 and 21 days after the last application. The residues at 0 days were 4.2 and 5.8 mg/kg.

The Meeting estimated a maximum residue level of 7 mg/kg and an STMR of 2.28 mg/kg for famoxadone in wheat straw.

There were too few trials to recommend a maximum residue level for famoxadone in wheat forage.

FATE OF RESIDUES IN PROCESSING

Grapes from vines treated with famoxadone were vinified by traditional French wine-making techniques, with alcoholic and malolactic fermentations. Residues in grapes were 1.4 and 1.6 mg/kg, decreasing in juice and wine, (processing factor (PF) of <0.01), in lees (PF 0.33) and in must (PF 0.81). Residues increased in raisins (PF 1.9), wet pomace (PF 2.0) and dry pomace (PF 3.6).

In four studies conducted in France, Spain and the USA, treated tomatoes were processed according to industrial manufacturing procedures. Residues in the tomatoes ranged from 0.09 to 0.86, decreasing after washing (PF 0.28, n=2), in juice (PF 0.22, n=2) and in purée (PF 0.44, n=4). Residues increased in tomato paste (PF 1.3, n=2), wet (PF 2.1, n=2) and dry pomace (PF 15, n=2).

Samples of treated winter barley from France and Germany were processed using traditional malting, brewing, milling and backing procedures. Residues were detectable only in pearling dust (PF 1.8) and in spent grain (PF 0.67). No residues (<0.02 mg/kg) were found in barley grits, pearl barley, wholemeal bread, malt, malt germ, trub, yeast (PF <0.5) or beer (PF <0.42, n=2).

Treated wheat from one site in France showed residues of 0.04 mg/kg, which increased in bran (PF 2). No residues (<0.02 mg/kg) were found in wholemeal, flour or wholemeal bread, with processing factors <0.5.

Residues in processed commodities

Estimates of residues in processed commodities were derived after multiplying the highest residue and/or STMR found in supervised trials on the raw commodity conducted according to GAP by the appropriate processing factor (PF) calculated from the processing studies. Maximum residue levels were only estimated for commodities of human consumption with a PF >1 with a Codex classification number and for commodities of animal consumption which can be used to estimate dietary burdens. An HR-P was estimated only when its use was required for the calculation of short-term exposure.

On the basis of a highest residue of 1.5 mg/kg and an STMR of 0.54 mg/kg in grapes the Meeting estimated an STMR-P of 0.005 mg/kg for famoxadone in wine and grape juice (PF 0.01), a maximum residue level of 5 mg/kg, an HR-P of 2.85 mg/kg and an STMR of 1.03 mg/kg for famoxadone in raisins (PF 1.9), and a maximum residue level of 7 mg/kg and an STMR of 1.94 mg/kg in dry pomace (PF 3.6).

On the basis of an STMR of 0.10 mg/kg for tomatoes the Meeting estimated an STMR-P of 0.022 mg/kg for famoxadone in tomato juice (PF 0.22), an STMR-P of 0.044 mg/kg for famoxadone in tomato purée (PF 0.44), and an STMR-P of 0.13 mg/kg for famoxadone in tomato paste (PF 1.3).

On the basis of an STMR of 0.02 mg/kg in barley, the Meeting estimated an STMR-P of 0.008 mg/kg for famoxadone in beer (PF 0.42) and an STMR-P of 0.01 mg/kg for famoxadone in wholemeal barley bread (PF 0.5).

On the basis of an HR of 0.04 mg/kg and an STMR of 0.02 mg/kg in wheat the Meeting estimated a maximum residue level of 0.2 mg/kg and an STMR-P of 0.04 for famoxadone in wheat bran (PF 2), and an STMR-P of 0.01 mg/kg for famoxadone in wheat flour and wheat wholemeal (PF 0.5).

Animal dietary burdens

The Meeting estimated the dietary burdens of famoxadone in cattle and poultry on the basis of the diets listed in Appendix IX of the FAO Manual (FAO, 2002) and the MRL and STMRs estimated at this Meeting.

Maximum dietary burden

Commodity	Group	Residues, mg/kg	Basis	% dry matter	Residues, on dry basis, mg/kg	% of diet			Residue contribution, mg/kg		
						Beef	Dairy	Poultry	Beef	Dairy	Poultry
Barley grain	GC	0.2	MRL	88	0.23	50	40	75	0.12	0.09	0.17
Wheat grain	GC	0.1	MRL	89	0.11	50	40	80			
Barley straw	AS	5	MRL	100	5.0	10	60	-	-	3.0	-
Wheat straw	AS	7	MRL	100	7.0	10	10	-	0.70	-	-
TOTAL						60	100	75	0.82	3.09	0.17

STMR dietary burden

Commodity	Group	Residues mg/kg	Basis	% dry matter	Residues, on dry basis, mg/kg	% of diet			Residue contribution, mg/kg		
						Beef	Dairy	Poultry	Beef	Dairy	Poultry
Barley grain	GC	0.02	STMR	88	0.023	50	40	75	0.012	0.009	0.017
Wheat grain	GC	0.02	STMR	89	0.022	50	40	80			
Barley straw	AS	0.99	STMR	100	0.99	10	60	-	-	0.594	-
Wheat straw	AS	2.28	STMR	100	2.28	10	10	-	0.228	-	-
TOTAL						60	100	75	0.24	0.603	0.017

Animal feeding studies

Famoxadone was given in gelatin capsules twice daily to lactating Holstein dairy cows for 28 days at feeding levels of 9, 27 and 90 ppm. Three cows at each dose were slaughtered on day 29, and one at the higher feeding level was slaughtered on each of days 42 and 48.

In whole milk, residue levels of famoxadone reached a plateau by the tenth day of dosing at all doses. The mean plateau level (from day 10 to 28) was 0.14, 0.43 and 1.5 mg/kg at feeding levels of 9, 27 and 90 ppm respectively. The average residues from day 1 to day 28 were 0.12, 0.33 and 1.2 mg/kg. Residues in milk from the cow killed on day 48 (highest feeding level) decreased from 1.5 mg/kg at day 28 to 0.02 mg/kg at day 47. Mean residues in milk fat from day 14 to day 28 were 10 times those in whole milk (1.4, 4.3 and 15 mg/kg respectively).

In tissues, famoxadone residues were detected at day 28 in liver (average of 0.69, 2.0 and 6.3 mg/kg, at the low, medium and high doses respectively), kidney (0.15, 0.59 and 1.5 mg/kg), muscle (0.07, 0.24 and 1.0 mg/kg) and fat (1.0, 4.1 and 17 mg/kg). Tissues from the cow killed 20 days after the end of dosing had decreased to 0.04, 0.02, 0.01 and 0.19 mg/kg in liver, kidney, muscle and fat respectively

Residue levels in animal commodities

Cattle. The maximum dietary burdens of beef and dairy cattle estimated by the Meeting were 0.82 and 3.1 ppm respectively and the higher value of 3.1 ppm was used for calculation of the residues. The levels were derived by applying the transfer factor (residue level in milk or tissue ÷ residue level in diet) from the lowest feeding level (9 ppm) to the calculated maximum dietary burden. For the STMR estimate, the same procedure was applied to the STMR dietary burden for dairy cattle of 0.60 ppm.

As the residue levels of famoxadone reached a plateau rapidly in milk (<14 days), the maximum residue levels in tissues were derived from the maximum dietary burden by applying the transfer factor to the highest individual residue levels found in the feeding study (FAO Manual, 2002). The STMRs were derived from the STMR dietary burden and the mean residue levels. For milk, the mean residue at the plateau level from the 9 ppm feeding group was used to estimate both the maximum residue level and the STMR.

Dose (ppm) (Extrapolated)	Milk fat	Whole milk	Famoxadone concentration (mg/kg)							
			Liver		Kidney		Muscle		Fat	
			Mean	Highest	Mean	Highest	Mean	Highest	Mean	Highest
MRL (3.1) [9.0]	(0.48) [1.4]		(0.24) [0.70]		(0.062) [0.18]		(0.031) [0.09]		(0.41) [1.2]	
STMR (0.60) [9.0]		(0.009) [0.14]		(0.046) [0.69]		(0.010) [0.15]		(0.005) [0.07]	(0.067) [1.0]	

Assuming the milk to contain 4% fat, the mean concentration of famoxadone in milk fat, expressed as whole milk, is 0.019 mg/kg (0.48 ÷ 25).

The Meeting estimated a maximum residue level of 0.03 mg/kg (F) and an STMR of 0.009 mg/kg (F) for famoxadone in milks, a maximum residue level of 0.5 mg/kg, an STMR of 0.046 mg/kg and an HR of 0.24 mg/kg for famoxadone in edible offal (mammalian), and a maximum residue level of 0.5 mg/kg for famoxadone in meat (fat) (from mammals other than marine mammals).

For the purpose of dietary intake calculations, the Meeting estimated an STMR of 0.067 mg/kg and an HR of 0.41 mg/kg in fat from mammals other than marine mammals, and an STMR of 0.005 mg/kg and an HR of 0.031 mg/kg for famoxadone in muscle from mammals other than marine mammals.

Poultry. The metabolism study conducted with laying hens at 10 ppm in the feed (7 days dosing) showed no radioactive residues in muscle, fat, skin or egg white (<0.01 mg/kg). Radioactive residues were detected only in egg yolk and liver, with a maximum of 0.003 mg/kg famoxadone found in yolk. The feeding level in this study is almost 60 times the calculated maximum dietary burden for poultry (0.17 mg/kg feed).

The Meeting agreed that it is unlikely that famoxadone residues would remain in poultry tissues and eggs after the animal had been fed with commodities containing the fungicide. The Meeting estimated a maximum residue level of 0.01* mg/kg for famoxadone in poultry meat, poultry edible offal and eggs, and an HR and an STMR of 0 for famoxadone in poultry edible offal and eggs.

For the purpose of dietary intake calculations, the Meeting estimated an HR and an STMR of 0 for famoxadone in poultry muscle and fat.

DIETARY RISK ASSESSMENT

Long-term intake

The ADI for famoxadone is 0-0.006 mg/kg body weight/day. The international estimated daily intake (IEDI) was calculated for commodities of human consumption for which STMRs were estimated in this evaluation. The results are shown in Annex 3.

International Estimated Daily Intakes for the five GEMS/Food regional diets, based on estimated STMRs, ranged from 1 to 7% of the maximum ADI. The Meeting concluded that the intake of residues of famoxadone resulting from its uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The International estimated short-term intakes (IESTI) for famoxadone were calculated for commodities for which STMR and HR values were estimated in this evaluation and for which data on consumption (large portion and unit weight) were available. The results are shown in Annex 4.

The acute RfD for famoxadone is 0.6 mg/kg bw. The IESTI represented 0 to 8% of the acute RfD for children and 0 to 3% of the acute RfD for the general population. The Meeting concluded that the short-term intake of residues of famoxadone from uses on the commodities that have been considered by the JMPR is unlikely to present a public health concern.

4.10 FENITROTHION (037)

RESIDUE AND ANALYTICAL ASPECTS

Fenitrothion, a contact insecticide which was first evaluated by the JMPR in 1969 and re-evaluated for residues several times up to 1989, is included under the CCPR Periodic Review Programme. At the 30th Session of the CCPR (ALINORM 99/24) fenitrothion was originally scheduled for periodic residue review by the 2001 JMPR but this was postponed until 2003.

The basic manufacturer supplied information on identity, metabolism and environmental fate, use patterns, residue analysis, residues from supervised trials on cereals, and the fate of residues during storage and processing. In addition information on GAP and/or national MRLs was reported by the governments of Australia, Germany, The Netherlands and the USA.

Animal metabolism

The Meeting received information on the fate of fenitrothion in orally-dosed lactating goats and in laying quail and hens.

Metabolism in laboratory mice, rats, guinea pigs, rabbits and dogs was evaluated by the WHO panel of the 2000 JMPR. It was concluded that orally-administered fenitrothion is rapidly and extensively absorbed from the mammalian intestinal tract (about 90-100% of the dose) and eliminated within 24 h. It is rapidly metabolized by mixed-function oxidases to the highly reactive fenitro-oxon by oxidative desulfuration. The oxon is then further metabolized by demethylation and hydrolysis to 3-methyl-4-nitrophenol and dimethyl hydrogen phosphate. A minor metabolic pathway involves further oxidation to 5-hydroxy-2-nitrobenzoic acid (3-carboxy-4-nitrophenol).

Six female Japanese Saanen goats were fed [phenyl-¹⁴C]fenitrothion mixed with 200 g of crushed hay for 7 days (0.5 mg ai/kg bw, corresponding to 7.6 ppm in the feed). The goats were milked twice daily and the evening milk samples were combined with the milk collected on the following morning. Whole milk was separated into cream and skimmed milk. Two goats were killed 1, 7 or 18 days after the last dose. The administered radiocarbon was almost quantitatively excreted during the 7-day post-treatment period; 50% of the dose was excreted in the urine, 44% in faeces and 0.1% eliminated in milk.

In whole milk a plateau of 0.011 mg/kg fenitrothion equivalents (mg/kg eq) was reached on the second day of dosing, with a maximum of 0.012 mg/kg eq on the 5th day. The residues in whole milk decreased to 0.003 mg/kg eq within 7 days of treatment. The four radioactive components detected in milk were acetylaminofenitro-oxon (5% of the TRR), sulfoaminofenitrothion (39% of the TRR), sulfoaminofenitro-oxon (22% of the TRR), and 4-acetyl-amino-3-methylphenyl methyl hydrogen phosphate (15% of the TRR). No parent, fenitro-oxon or 3-methyl-4-nitrophenol were detected. No radioactive residues could be detected in cream.

One day after the last dose liver contained the highest content of radiocarbon (0.85-1.5 mg/kg eq), with lower concentrations in kidneys (0.025 –0.031 mg/kg eq), muscle (0.002 to 0.005 mg/kg eq) and fat (0.008-0.012 mg/kg eq). After 18 days the radiocarbon was below 0.005 mg/kg eq in all tissues analysed except liver (0.1 mg/kg eq). The parent compound was not found (<0.001 mg/kg eq) and metabolites were not investigated.

[Phenyl-¹⁴C]fenitrothion was administered orally in gelatin capsules to 15 Japanese female quail as single doses of 5 mg/kg bw (about 20 mg/kg feed) and to six White Leghorn hens daily for 7 consecutive days at 2 mg/kg bw/day (about 35 mg/kg feed) and eggs were collected daily. The quail were killed 1 h, 1 or 7 days after their single doses, and the hens 1 or 7 days after their last doses. Radioactivity was very rapidly excreted by both: 93-94% of the applied radioactivity (AR) was excreted in the urine and faeces 6 h after dosing. The maximum radioactivity in the eggs was 0.2% of the AR.

The radioactive residues in hens' eggs did not reach a plateau during the 7-day dosing period, reaching maxima of 0.02 mg/kg eq on the 8th day in the whites and 0.1 mg/kg eq on the 7th day in the yolks (73% of the TRR in the yolks and 27% in the whites). In whole eggs, fenitrothion constituted 8% of the TRR (0.005 mg/kg eq). The main metabolite was 3-methyl-4-nitrophenyl sulfate (40% of the TRR), and others identified were 3-methyl-4-nitrophenol (22% of the TRR), the glucuronide of 5-hydroxy-2-nitrobenzyl alcohol (7% of the TRR), demethylfenitro-oxon (5% of the TRR) and demethylfenitrothion (2% of the TRR).

In the hens killed one day after treatment, residues were 0.098 mg/kg eq in liver, 0.1 mg/kg eq in kidney, <0.005 mg/kg eq in muscle and 0.016 mg/kg eq in fat.

In a quail killed one h after treatment 0.81 mg/kg eq radioactive residue was found in the liver (15% parent compound, 32% 3-methyl-4-nitrophenol, 4.4% fenitro-oxon, 1.6% fenitro-oxon-3-CH₂OH and 40% unextracted), 2.2 mg/kg eq in the kidney (5% parent, 10% 3-methyl-4-nitrophenol, 0.9% fenitro-oxon-3-CH₂OH, 64% unextracted and 18% unidentified), and 0.16 mg/kg eq in muscle (34% parent, 4.4% 3-methyl-4-nitrophenol and 61% unextracted). Fat was not investigated.

The metabolism of fenitrothion in laboratory animals was qualitatively similar to that in farm animals.

Plant metabolism

The Meeting received information on the fate of fenitrothion in grapes and tomatoes after spray application and in rice during storage.

Two Thompson Seedless grape vines were sprayed three times at 14-day intervals in the field (Madera County, California, USA) with an EC 500 formulation of [phenyl-¹⁴C]fenitrothion at a rate of 0.82 kg ai/ha and a spray volume of 1000 l/ha. Bunches of grapes were collected at mature harvest 35 days after the last treatment. Of the total recovered radioactive residue (TRR) in the grapes 97% was extractable (0.72 mg/kg eq). The main metabolites were a 3-methyl-4-nitrophenol conjugate (26% of the TRR) and 3-methyl-4-nitrophenol β -glucuronide (21%); the parent was not detected. 3-methyl-4-nitrophenol conjugates 2 to 6 constituted 23.5%, demethylfenitrothion 7.2% and 3-methyl-4-nitrophenol 0.97% of the TRR.

The foliage and fruit of F1 Shirley tomato plants were sprayed twice at a 14-day interval at normal and threefold rates in a greenhouse with a solution of [phenyl-¹⁴C]fenitrothion. The first application was at growth stage BBCH 85 (ripe fruit present). The application rates were 0.69 kg ai/ha with a spray volume of 4000 l/ha for the normal application and 2.1 kg ai/ha for the threefold application. Mature fruit, immature fruit and foliage were collected at harvest 15 days after the last treatment.

Of the total recovered radioactive residue 63%-70% was recovered in rinses and initial extracts of fruits and foliage. The parent was found at 13% of the TRR, 3-methyl-4-nitrophenol β -glucuronide at 7.3% and 3-methyl-4-nitrophenol at 7% in the mature fruit. When the remaining solids from mature fruit were further extracted with acetonitrile (ACN) followed by 1 M HCl and finally with 6 M NaOH, a further 19% of the TRR was extracted. The main metabolite in the extracts (24% of the TRR) did not correspond to any of the reference compounds available but could be hydrolysed with cellulase, resulting in the formation of both 3-methyl-4-nitrophenol (28%) and 3-methyl-4-nitrophenol β -glucuronide (44%) with 27% remaining as the unaltered metabolite. The main metabolite is considered to be a further conjugate of 3-methyl-4-nitrophenol β -glucuronide.

An emulsion of [α -methyl-¹⁴C]fenitrothion was applied to unpolished Nishikaze rice grain at rates of 6 and 15 g ai/t and samples were stored at 15° or 30°C in the dark for 12 months for analysis at intervals. Residues of fenitrothion gradually decreased with half-lives of about 4 and over 12 months at 30°C and 15°C respectively. The main metabolites were demethylfenitrothion and 3-methyl-4-nitrophenol. Demethylfenitrothion was formed in the early stages of degradation but the concentration remained fairly constant after 3 months. The concentration of 3-methyl-4-nitrophenol increased throughout the storage period. After 12 months at 15°C, 65% of the applied radioactivity was recovered as the parent compound, 10% as demethylfenitrothion and 16% as 3-methyl-4-nitrophenol, and after 12 months at 30°C 24% as parent, 18% as demethylfenitrothion and 38% as 3-methyl-4-nitrophenol.

Minor metabolites, found particularly at the end of the storage period, were fenitro-oxon, demethylfenitro-oxon, *S*-methyl-fenitrothion, demethylfenitrothion *S*-isomer, 1-methoxy-3-methyl-4-nitrobenzene, 3-hydroxymethyl-4-nitrophenol, 1,2-dihydroxy-4-methyl-5-nitrobenzene and 1,2-dimethoxy-4-methyl-5-nitrobenzene. These constituted together about 4% of the applied radioactivity

at 15°C, and at 30°C 1-methoxy-3-methyl-4-nitrobenzene constituted about 8%, 1,2-dihydroxy-4-methyl-5-nitrobenzene about 3%, and the remaining minor metabolites about 6%. One reference compound (1-methoxy-3-hydroxymethyl-4-nitrobenzene) was not detected. No radiolabelled carbon dioxide was present.

Autoradiography showed that the radioactivity was principally in the aleurone (part of the seed coat) but penetrated into the endosperm during storage. The concentration of fenitrothion in endosperm decreased from 4.5 to 3.3 mg/kg at 15°C and to 1.2 mg/kg at 30°C. The amount of fenitrothion in bran (seed coat plus germ) was approximately 40 times that in endosperm at all sampled intervals.

Although the main metabolites found in plants were also found in animals, some minor ones were not (*S*-methyl-fenitrothion, demethylfenitrothion *S*-isomer, 1-methoxy-3-methyl-4-nitrobenzene, 1,2-dihydroxy-4-methyl-5-nitrobenzene and 1,2-dimethoxy-4-methyl-5-nitrobenzene).

Environmental fate in soil

The Meeting received information on aerobic degradation in soil.

The aerobic degradation of [phenyl-¹⁴C]fenitrothion was studied in a US sandy loam soil for 365 days and in four European soils (two sandy loams, a silt loam and a clay loam) for 90 days.

In the first study, the parent decreased from 88% initially to 0.05% of the total applied radioactivity (TAR) at 365 days. At the end of the study accumulated volatile radioactivity was 71% of the TAR, most of which was present as ¹⁴CO₂ (67.3% of the TAR). Six degradation products were identified: fenitro-oxon, 3-methyl-4-nitrophenol, demethylfenitrothion, demethylfenitro-oxon, formylaminofenitrothion and 1-methoxy-3-methyl-4-nitrobenzene. 3-methyl-4-nitrophenol, the main product, amounted to 20% of the TAR at day 3, but decreased to <1% of the TAR at day 30. Other products were below 1% of the TAR. Unextractable residues increased to 35% of the TAR at day 21, but then decreased to 20% of the TAR at day 365. A number of fractions were not identified, but the sum of these did not exceed 4.4% of the TAR. Calculated half-lives were 2.0 days and 3.3 days for parent and 3-methyl-4-nitrophenol respectively.

In the second study, unextracted radioactivity increased to 37%-54% of the TAR after 7 days, decreasing to 23%-43% after 90 days, and trapped ¹⁴C as ¹⁴CO₂ to 51%-69% by the end of the study. Fenitrothion was detected at 91%-96% of the TAR immediately after application, but decreased rapidly to 2.4%-5.4% of the TAR after 7 days. The two products identified were 3-methyl-4-nitrophenol (17%-45% of the TAR at 1 day, decreasing rapidly to below 7% of the TAR after 7 days) and 1-methoxy-3-methyl-4-nitrobenzene at quantities below 0.5% of the TAR. A further unidentified compound was detected at a maximum of 3.2% of the TAR, and other unknowns and unresolved background occurred at maxima of 0.7% and 0.6% of the TAR respectively. Calculated half-lives ranged from 1 to 33 h for the parent compound, and from 42 to 68 h for 3-methyl-4-nitrophenol.

These results indicate that fenitrothion is mainly degraded via cleavage of the P-O-aryl linkage, and further breakdown occurs via opening of the phenyl ring with eventual mineralization to CO₂. The Meeting decided that studies on residues in succeeding crops were not necessary since the residues of fenitrothion in soil decrease rapidly.

Environmental fate in water-sediment systems

The Meeting received information on degradation in water and in water/sediment systems.

In a 30-day study at 25°C in the dark at pH 5, 7 and 9 in sterile solutions, fenitrothion (uniformly ¹⁴C-labelled in the phenyl ring) was hydrolysed faster at higher pH, with half-lives of 191-

200 days at pH 5, 180-186 days at pH 7, and 100-101 days at pH 9. Demethylfenitrothion and 3-methyl-4-nitrophenol were identified as degradation products.

Fenitrothion was rapidly photolysed with a half-life of 3.3-3.6 days. Photoproducts were further degraded to CO₂. In water/sediment systems the amount of fenitrothion decreased rapidly in the water phase with a concurrent initial increase of parent in the sediment phase. Unextractable radioactivity in the sediment increased to 71%-76% of the TAR at 59 days.

Methods of analysis

Several methods for the determination of fenitrothion in cereal grains and their processed products were reported to the Meeting. Extraction with acetone, acetone/water, methanol, acetonitrile/water or acetonitrile is followed by clean-up, partitioning into a suitable organic solvent and quantification by GC-FTD, GC-ECD, GC with an FPD, or GC-MS. LOQs in grain were 0.01-0.06 mg/kg, in straw 0.04-0.06 mg/kg, in bran 0.01-0.25 mg/kg, in pollard, white and brown bread 0.01-0.1 mg/kg, in germ 0.01-0.25 mg/kg and in flour 0.01-0.05 mg/kg.

The Meeting was informed by the government of The Netherlands of a multi-residue enforcement method for fruit and vegetables, consisting of extraction by a method for non-fatty samples and GC with an ion-trap detector. LOQ is 0.05 mg/kg.

Methods to determine fenitrothion in animal commodities were not provided.

Stability of residues in stored analytical samples

The Meeting received data on the stability of residues in cereal grain and straw. Information on storage stability in animal products was not available.

Fenitrothion and demethylfenitrothion residues were stable at -20°C for the times tested: wheat grain 113 days, barley grain 105 days, rice grain 149 days and straw 71 days.

Definition of the residue

Fenitrothion was rapidly excreted by goats, quail and hens. In whole goat milk a maximum of 0.012 mg/kg eq radioactive components was found: neither the parent compound, nor fenitro-oxon nor 3-methyl-4-nitrophenol were detected. The radioactivity was attributed to 4 metabolites of which the main one constituted 39% of the TRR (0.005 mg/kg eq). No radioactive residues could be detected in cream. The parent compound could not be detected in goat liver, kidney, fat or muscle, although maximum ¹⁴C levels of 1.5 mg/kg eq were found in liver, 0.031 mg/kg eq in kidney, 0.012 mg/kg eq in fat and 0.005 mg/kg eq in muscle. The nature of these residues was not investigated.

Of the total recovered radioactivity in eggs, 73% was in the yolk and 27% in the white. In whole egg, the parent was found at 8% of the TRR (0.005 mg/kg eq) and the main metabolites were 3-methyl-4-nitrophenyl sulfate (40% of the TRR) and 3-methyl-4-nitrophenol (22% of the TRR).

In a metabolism study on hens residues were 0.098 mg/kg eq in liver, 0.1 in kidney, <0.005 in muscle and 0.016 in fat, and in a study on quail the parent made up about 15% of the residue in liver, about 5% in kidney and about 34% in muscle; the main metabolite in the tissues was 3-methyl-4-nitrophenol.

The metabolism of fenitrothion in animals has not been fully elucidated, but in general it is expected that the levels of the individual metabolites will be <0.005 mg/kg at the expected exposure levels.

On the basis of the limited information available, the Meeting agreed that fenitrothion is a suitable marker molecule for enforcement in animal commodities and is also the compound of interest for dietary risk assessment.

The log K_{ow} of fenitrothion is 3.32. Taking into account the results of the metabolism studies (no radioactivity in cream, but found in yolk, only slightly more in fat than in muscle), the Meeting decided that fenitrothion should not be classified as fat-soluble.

After the pre-harvest treatment of grapes, the main metabolites were 3-methyl-4-nitrophenol conjugate 1 (26% of the TRR) and 3-methyl-4-nitrophenol β -glucuronide (21%); the parent was not detected. The main metabolite in tomatoes (24%) is considered to be a further conjugate of 3-methyl-4-nitrophenol β -glucuronide. The parent constituted 13% of the TRR. Information on residues in cereal grains after pre-harvest treatments was not reported.

After the post-harvest treatment of cereal grains, the residue consisted mainly of parent, demethylfenitrothion and 3-methyl-4-nitrophenol. The key effect that determines the ADI and the acute RfD for fenitrothion is inhibition of brain and/or red cell acetylcholinesterase. The Meeting concluded that 3-methyl-4-nitrophenol does not need to be considered for dietary risk assessment since it does not inhibit cholinesterase. Demethylfenitrothion was also not considered to be relevant for dietary risk assessment since it is not metabolized to a more potent oxon, and structure-activity considerations indicate that it is likely to be only a weak cholinesterase inhibitor.

The metabolism of fenitrothion in plants has also not been fully characterized. The supported uses of fenitrothion are pre-harvest applications on cereals and post-harvest on stored cereal grains. The Meeting concluded that the available studies were adequate only for the post-harvest uses on stored cereal grains. To support the pre-harvest uses on cereals, relevant metabolism studies are required.

Definition of the residue (for compliance with MRLs and for estimations of dietary intake):

fenitrothion, for both plant and animal commodities.

Results of supervised trials on crops

The Meeting received information on supervised trials on cereal grains (rice, wheat, barley, triticale) with pre-harvest treatments in Japan and Australia. In some trials pre-harvest treatments were combined with a seed treatment before planting. However, as data on metabolism in cereal grains after pre-harvest treatment were lacking the trials could not be evaluated.

No trials were reported on apples, head cabbages, cacao beans, cauliflower, cherries, citrus fruits, cucumbers, egg plants, grapes, leeks, head lettuce, bulb onions, peaches, pears, peas, peppers, potatoes, radishes, soya beans, strawberries, tea or tomatoes. The Meeting therefore recommended the withdrawal of the existing CXLs for these commodities.

Cereal grains (group 020)

Five trials on stored wheat were carried out in Australia and Argentina. The trial in Australia complied with Australian GAP for post-harvest use on wheat (912 g ai/t with a waiting period of 3 months) and the residue was 7.6 mg/kg. In Argentina the trials complied with Argentinean GAP for post-harvest use on cereals (6 g ai/t with a waiting period of 1 day) and residues were 3.1, 3.5, 5.0 and 5.6 mg/kg.

The Meeting estimated a maximum residue level for cereals based on the post-harvest use confirming the current CXL for cereal grains of 10 mg/kg (Po) and estimated an HR of 7.6 mg/kg and an STMR of 5.0 mg/kg.

Straw, fodder and forage of cereal grains and grasses (group 051)

The Meeting received details of supervised trials on cereal grains (rice, wheat, barley, triticale) with pre-harvest treatments in Japan and Australia. However, because details of metabolism were not provided the trials could not be evaluated.

Fate of residues in storage and processing

In storage

Hard red spring Neepawa wheat grains were evenly sprayed with fenitrothion at a rate of 12 g ai/t, and samples stored in screw-capped jars (240 ml) in the dark at 20°C for analysis after 0, 1, 3, 6 and 12 months. The concentration of fenitrothion in the stored samples decreased to about 5.5 mg/kg after 3 months and to about 2.5 mg/kg after 12 months. The main metabolites were demethylfenitrothion, 3-methyl-4-nitrophenol and dimethyl phosphorothioic acid. Residues of the first and the last increased to 2.0 and 0.55 mg/kg after 6 months, and decreased to 0.98 mg/kg and 0.21 mg/kg respectively after 12 months. 3-Methyl-4-nitrophenol increased from 0.38 mg/kg at 1 month to 0.96 mg/kg after 12 months. Neither fenitro-oxon nor *S*-methyl-fenitrothion was detected at any time point.

In processing

The Meeting received information on the fate of fenitrothion during simulated processing, in stored rice during polishing and cooking and in stored wheat during milling and baking.

A study with radiolabelled fenitrothion in sterile buffer solutions showed that fenitrothion is relatively stable during simulated pasteurisation (90°C for 20 min; 82% of the TAR left as parent, 12% demethylfenitrothion and 0.7% 3-methyl-4-nitrophenol formed) but is readily degraded to demethylfenitrothion during simulated baking/boiling (100°C for 60 min; 35% of the TAR left as parent, 62% demethylfenitrothion and 0.8% 3-methyl-4-nitrophenol formed) and sterilization (120°C for 20 min; 15% of the TAR left as parent, 82% demethylfenitrothion and 1.3% 3-methyl-4-nitrophenol formed).

When unpolished rice grains, treated post-harvest with 15 g ai/t [α -methyl-¹⁴C]fenitrothion and stored at 30°C, were cooked immediately after treatment, the amount of fenitrothion decreased to about 60%, with the formation of demethylfenitrothion and 3-methyl-4-nitrophenol. When cooked after storage about 40% of the fenitrothion was lost, and residues of demethylfenitro-oxon and 3-methyl-4-nitrophenol increased. Other metabolites, such as 1-methoxy-3-methyl-4-nitrobenzene and 1,2-dihydroxy-4-methyl-5-nitrobenzene, decreased.

When cooked after polishing and washing, 80% of the applied radioactivity remained in the bran and rinses. The combination of washing and boiling decreased the contents of fenitrothion, demethylfenitrothion and 3-methyl-4-nitrophenol by about a factor of 2. Processing factors could not be calculated since actual residue levels were not reported. The Meeting recommended the withdrawal of the existing CXLs for rice, polished (1 mg/kg PoP) and rice bran, unprocessed (20 mg/kg PoP).

Wheat stored for up to 3 months after post-harvest treatment with 12 g ai/t fenitrothion was milled and baked into white and brown bread. The parent compound was determined in all processed products. Processing factors from wheat stored for 1 and 3 months were comparable. Calculated processing factors were 4.0 and 3.9 for bran (mean 3.95), 1.7 for pollard, 3.7 and 3.2 for germ (mean 3.45), 0.21 and 0.26 for flour (mean 0.235), 0.60 for gluten, 0.089 and 0.11 for white bread (mean 0.10) and 0.43 and 0.33 for brown bread (mean 0.38).

From the highest residue and STMR for wheat (7.6 mg/kg and 5 mg/kg respectively) and the processing factors for wheat bran, flour, and white and brown bread, the Meeting estimated a maximum residue level of 30 mg/kg in bran, and STMR-Ps of 19.75 mg/kg in bran, 1.175 mg/kg in flour, 0.05 mg/kg in white bread and 1.9 mg/kg in brown bread.

Farm animal dietary burden

The Meeting estimated the dietary burden of diflubenzuron residues in farm animals from the diets listed in Appendix IX of the FAO Manual (FAO, 2002). One feed commodity only from each Codex Commodity Group was used, so the calculation includes wheat grain but no other cereals. Calculation from the MRL for wheat provides the concentrations in feed for estimating MRLs, while calculation from the STMR gives feed levels for estimating STMRs, for animal commodities. In the case of processed commodities, the STMR-P value would be used for both intake calculations.

Maximum farm animal dietary burden

Crop	Codex Code	Residue (mg/kg)	Basis	% Dry matter	Residue, dry wt (mg/kg)	Chosen Diets, %			Residue contribution of feeds (mg/kg)		
						Beef	Dairy	Poultry	Beef	Dairy	Poultry
Wheat grain	GC	10	MRL	89%	11.24	50	40	80	5.62	4.50	8.99
Total									5.62	4.50	8.99
Feeding levels in goat and hen metabolism studies									7.6	7.6	35

Mean farm animal dietary burden

Crop	Codex Code	Residue (mg/kg)	Basis	% Dry matter	Residue, dry wt (mg/kg)	Chosen Diets, %			Residue contribution of feeds (mg/kg)		
						Beef	Dairy	Poultry	Beef	Dairy	Poultry
Wheat grain	GC	5	STMR	89	5.62	50	40	80	2.81	2.25	4.50
Total									2.81	2.25	4.50
Feeding levels in goat and hen metabolism studies									7.6	7.6	35

Farm animal feeding studies

The Meeting received information on residues in the tissues cattle after grazing on fenitrothion-treated grass and in cattle fed with fenitrothion-treated maize.

Fenitrothion was applied as an EC formulation to two pastures at rates of 0.125 and 0.375 kg ai/ha. Ten cows were confined to each pasture immediately after spraying. Four animals, two from each field, were slaughtered after 1, 3, 7 or 10 days and breast muscle and omental fat only were analysed. Residues were found in the muscle and fat samples taken 1 day after spraying from cows from both pastures (0.007-0.014 mg/kg in muscle, <0.001-0.014 mg/kg in fat), at day 3 residues were

found only in samples from the cows grazing on the pasture treated with 0.375 kg ai/ha (<0.001-0.001 mg/kg in muscle, 0.004-0.007 mg/kg in fat), and after day 3 no residues could be detected.

For the feeding trial, maize was sprayed in the field with 1.1, 2.2 or 3.4 kg ai/ha fenitrothion as an EC formulation, cut the next day and aged for 76 days. Groups of four lactating Jersey cows were fed treated or control silage *ad libitum* for 56 days. Cows fed silage from corn treated with 1.1, 2.2 and 3.4 kg ai/ha ingested averages of 0.21, 0.41 and 0.66 mg/kg bw/day of fenitrothion and its metabolites. Animals were milked twice daily and at the end of each week a composite sample was prepared by combining the milk from 2 consecutive morning and evening milkings.

In the milk of cows fed silage from maize treated at 3.4 kg ai/ha aminofenitrothion was the only compound detected, at levels ranging from 0.001 to 0.005 mg/kg equivalents. No residues (<0.001 mg/kg eq) were found in the milk of cows consuming silage from maize treated at lower levels. Tissues were not analysed.

Animal commodity maximum residue levels

In a metabolism study when goats were dosed at 7.6 mg/kg eq in the feed, the parent compound was undetected in tissues and milk, so no residues are to be expected at the calculated dietary burden of 5.6 mg/kg feed for beef cattle and 4.5 mg/kg for dairy cattle.

The dietary burden for poultry was 9 mg/kg, lower than the feeding level in the metabolism study on hens (approximately 35 mg/kg feed); the resulting residues in eggs and poultry tissues were therefore calculated by applying the respective transfer factors (Transfer factor = residue level in egg or tissue ÷ residue level in diet) at this feeding level.

Since in the metabolism study only one residue was reported per tissue, this value was used in conjunction with the maximum dietary burden to calculate the highest likely poultry commodity residue levels, and it was used in conjunction with the STMR dietary burden to estimate the poultry commodity STMRs.

Calculation of MRLs and STMRs for poultry tissues and eggs

	Feeding level (ppm)	Fenitrothion Residues, mg/kg ^{1/}									
		Muscle		Fat		Liver		Kidney		Eggs	
		high ³	mean ⁴	high ³	mean	high	mean	high	mean	high	mean
MRL poultry	9	(0.001)		(0.004)		(0.025)		(0.016)		(0.001)	
	35	0.005		0.016		0.098		0.10		0.005	
STMR poultry	4.5		(0.0006)		(0.002)		(0.013)		(0.013)		(0.0006)
	35		0.005		0.016		0.098		0.100		0.005

¹ Residue values in parentheses in italics are extrapolated from residues found at the feeding level in the hen metabolism study

² Italics show the estimated dietary burdens. Normal font shows the feeding level in the hen metabolism study

³ High is the residue found in the feeding study combined with the maximum dietary burden

⁴ Mean is the residue found in the feeding study combined with the STMR dietary burden

The Meeting concluded that residues above the LOQ are unlikely to arise in poultry commodities, since the calculations were based on total radioactive residue levels. In the quail metabolism study 15% of the radioactive residue in liver was the parent, in kidney 5% and in muscle 34%.

However because a validated analytical method for the determination of fenitrothion in animal commodities was not available and no information on the storage stability of residues in analytical samples of animal commodities was reported, the Meeting decided it could not estimate maximum residue levels for animal commodities.

FURTHER WORK OR INFORMATION

Desirable

1. Metabolism in cereals (including rice) after pre-harvest treatment
2. Validated analytical method for the determination of fenitrothion in animal commodities
3. Freezer storage stability of residues in animal commodities
4. Farm animal transfer studies
5. Processing study on rice

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intake of fenitrothion, based on the STMRs estimated for 3 commodities, was 120-640% of the maximum ADI (0.005 mg/kg bw) for the GEMS/Food diets. The information provided to the Meeting precludes an estimate that the dietary intake would be below the ADI.

The Meeting noted that the intake calculations were conservative, since they did not take into account the reduction of the residue obtained by the processing of cereal grains, except the processing of wheat. Especially processing information on rice would be useful to refine the intake calculations.

Short-term intake

The International Estimated Short Term Intake (IESTI) for fenitrothion was calculated for the food commodities (and their processed fractions) for which maximum residue levels were estimated and for which consumption data were available. The results are shown in Annex 4.

The IESTI represented 1-150% of the acute RfD (0.04 mg/kg bw) for the general population and 2-240% of the acute RfD for children. The estimated short-term intakes from husked and polished rice were 120 and 150% respectively for the total population. The estimated short-term intakes from maize (fresh, flour, oil), husked rice and polished rice were 160, 240 and 240% respectively for children. The Meeting concluded that the short-term intake of residues of fenitrothion from uses, other than on these 3 commodities, that have been considered by the JMPR is unlikely to present a public health concern.

The Meeting noted that the intake calculations were conservative, since they did not take into account the reduction of the residue obtained by the processing cereal grains, except the processing of wheat. Especially processing information on rice would be useful to refine the intake calculations.

4.11 LINDANE (048)

RESIDUE AND ANALYTICAL ASPECTS

Lindane, a broad-spectrum insecticide, was originally evaluated by the JMPR in 1966 (under the name gamma-BHC) and re-evaluated for residues several times up to 1989. Lindane was scheduled for residue review by the 2003 JMPR under the Periodic Review Programme by the 30th Session of the CCPR (ALINORM 99/24).

At the 31st Session of the CCPR several delegations preferred revocation of the MRLs for lindane as (1) the TMDI greatly exceeded the temporary ADI; (2) it had been banned in many countries; (3) it has limited uses and (4) its last evaluation was in 1989. It was decided that at its next Session the Committee would consider the revocation of the existing CXLs, “(except those accompanied by the letter F)”, if not supported. The company confirmed support for cereals, sugar beet, maize and oil seed (sunflower and canola).

The Meeting received information on identity, metabolism and environmental fate, residue analysis, use pattern, residues resulting from supervised trials on wheat and canola, fate of residues during processing, animal feeding studies, and residues in food in commerce or at consumption. In addition information on GAP and/or national MRLs was supplied by the governments of Australia, Germany, The Netherlands, Poland and the USA.

Animal metabolism

The Meeting received information on metabolism in orally-dosed lactating goats, laying pheasants and laying hens. All studies were with uniformly-labelled [^{14}C]lindane.

Studies on metabolism in mice, rats, rabbits and dogs evaluated by the WHO Core Assessment Group of the 2002 JMPR indicated that lindane undergoes extensive metabolism in animals. Stepwise dehydrogenation, dechlorination, and dehydrochlorination may be followed by conjugation with sulfate or glucuronide. Lindane itself was considered to be the toxicologically significant compound.

Lactating goats. Animals dosed orally with [^{14}C]lindane at doses of 13, 20 or 200 ppm in the feed excreted 34-46% of the administered ^{14}C in the urine, 5.1%-13% in the faeces, and 1.1%-2.4% in milk, and 4.0%-4.4% was found in the tissues. The highest radioactive residues were found in body fat, followed by liver, kidney and muscle. 0.2%-1.0% of the administered radioactivity was recovered as expired $^{14}\text{CO}_2$. Total recoveries for each goat were low (51%-59%), probably owing to loss of volatile ^{14}C -metabolites untrapped by the solutions.

In fat and muscle, ^{14}C was mainly in the parent compound (73-85% and 28-81% of the TRR, corresponding to about 3 mg/kg and 0.02-0.16 mg/kg respectively at the lower doses). The metabolites identified in fat were 1,2,4-trichlorobenzene (3.6-11%), γ -pentachlorocyclohexene (5.8%), 1,2,4,5-tetrachlorobenzene (0.8-1.5%), 1,2,3,4,5,6-hexachlorocyclohexene (0.4-0.7%), and 1,2,3,4-tetrachlorobenzene and 1,2,3,5-tetrachlorobenzene (each <0.1%), and in muscle 1,2,4-trichlorobenzene and γ -pentachlorocyclohexene (5.8% and 3.5% of the TRR respectively).

In liver and kidney the parent compound constituted only about 16% and 4.5-36% of the TRR respectively, corresponding to about 0.36 mg/kg and 0.17 mg/kg at the 13 ppm feed level. In liver all

individual components were $\leq 1.3\%$ of the TRR (or 0.029 mg/kg eq). Identified, although not quantified, were 1,3,5-trichlorobenzene, 2,6-dichlorophenol and 2,3,4,5-tetrachlorophenol, and tentatively 2,3,4-trichlorophenol. In kidney, γ -tetrachlorocyclohexene and possibly 1,2-dichlorobenzene were identified at 4.5% and 5.8% of the TRR respectively.

In milk residues reached a plateau after 2-3 days. Approximately 55-87% of the TRR in whole milk was in the fat. Lindane was the major constituent in milk fat (55%-77% of the TRR of whole milk; 0.11 mg/kg at the 13 mg ai/kg feed level) with 1,2,4-trichlorobenzene up to 16% of the TRR and γ -pentachlorocyclohexene at about 5% of the TRR of whole milk. Skimmed milk contained 6-8 conjugated chlorophenols (5.9%-17% of the TRR of whole milk).

Laying hens. In this study 44-63% of the total applied radioactivity (TAR) was recovered from the excreta, 2.6-9.0% from eggs and 20-47% from tissues and organs. Total recovery of the administered radioactive dose was above 90%. The highest concentration of residues was found in the fat (5.5-13% of the TAR), followed by skin (5.5-10% of the TAR), thigh muscle (1.8-3.0% of the TAR), liver (0.43-0.97% of the TAR), breast muscle (0.2-0.5% of the TAR) and kidney (0.09-0.26% of the TAR).

Lindane was the main residue in all tissues analysed: fat 85%, thigh muscle 71%, liver 51%, breast muscle 100%, egg yolk 94%, egg white 100% of the identified residues. In breast muscle and egg whites no radioactive residue other than the parent was identified, whereas in fat and egg yolks the main metabolite was 2,3,4,5,6-pentachlorocyclohexene (6.1% and 4.2% of the identified residues respectively), and in liver 1,2,4-trichlorobenzene (19% of the identified residues) while dichlorobenzenes were present at 9.5% and 1,3,5-trichlorobenzene at 6.4%. In thigh muscle the main metabolite was 1,2,4,5- or 1,2,3,4-tetrachlorobenzene (18% of the identified residues). All other metabolites identified were $\leq 5\%$ of the TRR. During the dosing period (4-6 days) no plateau was reached in eggs.

Laying hen pheasants were dosed for 15 days. Eggs were collected daily for about 70 days for analysis. Residues in the yolks were highly variable, increasing sharply and reaching a mean maximum level in 8 days in a group dosed with capsules and gradually in a group fed treated seed reaching a mean maximum in 22 days. Thereafter levels decreased gradually to <0.5 mg/kg eq in both groups (in about 50 days in the former and about 70 days in the latter).

The metabolism of lindane in laboratory animals was qualitatively similar to that in farm animals.

Plant metabolism

The Meeting received information on the fate of lindane in plants grown from lindane-treated seeds, in spinach and cucumber plants after post-emergence spray applications and in apples after pre-harvest spray applications. The studies were conducted with uniformly-labelled [^{14}C]lindane.

Wheat seeds coated with lindane at an actual rate of 480 g ai/t were planted in the field and the resulting crops sampled 19 and 100 days after treatment. Significant amounts of residues were present in the seedlings and in the mature plants, indicating that lindane and/or its degradation products are readily translocated into growing plants. Extraction of the plant tissues with MeOH recovered more radioactive residues from the seedlings (91% of the TRR) than from any part of the mature plants (63% of the TRR from roots, 67% from straw, 34% from chaff), indicating that radioactive residues are more strongly bound in mature plant tissues.

No radioactive residue could be detected in grain. The parent was found at 36% of the TRR (0.2 mg/kg eq) in seedlings, 21% (0.48 mg/kg eq) in roots and 5.4% (0.006 mg/kg eq) in straw, and was undetected in chaff. In the seedlings, 26% of the TRR (0.14 mg/kg eq) was hydrophilic and 29% (0.16 mg/kg eq) hydrophobic. The proportion of the hydrophilic compounds increased in the mature plants: 27.4% of the TRR (0.63 mg/kg eq) in the roots, 53% (0.06 mg/kg eq) in the straw and 34%

(0.007 mg/kg eq) in the chaff. Roots contained eight non-acidic compounds (chlorobenzenes), each $\leq 5.7\%$ of the TRR (0.13 mg/kg eq), and four acidic compounds (chlorophenols).

Radish, sugar beet, spinach, mustard, maize, sweet corn, and spring wheat seeds were coated with uniformly-labelled [^{14}C]lindane (actual dose rates 380, 2290, 820, 590, 1770, 1440 and 370 g ai/t respectively) and planted outdoors under a clear protective roof. Sugar beet plants did not reach full maturity. Significant residues (>0.01 mg/kg eq) were found in all crop parts, except maize cobs and grains. The highest levels of radioactivity were found in spring wheat samples (foliage $>$ grain $>$ roots). Mustard seeds were not analysed.

Residues were extracted with acetonitrile (ACN) and analysed for lindane. In the ACN extracts of the fast-growing crops 81% of the TRR (mustard foliage) and 54% of the TRR (radish roots) was identified as the parent.

In the slow-growing crop extracts lindane constituted 30% of the TRR (0.09 mg/kg) in sugar beet roots, 19% (0.04 mg/kg) in sugar beet foliage, 20% (0.16 mg/kg) in maize roots, 12% (0.008 mg/kg) in maize foliage, 24% (0.012 mg/kg) in sweet corn foliage, 0.5% (0.016 mg/kg) in spring wheat foliage and 3.8% (0.002 mg/kg) in spring wheat grain. It should be noted that virtually all of the radioactivity in spring wheat foliage (109%; 3.2 mg/kg) and grain (217%; 0.11 mg/kg eq) was unextracted. (The author's figures are quoted although clearly in error; no explanation was suggested.)

A single Red Delicious apple tree was treated once with 1 kg ai/ha uniformly-labelled [^{14}C]lindane, just before petal fall. Lindane and metabolites were found in both leaves and fruit. The presence of lindane in the fruit indicate that it was distributed throughout the tree and transferred to the maturing fruit from the leaves and twigs. Total radioactive residues decreased during the maturation period and those in the apples were about one fifth of the levels in the foliage at each collection. The amount of unextracted residue increased with time from about zero initially to 30-40% of the TRR in the foliage and 25% of the TRR in the mature fruit.

At harvest at 131 days, radioactive residue in foliage consisted of 3.2% of the TRR of lindane, minute quantities of chlorinated phenols (2.0% of the TRR), TLC-origin material (19% of the TRR), water-soluble material (40% of the TRR) and unextracted residues (32% of the TRR). Residues in the fruit consisted of 11% of the TRR as parent, 14% as pentachlorophenol, minute quantities of two other chlorinated phenols (0.6% of the TRR), TLC-origin material (12% of the TRR), water-soluble material (38% of the TRR) and unextracted residues (25% of the TRR). In mature apples the levels of unextracted residues and residues in the aqueous layer were too low (<0.02 mg/kg eq) to justify further investigation.

Fenumex cucumber plants were treated three times with EC foliar applications of [^{14}C]lindane at a rate of 0.71 kg ai/ha each. Autoradiography indicated that radioactivity spread very rapidly throughout the plant. Radioactivity in the stem and root detected immediately after treatment disappeared after 24 h, and after seven days most had disappeared from the leaves.

Most of the radioactivity was in the leaves and extractable radioactivity decreased rapidly. Growth dilution appeared to be important in reducing the residue on a weight/weight basis. Residues in cucumber fruits ranged from 0.00009-0.0032 mg/kg eq and were therefore not further investigated. In the initial plant extracts that contained sufficient radioactivity no radioactive components co-eluted with potential metabolites, including chlorinated benzenes, cyclohexanes, and phenols (it was not stated which were used as reference standards). Lindane was the only residue identified. Hydrolysis of the solids released additional radioactivity consisting of multiple low-level radioactive components.

Separate recovery studies were conducted on a cucumber plant grown in an aerated glass enclosure. Volatiles were collected in traps for CO_2 and volatile organic compounds. Radioactivity at 7 days was distributed among leaves (41% of the TAR), stems (3.9% of the TAR), roots (0.9% of the

TAR), soil (14% of the TAR) and traps (17% of the TAR) or remained stuck to tanks, tubes and pots (27% of the TAR).

Perpetual spinach plants at the two-leaf stage were treated with a single foliar application of uniformly-labelled [¹⁴C]lindane at a rate of 1.5 kg ai/ha. Autoradiography showed that lindane was translocated rapidly throughout the plants. At 1 day no radioactivity was associated with the roots and at 7 days the greater part of the residue had disappeared from the leaves. Total radioactive residues (TRR) had decreased markedly by day 7 to below 1% of the TAR. By the time the plants matured (60-92 days) the TRR was at most 0.0004 mg/kg eq, too low to allow identification of metabolites. In acetone extracts of immature plants at 0, 1 and 3 days, lindane was the only radioactive component observed.

Lindane is intended for use as a seed treatment on oilseeds and cereal grains. After seed treatment, significant amounts of residues were present in the seedlings and in the mature plants, indicating that lindane and/or its degradation products are readily translocated. Extraction efficiency decreased when plants matured indicating that radioactive residues are more strongly bound in the mature plant tissues. This is also consistent with the fact that lindane was a major residue in fast-growing crops, but its contribution decreased in slow-growing crops. In one study on wheat plants grown from seeds treated with lindane according to GAP, no radioactivity could be detected in the grain at harvest. In a second study, only 0.052 mg/kg eq radioactive residue was found in the wheat grain, of which virtually all (217% according to the author's figures) was unextractable. Of the very small amount extracted, 3.8% of the TRR (corresponding to 0.002 mg/kg eq) was the parent compound. Also in wheat foliage at harvest, only about 5% of the radioactive residue was extractable, corresponding to 0.14 mg/kg equivalents. Of this, 10% (0.016 mg/kg) was identified as the parent compound.

All metabolites found in plants were also characterized in animals.

Environmental fate in soil

In a field rotational crop study soil was treated with [¹⁴C]lindane at a rate of 0.85 kg ai/ha as an EC formulation in a spray volume of 700 l/ha before planting. Lindane was incorporated to a depth of 5 or 10 cm. Soil cores (30 cm in depth) were collected before and immediately after treatment, at each crop planting, and at harvest. Subsequently each core was divided into 0-15 and 15-30 cm sub-cores. Walmann's Green Leaf lettuce, Goldmine carrots, and BB882 barley were planted 30 days, 121 days and 365 days respectively after spraying.

With one exception, the 15-30 cm sub-cores contained TRRs of ≤ 0.01 mg/kg eq, so only the 0-15 cm sub-cores were extracted with acetone. Lindane was the only component found to be extractable, at 28-88% of the TRR, suggesting that the rotational crops were exposed only to lindane and soil-bound (unextracted) residues. Lindane was found to be rather persistent in soil: 73% of the parent compound found 2 h after treatment was still present 240 days later. The TRR in crops did not appear to be strongly related to the TRR in soil. An approximately linear relationship between crop and soil TRR levels was observed only in mature barley grain and straw. In mature lettuce plants, radioactive residues decreased with increasing plant-back intervals, from 0.04 mg/kg eq at 30 days to 0.009 mg/kg eq at 365 days. 43% of the TRR was identified as lindane, 19% as 3 different chlorophenols, and 35% was unextracted.

In mature carrot roots the amount of radioactive residue remained constant at the different plant-back intervals at 0.4 mg/kg equivalents. Approximately 86% of the TRR was identified as lindane, 4.4% as 1,3,4,5,6-pentachlorocyclohexene, 3% was unidentified and 1.7% was unextracted.

In barley forage, 0.10-0.4 mg/kg eq radioactive residue was found at the different plant-back intervals, of which 16-26% of the TRR was lindane, about 9% was 3 different chlorophenols, 39-52% was unextracted, and 17-18% was unidentified. In barley grain, radioactivity (0.05-0.09 mg/kg eq)

was either unextracted (71-112% of the TRR) or uncharacterized (0-32% of the TRR). About half of the uncharacterized radioactivity could later be attributed to 3 different chlorophenols. In barley straw, 68-78% of the TRR (0.1-0.9 mg/kg eq) was unextracted, 11-34% was uncharacterized, 0.36-2.4% was lindane, and about 4% was 3 different chlorophenols.

At each sampling lindane degradation products, if present in soil, were too low to quantify so only lindane was available for uptake, and degradation products in crops arose from metabolism of lindane within the plants. The metabolites identified in crops from the rotational study are among those identified in the seed-treatment metabolism study on wheat, confirming that degradation of lindane taken up by roots proceeds by hydroxylation and successive losses of chlorine.

Environmental fate in water-sediment systems

Solutions of 1 mg/l uniformly-labelled [¹⁴C]lindane at pH 5, 7 and 9 at two ionic strengths were kept in the dark at 25 ± 1°C for 30 days. At pH 5 and 7 lindane was stable with a half-life of 115-173 and 282-309 days respectively, with 5% transformation after 30 days. At pH 9, lindane was unstable with a half-life of 35-36 days. After 30 days, 43-44% transformation was found with 7% 2,3,4,5,6-pentachlorocyclohexene and 4% trichlorobenzenes (1,2,4- and 1,2,3-), and 32-33% not accounted for.

In water as well as in an acetone-sensitized aqueous solution, [¹⁴C]lindane was resistant to natural sunlight. After 28 days recovery was comparable to the dark control and no degradation products were observed. Lindane was also resistant to simulated sunlight. After 15 days irradiation equivalent to 44.5 days of natural sunlight at 40° N in summer, in water at pH 7 at 25°C, recovery was ≥92% (dark control ≥91% recovery). Again no degradation products were observed.

It was concluded that lindane is resistant to hydrolysis (except at high pH) and photolysis.

Methods of analysis

Analytical methods proposed as enforcement methods, and those used in supervised residue trials, storage stability studies, processing studies and feeding studies were reported.

Two enforcement methods were reported. A Dutch multi-residue method for fruit and vegetables involves extraction by a method for non-fatty samples and GC with ion-trap detection with an LOQ of 0.03 mg/kg. The AOAC method is a multi-residue method for organochlorine and organophosphorus pesticide residues and is suitable for non-fatty foods, dairy products and whole eggs. After extraction lindane is quantified by GC with ECD or KCl-thermionic detection. The LOQ was not stated.

Method 109, a GC-MS method, was used in supervised trials, storage stability studies and processing studies on wheat and canola. The reported LOQ was 0.005 mg/kg in wheat and canola commodities.

Modified AOAC methods were used in feeding studies on poultry, cows, sheep and pigs and storage stability studies on animal commodities. Reported LOQs were 0.01 mg/kg for liver, kidney, muscle and fat, 0.001 mg/kg for milk and 0.005 mg/kg for eggs, but the validated LOQs were liver and kidney 0.05 mg/kg, muscle 0.02 or 0.03 mg/kg, milk 0.005-0.2 mg/kg, and eggs 0.1 mg/kg.

Stability of residues in stored analytical samples

The Meeting received data on the stability of residues in wheat forage, hay, straw and grain, in canola seed, meal and refined oil, and in animal tissues, eggs and milk stored frozen.

Lindane residues in wheat and canola were stable at -20°C for the time tested (wheat forage 14 months, wheat hay, wheat straw and wheat grain 18 months, canola seed 6 months, canola meal 1.5 months, refined canola oil 1.8 months).

Lindane was stable at -18°C for 9 months in animal tissues and for at least 12 months in milk and eggs.

Definition of the residue

In goat fat and muscle, the residue was mainly present as the parent compound (82-86% and 62-90% of the TRR respectively). In goat liver and kidney, the parent compound was present at 0.4-16% and 4.7-36% of the TRR respectively. Approximately 55-87% of the TRR in whole milk was associated with the milk fat where lindane was the major constituent (55%-77% of the TRR of whole milk). In laying hens lindane was the major radioactive residue in all tissues tested: fat 87%, thigh muscle 77%, liver 39%, breast muscle >100%, egg yolk >100%, egg white 67% of the TRR. In breast muscle and egg white, no radioactive residue besides lindane was identified.

Since the parent compound is the major residue in all animal commodities, and since the remaining residue is made up not of one single component but of a wide range of chlorocyclohexenes, chlorobenzenes, and chlorophenols, the Meeting agreed that the parent is a suitable marker molecule for enforcement in animal commodities and is also the compound of interest for dietary risk assessment.

The log K_{ow} of lindane is 3.2–3.7. Taking into account results from farm animal feeding studies, the Meeting concluded that lindane should be classified as fat-soluble.

Lindane is intended for use as a seed treatment on oilseeds and cereal grains. As discussed in the section on plant metabolism, after pre-planting seed treatment virtually all the radioactive residue in wheat grain (>100% of the TRR) and wheat foliage (95% of the TRR) at harvest is unextractable.

In view of the low levels of radioactive residue present at harvest (0.052 mg/kg eq in grain), the lack of an alternative marker molecule, the fact that lindane was considered to be the toxicologically significant compound, and the fact that the existing definition of the residue is lindane, the Meeting agreed that the definition of the residue for compliance with MRLs and for estimation of dietary intake should be:

lindane, for both plant and animal commodities.

The residue is fat-soluble.

Supervised residue trials

Trials were reported on wheat and canola.

Root and tuber vegetables (group 016)

There is a current CXL for carrot of 0.2 E mg/kg, which stems from 1977 and was based on a rotational crop study. The rotational crop study described above confirms that carrots can take up relatively large amounts of the parent compound. Since neither information on GAP nor supervised trials on carrots were reported, the Meeting decided to recommend withdrawal of the existing CXL for carrot.

Neither information on GAP nor supervised trials were reported for sugar beet. The Meeting decided to recommend withdrawal of the current CXLs for sugar beet and sugar beet leaves or tops, both 0.1 mg/kg.

Cereal grains (group 020)

Lindane is registered in Canada and the USA for use on barley, maize, sweet corn, oats, rye, sorghum and wheat with DS, LS, FS, and ES formulations with a single treatment of the seeds immediately before sowing. Fifteen residue trials on wheat were conducted in the USA (1997, 1998) using an application rate of 328 g ai/t. In the USA, there are 13 labels for use on wheat. On 12 of those the application rate ranges from 163 to 391 g ai/t, but on one label the application rate is 2085 g ai/t and therefore the trials cannot be considered to be at the maximum US GAP.

In Canada two labels for use on wheat are registered; the critical label specifies an application rate of 390 g ai/t, so all 15 US trials were according to maximum Canadian GAP. Residues in wheat grain were all <0.005 mg/kg.

From the rotational crop study it became clear that the behaviour of lindane in barley is comparable to that in wheat. The metabolism study with several lindane-treated seeds showed that wheat grain and foliage contained more lindane than maize grain and foliage. Therefore the Meeting decided to extrapolate the results from the supervised trials in wheat to all registered pre-planting seed treatments of lindane on cereal grains, i.e. barley, maize, sweet corn, oats, rye, and sorghum.

The Meeting estimated a maximum residue level of 0.01* mg/kg in wheat, barley, maize, sweet corn, oats, rye and sorghum, with STMRs and HRs of 0.005 mg/kg.

Oilseeds (group 023)

Lindane is registered for use on mustard in Canada. Six residue trials on canola were conducted in the USA (1998), but no relevant GAP was available for evaluation of the data.

The Meeting decided to recommend withdrawal of the current CXL for rape seed of 0.05* mg/kg.

Straw, fodder and forage of cereal grains and grasses (group 051)

The wheat trials that were evaluated for grain residues were also evaluated for residues in wheat forage, hay and straw. The results were again extrapolated to barley, maize, sweet corn, oats, rye and sorghum.

Residues in wheat forage were <0.005 (8), 0.0087, 0.0097, 0.014, 0.017, 0.021, 0.032 and 0.036 mg/kg.

The Meeting estimated a highest residue level of 0.036 mg/kg in wheat, barley, maize, sweet corn, oat, rye and sorghum forage, and an STMR of 0.005 mg/kg.

Because of matrix interferences in wheat hay up to 0.0037 mg/kg, the reported LOQ for wheat hay should be increased to 0.01 mg/kg. Taking this into account, residues in wheat hay were <0.01 (14) and 0.023 mg/kg.

The Meeting estimated a highest residue level of 0.023 mg/kg in wheat, barley, maize, sweet corn, oats, rye and sorghum hay, and an STMR of 0.01 mg/kg.

Residues in wheat straw were <0.005 (15) mg/kg.

The Meeting estimated a maximum residue level of 0.01* mg/kg in wheat, barley, maize, sweet corn, oats, rye and sorghum straw, with STMRs and HRs of 0.005 mg/kg.

Fate of residues during processing

The Meeting received information on the fate of residues in the processing of canola seeds to oil.

Canola seeds with incurred residues were processed on a small scale into meal, refined oil and edible oil. No residues could be detected in seed, meal or edible oil, but a residue of 0.013 mg/kg was found in the refined oil. Because no residues were found in the seed, processing and transfer factors could not be calculated.

Farm animal dietary burdens

The Meeting estimated the dietary burden of lindane residues in farm animals from the diets listed in Appendix IX of the FAO Manual (FAO, 2002). One feed commodity only from each Codex Commodity Group is used. Calculation from the MRLs or HR values provides the concentrations in feed suitable for estimating MRLs for animal commodities, while calculation from the STMRs for feed is suitable for estimating STMRs for animal commodities. In the case of processed commodities, the STMR-Ps are used for both calculations.

Maximum farm animal dietary burden

Commodity	group	Residue mg/kg	basis	% dry matter	Residue on dry wt mg/kg	Chosen diets, %			Residue contribution, mg/kg		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
Wheat grain	GC	0.01	MRL	89	0.011	50		80	0.006		0.009
Wheat forage	AF	0.036	HR	25	0.144	25	60		0.036	0.086	
Wheat hay	AS	0.023	HR	88	0.026	25	40		0.006	0.01	
						Maximum dietary burden			0.05	0.1	0.009

Mean farm animal dietary burden

Commodity	group	Residue mg/kg	basis	% dry matter	Residue on dry wt mg/kg	Chosen diets, %			Residue contribution, mg/kg		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	
Wheat grain	GC	0.005	STMR	89	0.006	50	40	80	0.003	0.002	0.005
Wheat forage	AF	0.005	STMR	25	0.02	25	60		0.005	0.012	
Wheat hay	AS	0.005	STMR	88	0.006	25			0.002		
						Mean dietary burden			0.011	0.014	0.005

Farm animal feeding studies

Animal feeding studies were reported for dairy cattle, sheep, pigs and chickens. In all the studies, only the parent compound was determined.

Three milking Holstein cows were dosed orally with lindane at levels equivalent to 20, 60 or 200 ppm in the feed. Dosing took place for 28 days after the morning milking (by gelatin capsule using a balling gun). Milk samples were taken on days 1, 3, 7, 14, 21, 25 and 28. Animals were slaughtered 20 h after the last dosing. Residues in fat were 12, 20 and 158 mg/kg for the 20, 60 and 200 ppm cows respectively. Residues in muscle were 0.97, 1.8 and 8.8 mg/kg, in liver 0.10, 0.19, and 0.72 mg/kg and in kidney 0.34, 1.1 and 4.9 mg/kg. Residues in milk were 0.37, 1.0 and 6.0 mg/kg (mean for day 7-28), but results above 0.6 mg/kg lindane in milk are considered invalid because of bad procedural recoveries (48%-142%).

Hampshire cross-bred feeder lambs (one male and one female per group) were dosed orally with lindane at levels equivalent to 17.5, 52.5 and 175 ppm in the feed for 28 days as before and slaughtered 10-12 h after the last dosing. No difference between residues in male and female lambs was observed, so results are given as the mean for each group. Results below 0.2 mg/kg are considered invalid because of matrix interferences in control samples. Residues in fat were 19, 43 and 198 mg/kg for the 17.5, 52.5 and 175 ppm lambs respectively. Residues in muscle were 0.73, 1.6 and 7.7 mg/kg, in liver 0.02, 0.02, and 0.12 mg/kg and in kidney 0.74, 1.8 and 4.8 mg/kg.

Yorkshire/Landrace cross-bred pigs (one male and one female per group) were dosed orally with lindane at levels equivalent to 7.0, 21 and 70 ppm in the feed for 28 days as before and slaughtered 6-10 hrs after the last dosing. No difference between residues in males and females was observed, so results are given as the mean for each group. Residues in fat were 1.7, 5.6 and 16 mg/kg, in muscle 0.086, 0.24 and 0.78 mg/kg, in liver <0.02, <0.02, and <0.02 mg/kg and in kidney 0.049, 0.21 and 0.39 mg/kg.

Leghorn laying hens (four birds per group) were dosed orally by gelatin capsule with lindane at levels equivalent to 1.5, 4.5 and 15 ppm in the feed for 28 or 60 days after the morning egg collection (two groups of 4 hens at each level for each period). Eggs from days 0, 1, 3, 7, 14, 21, 25, 28, 35, 42, 49, 56 and 60 were analysed. Birds were killed 20 h after the last dosing. Samples were composited by group. Residues were similar in the four groups at each dose level. Mean residues in fat were 2.5, 8.3 and 28 mg/kg for the 1.5, 4.5 and 15 ppm hens respectively. Mean residues in thigh muscle were 0.18, 0.44 and 1.4 mg/kg, in breast muscle 0.03, 0.09 and 0.35 mg/kg, in liver 0.11, 0.38 and 0.84 mg/kg, and in kidney 0.18, 0.49 and 2.0 mg/kg. The highest individual residues at 1.5, 4.5 and 15 ppm were 2.7 mg/kg, 9.7 mg/kg and 29 mg/kg in fat, 0.19 mg/kg, 0.60 mg/kg and 1.6 mg/kg in thigh muscle, 0.04 mg/kg, 0.12 mg/kg and 0.40 mg/kg in breast muscle, 0.21 mg/kg, 0.71 mg/kg and 2.5 mg/kg in kidney, and 0.14 mg/kg, 0.55 mg/kg and 0.95 mg/kg in liver. The mean residues in eggs were 0.21, 0.59 and 2.2 mg/kg, and the highest residues in individual group composites were 0.35, 0.68 and 2.6 mg/kg at the three dose levels.

Residues in animal commodities

The estimated maximum dietary burdens for beef and dairy cattle were 0.05 and 0.1 mg/kg feed respectively, so the dairy cattle burden represents the worst case. In the feeding study with dairy cows, the lowest dosing level was 20 mg ai/kg feed. The resulting residues in tissues and milk were calculated by applying the transfer factors at this level to the dietary burdens. (Transfer factor = residue level in sample ÷ feeding level). The dietary burden for poultry was 0.009 ppm, which was lower than the lowest feeding level in the feeding study (1.5 ppm) so, the resulting residues in eggs and poultry tissues were calculated by applying the appropriate transfer factors at this feeding level. Residues in pork commodities were similarly calculated from the lowest level fed in the pig feeding study (7 ppm).

The highest individual residues in tissues and eggs from the lowest levels fed in the feeding studies were used in conjunction with the maximum dietary burdens to calculate the highest likely residue levels, and in conjunction with the STMR dietary burdens, to estimate the STMRs, in commodities derived from cattle, poultry and pigs.

Calculation of MRLs and STMRs for animal tissues

	Feeding level (ppm)	Lindane residues, mg/kg ^{1/}												
		<i>(Extrapolated)</i>	Milk		Muscle		Fat		Liver		Kidney		Eggs	
			actual ²	mean	high ⁴	mean ³	high ⁴	mean	high	mean	high	mean	high	mean
MRL dairy	0.1	<i>(0.002)</i>	<i>(0.005)</i>		<i>(0.06)</i>		<i>(0.0005)</i>		<i>(0.002)</i>					
	20	0.37	0.97		12		0.1		0.34					
MRL poultry	0.009		<i>(0.001)</i>		<i>(0.016)</i>		<i>(0.0008)</i>		<i>(0.001)</i>		<i>(0.002)</i>			
	1.5		0.19		2.7		0.14		0.21		0.35			
STMR dairy	0.014	<i>(0.0003)</i>	<i>(0.0007)</i>		<i>(0.008)</i>		<i>(0.00007)</i>		<i>(0.0002)</i>					
	20	0.37	0.97		12		0.1		0.34					
STMR poultry	0.005			<i>(0.0006)</i>		<i>(0.008)</i>		<i>(0.0004)</i>		<i>(0.0006)</i>		<i>(0.0007)</i>		
	1.5			0.18		2.5		0.11		0.18		0.21		

¹Values in italics are the estimated dietary burdens. Values in normal font are the lowest feeding levels in feeding studies.

²Residue values in parentheses in italics are extrapolated to the dietary burdens from the lowest feeding levels used in the feeding studies and the residues found in those studies.

³Mean (in roman) is the mean tissue or milk residue in the relevant feeding group.

⁴High (in roman) is the highest individual animal tissue residue in the relevant feeding group.

The Meeting estimated maximum residue levels of 0.1 mg/kg (fat) for meat from mammals other than marine mammals, 0.01* mg/kg for edible offal and 0.01* mg/kg for milks, and STMRs of 0.0007 mg/kg and 0.008 mg/kg in muscle and fat from mammals other than marine mammals respectively, 0.0002 mg/kg for edible offal and 0.0003 for milks, and HRs of 0.005 mg/kg and 0.06 mg/kg in muscle and fat from mammals other than marine mammals respectively, and 0.002 mg/kg for edible offal.

CXLs exist for eggs (0.1 mg/kg E) and poultry meat (0.7 mg/kg (fat) E). These recommendations stem from 1968/1969 and 1973, when maximum residue levels for animal commodities were defined as EMRLs. Currently, this designation is reserved for pesticide residues arising from environmental sources other than the use directly or indirectly on the commodity.

The Meeting recommended MRLs of 0.05 mg/kg for lindane in poultry meat (fat), 0.01* mg/kg in edible offal of poultry and 0.01* mg/kg in eggs to replace the current CXLs of 0.1 mg/kg E for eggs and 0.7 mg/kg (fat) E for poultry meat, and estimated STMRs of 0.0006 mg/kg and 0.008 mg/kg for poultry muscle and fat, 0.0004 mg/kg in edible offal of poultry and 0.0007 mg/kg in eggs, and HRs of 0.001 mg/kg and 0.016 mg/kg in poultry muscle and fat, 0.001 mg/kg in edible offal of poultry and 0.002 mg/kg in eggs.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes of lindane, based on the STMRs estimated for 13 commodities, for the five GEMS/Food regional diets were in the range of 0 to 1% of the maximum ADI of 0.005 mg/kg bw (Annex 3). The Meeting concluded that the long-term intake of residues of

lindane resulting from its 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 lindane was calculated for 13 food commodities for which maximum residue levels were estimated and for which consumption data were available. The results are shown in Annex 4.

The IESTI represented 0% of the acute RfD for the general population and 0% of the acute RfD for children. The Meeting concluded that the short-term intake of residues of lindane resulting from its uses that have been considered by the JMPR is unlikely to present a public health concern.

4.12 MALATHION (049)

TOXICOLOGY

Malathion was evaluated by JMPR in 1963, 1965 and 1966. An ADI of 0–0.02 mg/kg bw was assigned at each Meeting. Malathion was re-evaluated by the JMPR in 1997, when an ADI of 0–0.3 mg/kg bw was assigned. Malathion was re-evaluated at the present Meeting in order to establish an acute reference dose (RfD), at the request of the Codex Committee on Pesticide Residues. The Meeting reviewed a study in humans and some studies of toxicity in animals and studies of genotoxicity which were produced since the last evaluation by the JMPR. The FAO and WHO are in the process of revising the specifications for malathion technical material.

As a supplement to a study of developmental neurotoxicity, a study was undertaken on the effects of orally administered malathion on the activity of cholinesterase. In this study, single or repeated doses of malathion of up to 450 mg/kg bw were administered orally to pregnant rats, pre-weaning offspring at various stages of development, and young adults. The NOAEL for the study was 50 mg/kg bw. Inhibition of brain cholinesterase activity was observed in offspring of untreated females who were given a single direct dose of 150 mg/kg bw on post-natal day 11.

A study of developmental toxicity in rabbits was evaluated at the 1997 JMPR. This study was re-evaluated in 2002. Malathion was administered by gavage at doses of 25, 50 and 100 mg/kg bw per day to groups of mated female rabbits from day 6 to day 18 of gestation. The NOAEL for maternal toxicity was 25 mg/kg bw per day, on the basis of decreased maternal body-weight gain during dosing. There was no difference in fertility, number of corpora lutea, implantation sites, litter size or fetal weight and length. The NOAEL was 100 mg/kg bw per day for fetal toxicity, on the basis of the absence of developmental toxicity at any dose.

A study of developmental neurotoxicity in which malathion was administered orally to rats was undertaken. Malathion was administered to groups of mated females from day 6 of gestation to post-natal day 10 and to their offspring from post-natal day 11 to post-natal day 21 at doses of 5, 50 or 150 mg/kg bw per day. Behavioural assessments were performed on both dams and pups, in the latter at intervals up to postnatal day 60. The NOAEL for the study was 50 mg/kg bw per day for developmental neurotoxicity (slower surface righting reflex at the highest dose of 150 mg/kg bw per day on post-natal day 11, but not subsequently) and 150 mg/kg bw per day for maternal toxicity. It was considered that the effects observed were likely to have been caused by current treatment rather than any permanent developmental neurotoxic effect because neurotoxicity was not observed in the offspring at later time points in the study.

The results of tests for chromosomal aberrations in human lymphocytes and gene mutation in mouse lymphoma cells were positive at cytotoxic concentrations. A test for unscheduled DNA synthesis *in vivo* in male rats gave negative results. This is consistent with the conclusions of the 1997

JMPR, which recorded that although the results of some tests in vitro on malathion were positive, malathion was not genotoxic in vivo.

An acceptable¹ randomized double-blind placebo-controlled ascending single oral dose study was carried out in healthy men and women aged 18–50 years, using malathion in gelatine capsules. Doses of malathion used were 0.5, 1.5, 5, 10 or 15 mg/kg bw. No test-material-related clinical changes were seen, nor were electrocardiograms (ECGs), haematology and clinical chemistry parameters affected by treatment with malathion. No significant changes in plasma or erythrocyte cholinesterase activity were observed when compared to pre-dosing activity or placebo controls at any dose. As no test-material-related effects were observed during the study, the NOAEL was considered to be 15 mg/kg bw.

After considering the new data made available to the Meeting and also the previous monograph, the Meeting established an acute RfD of 2 mg/kg bw on the basis of the study in humans and a safety factor of 10. It should be noted that this acute RfD is likely to be conservative as erythrocyte cholinesterase was more sensitive to inhibition by malathion than brain cholinesterase in the studies available to the Meeting. The Meeting considered that the use of data from studies in which pre-weaning pups received bolus doses of pesticides by direct dosing, particularly when they were also receiving the pesticide in unknown amounts from the dams via their milk, was inappropriate for the establishment of an acute RfD.

An addendum to the toxicological monograph was prepared.

Estimate of acute RfD

2 mg/kg bw

Further studies that would provide information useful for continued evaluation of the compound

Further observations in humans

4.13 METHAMIDOPHOS (100)

RESIDUE AND ANALYTICAL ASPECTS

Methamidophos was evaluated initially in 1976 for residues and toxicology and the latest evaluation for residues was in 1997. It was identified as a priority compound under the Periodic Review Programme of the 29th Session of the CCPR for review by the 2002 JMPR (ALINORM 97/24A). At the 31st Session of the CCPR, the Committee noted that an acute RfD would be established by the 2000 JMPR, but this was finally established only at the 2002 Meeting. The present Meeting received information on methamidophos 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. Some information on GAP, national MRLs and residue trials was reported by the governments of Australia, Germany and The Netherlands.

The 2002 JMPR established an ADI and acute RfD for methamidophos of 0-0.004 mg/kg bw and 0.01 mg/kg bw respectively.

¹ Annex 5, reference 83, page 5

Methamidophos is a broad-spectrum organophosphorus insecticide with uses on many crops. It is also formed as a metabolite of the insecticide acephate.

The following abbreviations are used for the metabolites discussed below.

DMPT = *O,S*-dimethyl *O*-hydrogen phosphorothioate

SMPAA = *O,S*-methyl *O*-hydrogen phosphoramidothioate

Animal metabolism

The Meeting received reports of studies of methamidophos metabolism in lactating goats and laying hens.

Methamidophos is rapidly metabolized and was not identified as a component of the residue in ruminant (goat) kidney, liver, muscle or fat and only at low levels in milk. In laying hens low levels of methamidophos were detected in liver and eggs.

In three lactating goat metabolism studies with [*S*-methyl-¹⁴C]methamidophos daily doses were administered in one, two or three parts and the interval between the last dose and slaughter ranged from 3 h to 11 days. Generally, methamidophos accounted for <3% of the ¹⁴C in milk with the majority of radioactivity incorporated into lactose, proteins/amino acids and triglycerides. In tissues, most of the ¹⁴C was incorporated into natural products: proteins, and amino acids in kidney, liver and muscle and triglycerides in fat. Methamidophos was not detected in any tissues and only low levels of the metabolites DMPT and SMPAA were detected in kidney but not in other tissues or milk.

In laying hens administered [*S*-methyl-¹⁴C]methamidophos, the parent compound was identified as a minor component of the ¹⁴C residues in liver (<1%) and represented <7% of the ¹⁴C residue in egg white and yolk. Natural products (lipids, proteins and amino acids) accounted for most of the ¹⁴C with only trace amounts of the metabolites SMPAA and DMPT.

Plant metabolism

The Meeting received reports of metabolism studies of methamidophos in tissue cultures of sweet potatoes and tobacco, glasshouse-grown bean, cabbage, lettuce and tomato plants and outdoor-grown lettuce, potato and tobacco plants.

Radioactivity in glasshouse-grown cabbage and tomato plants was mostly associated with natural products, mainly lipids, pigments and amino acids, although trace amounts of the metabolite DMPT were detected. Most of the residue on exposed foliage of tomato and lettuce plants was methamidophos. Methamidophos is systemic.

Comprehensive studies of the nature of the residue followed the foliar application of [*S*-methyl-¹⁴C]methamidophos to lettuce and potato plants. Most of the ¹⁴C residue in lettuce leaves harvested 21 days after application was methamidophos (about 66%). A minor metabolite, a conjugate of *S*-methyl phosphorothiolate, was detected at <2% of the ¹⁴C with the remainder associated with natural products, principally sugars and starch.

Radioactivity in potato tubers harvested 14 days after the last of four foliar sprays with [*S*-methyl-¹⁴C]methamidophos was essentially accounted for by incorporation into starch and other natural products; methamidophos represented only 0.2% of the total radioactive residue.

In a comparison of the decline of radioactive and methamidophos residues in field- and glasshouse-grown tobacco plants, methamidophos was also the major component of the ¹⁴C residue in glasshouse tobacco leaves. The decline in methamidophos residues was more rapid in the field (half-life 5 days) than in the glasshouse (half-life 15 days).

In both animals and plants, methamidophos undergoes hydrolysis of the ester and thioester moieties, liberating small carbon fragments to the general metabolic pool for incorporation into natural products. The main identified residue component is methamidophos *per se*.

Environmental fate in soil

Information was provided on the soil adsorption of methamidophos and its fate during soil photolysis, aerobic and anaerobic soil degradation, the column leaching of aged residues and field dissipation.

Methamidophos degradation on soil surfaces by photolysis occurred with a half-life of about 60 h. The major product was SMPAA with small amounts of DMPT also observed.

The half-lives of methamidophos in soil under aerobic test conditions were estimated to be ≤ 6 days in the laboratory and ≤ 3 days in the field. Degradation occurred by hydrolysis of ester and amino groups to form SMPAA and DMPT. The principal mechanism of degradation appears to be microbial metabolism.

Methamidophos and DMPT are only very weakly adsorbed by soils and can be classified as mobile. The rate of degradation both in the laboratory and in the field is such that residues are not expected to persist at detectable levels for more than a few days. Methamidophos is not persistent.

Environmental fate in water-sediment systems

The Meeting received information on the sterile aqueous hydrolysis of methamidophos and its fate in water-sediment systems.

Methamidophos is stable to hydrolysis at low pH but is readily degraded at neutral and high pH (half-life 27 and 3.2 days at pH 7 and 9 respectively).

The half-life for the degradation of methamidophos in the water-sediment systems was estimated to be 4-6 days.

In summary, chemical hydrolysis is only expected to occur in waters having high pH values. Indirect photochemical transformation of methamidophos is expected to occur but is considered to be only a minor route of degradation. Biodegradation in the aquatic environments is expected to be rapid, so that methamidophos is not expected to persist in the environment.

Analytical methods

Samples in field trials were analysed for methamidophos by solvent extraction (ethyl acetate, acetone/water and in the case of oily crops and animal commodities acetonitrile/hexane), clean-up by solvent partition and/or silica gel or gel permeation chromatography, and determination by gas chromatography with a thermionic detector. A typical LOQ was 0.01 mg/kg.

Stability of pesticide residues in stored analytical samples

The Meeting received information on the stability of methamidophos in various commodities under freezer storage (-20°C). Residues were stable in or on the following commodities (storage period, in parentheses): broccoli (9 months); lettuce (2 months); cabbage (8 months); cauliflower (6 months); Brussels sprouts (5 months); celery, peppers, peanut forage (26 months); sorghum grain (6 months); sorghum forage (10 months); rape seed, potato tubers, granules and dry peel, tomato fruit, purée and dry pomace (24 months); bovine milk, meat and fat, eggs (3 months) and poultry liver and heart/gizzard (2 months).

Methamidophos residues were not stable in cattle liver, with only 26% of the residues remaining after 3 months frozen storage.

Definition of the residue

Methamidophos is the principal residue in crops. Significant residues of methamidophos and metabolites were not observed in animal commodities. The Meeting agreed that the residue should be defined as methamidophos.

The log P_{ow} of -0.8 and the animal metabolism and feeding studies suggest that methamidophos should not be described as fat-soluble.

Definition of methamidophos residue (for compliance with MRLs and for estimation of dietary intake):

methamidophos.

The definition applies to plant and animal commodities. Methamidophos residues may arise from the use of methamidophos and/or acephate.

Supervised trials

Supervised trials were reported for the use of methamidophos on broccoli, cabbage, cauliflower, cotton seed, fodder beet, maize, nectarines, peaches, peppers (including chili peppers), potatoes, soya beans, sugar beet and tomatoes.

Trials data or relevant GAP were not reported for the following crops with current CXLs: alfalfa forage, green (2 mg/kg), head lettuce, (1 mg/kg), and tree tomato (0.01 mg/kg). The Meeting agreed to recommend withdrawal of the CXLs for these commodities.

In cases where maximum residue levels have been estimated for acephate, it is also necessary to ensure that the resulting methamidophos residues are covered by a maximum residue level estimate for methamidophos. Residues of methamidophos arising from the use of acephate and derived from the same trials as were used to estimate the maximum residue, STMR and HR levels for acephate are reported below.

Citrus fruits

Methamidophos residues arising from the use of acephate on mandarins were 0.02, 0.03, 0.04, 0.05, 0.06, 0.08, 0.08, 0.09, 0.09, 0.13, 0.14, 0.15, 0.25 and 0.26 mg/kg. The Meeting estimated a maximum residue level, STMR and HR for methamidophos in mandarins of 0.5, 0.085 and 0.26 mg/kg, all based on whole fruit as insufficient information was available to estimate residues in the edible portion.

Pome fruits

Methamidophos residues in apples and pears from the use of acephate (n=13) were <0.1, <0.1, 0.03, 0.03, 0.04, 0.04, 0.06, 0.06, 0.13, 0.14, 0.16, 0.22 and 0.28 mg/kg. The Meeting estimated a maximum residue level, STMR and HR for methamidophos in pome fruits of 0.5, 0.06 and 0.28 mg/kg.

Stone fruits

Methamidophos trials on nectarines were conducted in Italy (GAP for peaches 0.03-0.06 kg ai/hl, maximum 2 sprays, PHI 35 days) and Portugal (GAP for peaches 0.6 kg ai/ha, 0.06 kg ai/hl, maximum 1 spray, PHI 35 days). No trials matched GAP as either the application rates were too low or samples were not collected after an appropriate interval.

Data reported from supervised trials on peaches in France (GAP 0.05 kg ai/hl, PHI 14-21 days), Italy, Portugal and Spain (GAP 0.05-0.08 kg ai/hl, PHI petal fall + 10 days). The trials in France and Spain did not match GAP in these countries. The Meeting decided to evaluate the trials in Spain according to the GAP of Italy and Portugal.

Four trials in Italy approximated Italian GAP with methamidophos residues of 0.04, 0.06, 0.11 and 0.13 mg/kg, all on a pulp basis (calculated whole fruit residues 0.04, 0.05, 0.11 and 0.12 mg/kg) 28 days after application at 0.05-0.06 kg ai/hl. A further six trials in Spain matched GAP in Italy and/or Portugal and showed residues of 0.01, 0.02, 0.03, 0.04, 0.09 and 0.15 mg/kg.

The residues in peaches from trials with methamidophos according to GAP were 0.01, 0.02, 0.03, 0.04, 0.04, 0.05, 0.09, 0.11, 0.12 and 0.15 mg/kg. Residues of methamidophos in peaches arising from the use of acephate according to Greek GAP were 0.09, 0.1, 0.16, 0.22, 0.28 and 0.35 mg/kg, and since this use gave higher residues than the use of methamidophos, the Meeting used the acephate data to estimate a maximum residue level, STMR and HR.

The Meeting also considered that the residues of methamidophos on peaches and nectarines treated at the same rate would be similar and noted that GAP for the use of acephate in Greece was for stone fruit which includes both peaches and nectarines. The Meeting estimated a maximum residue level, STMR and HR for peaches and nectarines of 0.5, 0.19 and 0.35 mg/kg and recommended withdrawal of the draft MRL of 1 mg/kg for peach.

Brassica vegetables

Trials reported from Belgium (no GAP), Canada (GAP 0.53-1.1 kg ai/ha, PHI 7 days for cauliflower, 14 days for broccoli), Germany (GAP 0.36 kg ai/ha, PHI 21 days), and the UK (no GAP) on broccoli and cauliflower.

No trials on broccoli matched GAP. Residues in eight trials on cauliflower from Germany approximating GAP in that country were <0.01 (5), 0.01 (2) and 0.04 mg/kg while the residue of methamidophos in one trial in Canada approximating Canadian GAP was 0.08 mg/kg.

The residues in trials according to GAP in Canada and Germany appeared to be from different populations and could not be combined for estimating a maximum residue level. Residues in cauliflower complying with GAP in Germany in rank order, median underlined, were <0.01 (5), 0.01 (2) and 0.04 mg/kg.

Residues of methamidophos in broccoli and cauliflower from the use of acephate (n=14) were <0.01(5), 0.01, 0.01, 0.03, 0.03, 0.08, 0.09, 0.1, 0.2 and 0.33 mg/kg, giving a higher maximum residue level than the trials with methamidophos. The Meeting used the acephate data to estimate a maximum residue level, STMR and HR for methamidophos in flowerhead brassicas of 0.5 mg/kg, 0.02 mg/kg and 0.33 mg/kg respectively. The estimated maximum residue level of 0.5 mg/kg is recommended to replace the existing CXL of 0.5 mg/kg for cauliflower.

Trials on head cabbage were reported from Canada (GAP 0.53-1.1 kg ai/ha, PHI 7 days) and Germany (GAP 0.36 kg ai/ha, PHI 14 days).

Residues in head cabbage in three trials in Canada approximating GAP in that country were 0.04, 0.60 and 0.62 mg/kg. Residues in eight trials on head cabbage in Germany approximating German GAP were <0.01 (2), 0.01, 0.03, 0.04, 0.07, 0.09 and 0.20 mg/kg.

The residues evaluated according to the GAP of Canada and Germany appeared to be from the same population and could be combined to estimate a maximum residue level. The residues in rank order, median underlined (n=11) were <0.01 (2), 0.01, 0.03, 0.04, 0.04, 0.07, 0.09, 0.20, 0.60 and 0.62 mg/kg.

The Meeting estimated a maximum residue level, STMR and HR for methamidophos in head cabbages of 1 mg/kg, 0.04 mg/kg and 0.62 mg/kg respectively. The maximum residue level of 1 mg/kg is recommended to replace the existing CXL of 0.5 mg/kg.

Tomatoes. Trials on tomatoes with methamidophos were reported from Brazil (no GAP), France (no GAP), Germany (no GAP), Greece (GAP 0.6-0.9 kg ai/ha, PHI 21 days), Italy (no GAP), Mexico (GAP 0.6-0.9 kg ai/ha, PHI 7 days), Spain (no GAP), Turkey (no GAP) and the USA (GAP 0.84-1.1 kg ai/ha, maximum 5.6 kg ai/ha/season, PHI 7 days).

Methamidophos residues in 18 trials in the USA matching GAP \pm 30% in rank order, median underlined, were 0.05, 0.08, 0.12, 0.14, 0.14, 0.16, 0.22, 0.24, 0.26, 0.31, 0.36, 0.36, 0.42, 0.56, 0.86, 1.3, 1.4 and 1.5 mg/kg.

The Meeting estimated a maximum residue level, STMR and HR for methamidophos in tomatoes of 2 mg/kg, 0.285 mg/kg and 1.5 mg/kg respectively. The maximum residue level is recommended to replace the draft MRL of 1 mg/kg for tomato.

Peppers. In Mexico methamidophos is registered for use on peppers at 0.6-0.9 kg ai/ha with harvest permitted 14 days after the last application. In five trials in the USA matching those conditions methamidophos residues on sweet peppers were 0.04, 0.07, 0.22, 0.38 and 0.95 mg/kg.

Methamidophos residues in peppers from the use of acephate (n=9) were 0.05, 0.22, 0.24, 0.25, 0.25, 0.29, 0.34, 0.35 and 1.6 mg/kg. As the acephate trial showed higher residues the Meeting used the acephate data to estimate a maximum residue level, STMR and HR for methamidophos in peppers of 2, 0.25 and 1.6 mg/kg. The maximum residue level is recommended to replace the existing CXLs for chili peppers of 2 mg/kg and sweet peppers of 1 mg/kg.

Common beans. Residues of methamidophos in beans, except broad bean and soya bean, from the use of acephate in rank order, median underlined (n=8) were 0.01, 0.04, 0.15, 0.15, 0.19, 0.34, 0.45 and 0.54 mg/kg

The Meeting estimated a maximum residue level, STMR and HR for methamidophos in beans, except broad bean and soya bean, of 1, 0.17 and 0.54 mg/kg respectively.

Soya beans. Field trials were reported from Brazil (GAP 0.15-0.5 kg ai/ha, PHI 23 days). Residues in four trials approximating GAP were <0.01, <0.01, <0.04 and <0.04 mg/kg.

The Meeting decided that four trials were not sufficient to recommend a maximum residue level for such an important crop. However, the Meeting noted that in an additional four trials conducted at twice the maximum application rate, residues were all below the LOQ (<0.01, <0.01, <0.04, <0.04 mg/kg). Those trials were considered as support for the trials complying with GAP.

Residues of methamidophos in soya beans from the use of acephate in rank order, median underlined (n=7) were <0.01, <0.01, <0.01, <0.01, 0.02, 0.06 and 0.06 mg/kg. The Meeting noted that the residues from the use of acephate would lead to the higher estimates for a maximum residue level, STMR and HR for methamidophos in soya beans and estimated values of 0.1, 0.01 and 0.06 mg/kg respectively. The maximum residue level is recommended to replace the existing CXL of 0.05 mg/kg for soya bean (dry).

Potatoes. Field trials were reported from Canada (GAP 0.9-1.1 kg ai/ha, PHI 14 days), France (no GAP), Germany (GAP 0.5-0.6 kg ai/ha, PHI 14 days), Greece (GAP 0.045-0.09 kg ai/hl, PHI 21 days), Italy (GAP 0.57 kg ai/ha, PHI 21 days), Spain (no GAP) and the USA (GAP 0.84-1.1 kg ai/ha, maximum 4.5 kg ai/ha, PHI 14 days). The Meeting decided to evaluate the trials conducted in Spain against the GAP of Italy.

Twenty-nine trials in Germany matched GAP in that country with residues in potatoes of <0.01 (25), 0.01, 0.01, 0.02 and 0.02 mg/kg. In two trials in Greece according to GAP, residues in potatoes were <0.01 mg/kg at 21 and 22 days after application, and were also <0.01 mg/kg in two trials in Italy according to GAP, and in four trials in Spain approximating the GAP of Greece.

In 3 trials in Canada matching GAP methamidophos residues in potatoes were all <0.01 mg/kg. In 23 trials in the USA matching GAP from that country the residues were <0.01 (5) and <0.05 (18) mg/kg.

The Meeting considered that to estimate a maximum residue level the trials could be considered to come from the same population. Residues in rank order, median underlined, were <0.01 (41), 0.01 (2), 0.02 (2) and <0.05 (18) mg/kg.

The Meeting estimated a maximum residue level, STMR and HR for methamidophos in potatoes of 0.05, 0.01 and 0.02 mg/kg respectively. The estimated maximum residue level of 0.05 mg/kg confirms the existing CXL.

Sugar beet. Field trials on sugar and fodder beet were reported from France (no GAP), Germany (GAP 0.36-0.48 kg ai/ha, PHI 28 days), Greece (no GAP), Italy (GAP 0.4-0.57 kg ai/ha, PHI 21 days) and Spain (no GAP). The Meeting evaluated the trials in France against the GAP of Germany.

Two trials in France and three in Germany matched GAP in Germany with residues in sugar beet roots (only 4 results at GAP PHI) of <0.01 (3) and 0.01 mg/kg, and in tops of 0.9, 1.4, 1.5, 2.3 and 6.1 mg/kg. In six trials in Germany according to GAP, residues in fodder beet were all <0.01 mg/kg at 28 days after application and in tops 0.49, 0.54, 2.1, 2.8, 2.9 and 3.1 mg/kg. The Meeting agreed to combine the trials results for sugar and fodder beet to give a combined data set of <0.01 (9) and 0.01 mg/kg and estimated a maximum residue level, STMR and HR for methamidophos in sugar and fodder beet of 0.02, 0.01 and 0.01 mg/kg respectively. The maximum residue level of 0.02 mg/kg for sugar beet is recommended to replace the existing CXL of 0.05 mg/kg.

Residues in beet leaves or tops on a fresh weight basis from the combined trials approximating GAP and arranged in rank order, median underlined, were 0.49, 0.54, 0.9, 1.4, 1.5, 2.1, 2.3, 2.8, 2.9, 3.1 and 6.1 mg/kg. Allowing for an average dry weight of 23%, the Meeting estimated a maximum residue level, an STMR and HR for methamidophos in sugar and fodder beet leaves or tops of 30, 9.1 and 26.5 mg/kg respectively on a dry weight basis. The estimate of a maximum residue level of 30 mg/kg for sugar beet leaves or tops is recommended to replace the existing CXL of 1 mg/kg.

Globe artichokes. Methamidophos residues in globe artichokes from the use of acephate (n=4) were 0.02, 0.02, 0.04 and 0.08 mg/kg. The Meeting estimated a maximum residue level, STMR and HR for methamidophos in globe artichokes of 0.2, 0.03 and 0.08 mg/kg.

Maize. Field trials were reported from Germany (4 trials: no GAP), Greece (4 trials: GAP 0.6-0.8 kg ai/ha, PHI 21 days) and Spain (4 trials: GAP 0.05-0.08 kg ai/hl, PHI 35 days).

A single trial in Spain approximated GAP \pm 25% for that country with residues of <0.01 mg/kg in both the cob and grain. The Meeting agreed that the available data were insufficient to estimate a maximum residue level.

Cotton seed. Trials on cotton in Brazil (GAP 0.21-1.2 kg ai/ha, PHI 21 days), India (no GAP) and the USA (GAP 0.11-1.12 kg ai/ha, PHI 50 days) were reported to the Meeting.

In one trial in Brazil, with 21 days PHI methamidophos residues in cotton seed were below the LOQ (0.01 mg/kg).

In 15 US trials matching the GAP of the USA residues in fuzzy seed in rank order, median underlined, were ≤0.01 (9), 0.01, 0.05, 0.06, 0.06, 0.09 and 0.16 mg/kg.

The Meeting decided that the Brazilian trial could be combined with the USA trials to estimate a maximum residue level, HR and STMR. Residues in cotton seed in rank order, median underlined, were ≤0.01 (11), 0.01, 0.05, 0.06, 0.06, 0.09 and 0.16 mg/kg.

Residues in cotton gin trash were 0.1, 0.2, 0.2, 0.35, 0.69, 0.85, 0.9, 1.5, 4.3 and 7.7 mg/kg.

The Meeting estimated a maximum residue level, STMR and HR for methamidophos in cotton seed of 0.2, 0.01 and 0.16 mg/kg respectively. The maximum residue level of 0.2 mg/kg for cotton seed is recommended to replace the existing CXL of 0.1 mg/kg.

Processing

Processing studies with methamidophos on apples, peaches, tomatoes, potatoes, soya beans, sugar beet and cotton seed were reported, together with a range of studies on the effects of washing, cooking or dehydration on residues in brassica vegetables, tomatoes, peppers and potatoes.

Two studies on peaches investigated residues in home-prepared jam as well as simulated commercially produced preserve and juice. With initial residue levels of 0.1 mg/kg, processing factors were estimated for washed peaches (0.75), jam (0.62), juice (0.33) and preserve (0.52).

The transfer of residues from field-treated raw tomatoes to juice, purée, paste and pomace, as well as the effect of canning on incurred residues, was investigated using simulated commercial practices. The Meeting estimated average processing factors for processed tomato commodities of: 0.74 for juice, 0.84 for purée, 0.8 for wet pomace and 3.8 for dry pomace.

The Meeting derived processing factors of 13.5 for soya bean hulls, 1.6 for soya bean meal and 0.75 for soya bean flakes, based on a processing study in which soya beans treated with methamidophos in a field trial in the USA, containing initial residues of 0.08 mg/kg methamidophos, were processed using procedures that simulated commercial practice. No residues were detectable in any of the oil fractions or in the soapstock.

The Meeting estimated a maximum residue level, HR and STMR for methamidophos in soya beans to accommodate methamidophos residues arising from the use of acephate. As some acephate may be converted to methamidophos on processing, the relevant processing factors for the estimation of residues in crude soya bean oil (<0.5) and animal feed commodities (2.0 for soya bean meal and 4.5 for soya bean hulls) were based on the acephate processing study.

One processing study with sugar beet was reported in which sugar beet roots from a field trial in the USA, containing 0.05 mg/kg methamidophos, were processed into juice, pulp, molasses and sugar. The Meeting noted that no residues were detectable in any of the fractions analysed.

Cotton seed from a residue trial in the USA in which fivefold rates of methamidophos were applied, was processed in a way that simulated commercial practice. Initial residues in the cotton seed were 0.74 mg/kg and no residues were detectable in the crude or refined oil, or the soapstock. Residues were found in the meal and hulls, and the Meeting estimated processing factors of 0.014 for cotton seed oil (crude), 0.58 for cotton meal and 0.76 for cotton hulls.

Farm animal dietary burden

The Meeting estimated the dietary burdens of methamidophos residues for livestock using the diets in Appendix IX of the FAO Manual. The calculation from MRLs or HRs in feed provides the feed levels

suitable for estimating animal commodity maximum residue levels, while the calculation from feed STMRs is suitable for the estimation of animal commodity STMRs.

Maximum burden

Commodity	MRL or HR	Group	% DM	MRL ÷ DM	Chosen diets, %			Residue contribution, mg/kg		
					Beef	Dairy	Poultry	Beef	Dairy	Poultry
Apple pomace, wet	$0.28 \times 1.35 = 0.378$	AB	40	0.945						
Potato culls	0.02	VR	20	0.1						
Potato processed waste	0.02	AB	15	0.13						
Beet, fodder tops	6.1	AV	23	26.5	20	10		5.3	2.65	
Cotton seed	0.16	SO	88	0.18	25	25		0.045	0.045	
Cotton gin by-products	7.7	AM	90	8.56						
Cotton meal	$0.16 \times 0.58 = 0.093$	-	89	0.104			20			0.0208
Cotton hulls	$0.16 \times 0.76 = 0.122$	AM	90	0.135						
Soya bean seed	0.06	VD	89	0.067			20			0.0134
Soya bean meal	$0.06 \times 2.0 = 0.12$	AL	92	0.13						
Soya bean hulls	$0.06 \times 4.5 = 0.27$	AL	90	0.3						
TOTAL					45	35	40	5.3	2.7	0.0342

STMR burden

Commodity	STMR	Group	% DM	STMR ÷ DM	Chosen diets, %			Residue contribution, mg/kg		
					Beef	Dairy	Poultry	Beef	Dairy	Poultry
Apple pomace, wet	$0.06 \times 1.35 = 0.081$	AB	40	0.2025						
Potato culls	0.01	VR	20	0.05						
Potato processed waste	0.01	AB	15	0.067						
Beet, fodder tops	2.1	AV	23	9.1	20	10		1.82	0.91	
Cotton seed	0.01	SO	88	0.011	25	25		0.00275	0.00275	
Cotton gin by-products	0.77	AM	90	0.86						
Cotton meal	$0.01 \times 0.58 = 0.0058$	-	89	0.0065			20			0.0013
Cotton hulls	$0.01 \times 0.76 = 0.0076$	AM	90	0.008						
Soya bean seed	0.01	VD	89	0.0122			20			0.0024
Soya bean meal	$0.01 \times 2 = 0.02$	AL	92	0.022						
Soya bean hulls	$0.01 \times 4.5 = 0.045$	AL	90	0.05						
TOTAL					45	35	40	1.82	0.91	0.0037

The methamidophos dietary burdens for estimating animal commodity maximum residue levels and STMRs (residue levels in animal feeds expressed on dry weight) are beef cattle 5.3 and 1.8 ppm, dairy cattle 2.7 and 0.91 ppm and poultry 0.034 and 0.0037 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 methamidophos for 28 days at the equivalent of 0.2, 1.0 and 5.0 ppm in the diet. Residues in tissues were all <0.01 mg/kg. Owing to the interval between sample collection and analysis, liver residues were estimated to be <0.07 mg/kg from the rate of decomposition of residues in liver during frozen storage and the storage period. In a supplementary study residues in liver after dosing for 30 days at 10 and 20 ppm in the diet were <0.01 mg/kg for the 10 ppm dose group and up to 0.03 mg/kg for the 20 ppm dose group. Residues in milk were a maximum of 0.021 mg/kg from the 5 ppm feeding level.

The Meeting also received information on the residue levels arising in tissues and eggs when laying hens were dosed with methamidophos for 28 days at the equivalent of 2, 6 and 20 ppm in the diet. Residues in composite tissue and egg samples were highest in eggs. Transfer factors based on average residues in tissues and eggs from the 20 ppm feeding level were 0.0001, 0.00015, 0.0002, 0.0009, 0.0011, 0.002 and 0.006 for fat, liver, kidney, skin, heart/gizzard, muscle and eggs respectively.

Maximum residue levels and STMRs in animal commodities

The maximum dietary burdens for beef and dairy cattle are 5.3 and 2.7 ppm respectively, so the levels of residues in tissues and milk can be obtained from the highest residues in tissues and the mean residue in milk at the 5 ppm feeding level (10 ppm for liver) and by noting the results of the metabolism study on lactating goats. The maximum residues expected in tissues are <0.01 mg/kg and the mean residue in milk is 0.011 mg/kg.

The Meeting estimated maximum residue levels in meat (from mammals other than marine mammals) of 0.01* mg/kg; in edible offal (mammalian) of 0.01 (*) mg/kg, and in milks of 0.02 mg/kg. These are recommended to replace the existing CXLs of 0.01 (*) mg/kg for cattle fat, cattle meat, goat meat, goat fat, sheep meat, sheep fat and milks.

The STMR dietary burdens for beef and dairy cattle are 1.8 and 0.91 ppm respectively. The estimated STMRs are meat (from mammals other than marine mammals) <0.01 mg/kg, fat (from mammals other than marine mammals) <0.01 mg/kg, edible offal (mammalian) <0.01 mg/kg and milks <0.01 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 highest likely residue level in the animal commodity.

Dietary burden (ppm) ¹ Feeding level [ppm] ²		Methamidophos residues, mg/kg ³									
		Milk		Fat		Muscle		Liver ⁴		Kidney	
		mean	high	mean	high	mean	high	mean	high	mean	high
MRL beef	(5.3) [5]		(<0.01) <0.01		(<0.01) <0.01		(<0.01) <0.01		(<0.01) <0.01		(<0.01) <0.01
MRL dairy	(2.7) [5]	(0.011) 0.021									
STMR beef	(1.8) [5]		(<0.01) <0.01		(<0.01) <0.01		(<0.01) <0.01		(<0.01) <0.01		(<0.01) <0.01
STMR dairy	(0.91) [5]	(<0.01) 0.021									

¹ Values in parentheses are the estimated dietary burdens

² Values in square brackets are the actual feeding levels in the feeding study

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

⁴ The dietary level for liver in the feeding study was 10 ppm for the estimation of both the maximum residue level and the STMR

The maximum dietary burden for poultry is 0.034 ppm. The levels of residues in tissues and eggs are all expected to be <0.01 mg/kg at this level.

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

As no residues are expected at the maximum feeding level in poultry, the STMRs for poultry meat, edible offal and eggs are estimated to be zero.

DIETARY RISK ASSESSMENT

Long-term intake

The evaluation of methamidophos has resulted in recommendations for maximum residue levels and STMRs for raw and processed commodities. Consumption data were available for 17 food commodities and were used in the dietary intake calculation. The results are shown in Annex 3.

The International Estimated Daily Intakes for the 5 GEMS/Food regional diets based on STMRs were in the range 0-10% of the maximum ADI of 0.004 mg/kg bw (Annex 3). The Meeting concluded that the long-term intake of residues of methamidophos 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) of methamidophos was calculated for the food commodities (and their processed fractions) for which HRs arising from the use of methamidophos and acephate were estimated and for which consumption data were available. The results are shown in Annex 4.

The IESTI varied from 0 to 150% of the acute RfD (0.01 mg/kg bw) for the general population and from 0 to 410% of the acute RfD for children aged 6 years and below. The short-term intakes for cabbage, sweet peppers and tomatoes were 120% to 150% of the acute RfD for the general population. For children 6 years and below, short-term intakes of between 110% and 410% of the acute RfD for broccoli, cauliflower, apples, sweet peppers, cabbages and tomatoes. The information provided to the Meeting precluded a conclusion that the acute dietary intake for these commodities would be below the acute RfD.

The Meeting concluded that the short-term intake of residues of methamidophos arising from the uses of methamidophos that have been considered by the JMPR is unlikely to present a public health concern, with the exception of cabbage (head) and tomatoes.

4.13 METHOXYFENOZIDE (209)

TOXICOLOGY

Methoxyfenozide (N-*tert*-butyl-N'-(3-methoxy-*o*-toluoyl)-3,5-xylohydrazide) is a diacylhydrazine insecticide that acts as an ecdysone agonist. Methoxyfenozide has not been evaluated previously by the JMPR. The Meeting noted that the purity of the material tested (> 98%) was higher than that of

the material proposed for commercialization (97%), but concluded that the findings were applicable to the proposed technical specification and production material.

Orally administered [¹⁴C]-methoxyfenozide is absorbed rapidly, with 58–77% of the dose being excreted within 24 h in rats. Peak plasma concentrations of radioactivity (C_{max}) were seen approximately 30 minutes after dosing. Excretion occurs mainly via faeces, after absorption followed by secretion in bile. On the basis of the quantities of radioactivity excreted in the bile and urine, it can be concluded that approximately 60–70% of an orally administered dose of 10 mg/kg bw was absorbed. Absorption and excretion profiles were similar irrespective of dose (10 or 1000 mg/kg bw), single or repeated dosing (over 14 days) or sex, the only differences being evidence of saturation at the high dose and a slightly increased level of urinary excretion in females. Concentrations of radioactivity at C_{max} were highest in the liver, with concentration in the adrenals and in the spleen also being higher than that in whole blood.

More than 30 metabolites of methoxyfenozide were identified in rat urine, faeces and bile. The primary reactions were demethylation, glucuronidation and hydroxylation. Less than 5% of the methoxyfenozide administered was cleaved at the amide bridge between the two aromatic rings. Repeated dosing at 10 mg/kg bw for 14 days altered the metabolite profile to a limited extent, with an increase in the concentration of multiple hydroxylated compounds.

Methoxyfenozide has low acute toxicity when administered by the oral, dermal or inhalation routes. The acute LD_{50} was > 5000 mg/kg bw in rats after oral or dermal administration. Methoxyfenozide was not irritating to rabbit skin, and produced minimal transient irritation of the rabbit eye. Methoxyfenozide did not induce skin in a Magnusson and Kligman maximization test for sensitization in guinea-pigs.

Short-term studies in rats, mice and dogs fed with methoxyfenozide show that these animals tolerated high concentrations of methoxyfenozide in the diet, equivalent to about 1000 mg/kg bw per day, with no marked adverse effects. Effects seen to varying degrees in all species were increased liver weight, hepatocyte hypertrophy and alterations in erythrocyte parameters consistent with a mild haemolytic effect, accompanied by formation of methaemoglobin. Findings were not always consistent between studies in the same species and comparison was also hindered to a certain extent by variations in blood sampling procedure and in the range of parameters investigated. The NOAEL in mice was 2500 ppm, equal to 428 mg/kg bw per day, on the basis of reduced body-weight gain at 7000 ppm, equal to 1149 mg/kg bw per day, in the 90-day study. In rats, the NOAEL was 1000 ppm, equal to 69 mg/kg bw per day, on the basis of increased (by > 10%) relative liver weights and periportal hepatocyte hypertrophy at 5000 ppm, equal to 353 mg/kg bw per day, in the 90-day study in rats. Thyroid follicular cell hypertrophy/hyperplasia seen in the 2-week study in rats receiving 1000 ppm methoxyfenozide, equal to 98 mg/kg bw per day, was not reproduced in the 90-day study. In dogs, increases in the formation of methaemoglobin and abnormal erythrocyte morphology were seen in two 14-day studies, with increases in spleen weights also noted in one of these studies. The overall NOAEL in the 14-day studies in dogs was 500 ppm, equal to 20 mg/kg bw per day, with a LOAEL of 3500 ppm, equal to 154 mg/kg bw per day. No treatment related adverse effects were seen in a 90-day study in dogs receiving doses of up to 5000 ppm, equal to 198 mg/kg bw per day. In a 1-year study in dogs fed with a diet containing methoxyfenozide at concentrations of 0 to 30 000 ppm (0, 60, 300, 3000, 30 000 ppm), there was evidence of haemolysis, methaemoglobinaemia, increased concentrations of bilirubin in blood and urine and increases in numbers of platelets. The presence of increased quantities of iron-positive pigment in the liver and spleen is consistent with phagocytosis of damaged erythrocytes. The NOAEL was 300 ppm, equal to 9.8 mg/kg bw per day, with a LOAEL of 3000 ppm, equal to 106 mg/kg bw per day. Extensive reversibility of haematological effects was demonstrated in dogs examined 4 weeks after the end of a 4-week exposure to 30 000 ppm, equal to 1036 mg/kg bw per day, of methoxyfenozide in the diet. This is consistent with the increases in reticulocytes and bone marrow hyperplasia observed in other studies and indicates that the effects on erythrocytes are not due to a direct effect on stem cells.

The chronic toxicity and carcinogenicity of methoxyfenozide has been investigated in mice

and rats at concentrations in the diet equating to >1000 mg/kg bw per day in the groups receiving high doses. There was no treatment related increase in the incidence of any tumour type. There were no significant treatment related non-neoplastic effects. The NOAEL for carcinogenicity and non-neoplastic effects in mice was 7000 ppm, equal to 1020 mg/kg per day, the highest dose tested. The Meeting concluded that methoxyfenozide was not carcinogenic in mice.

In the study in rats, poor survival (< 50% at week 90) in all groups resulted in the study being terminated at 99 weeks. This reduction in the duration of exposure reduces the power of the study, but the study was considered to be adequate for the assessment of carcinogenic potential in rats. Non-neoplastic findings were consistent with those of the short-term studies. Changes in erythrocyte parameters, increases in numbers of platelets, serum gamma-glutamyl transferase activity, liver weight, hepatocyte hypertrophy, glomerular nephropathy, thyroid follicular hyperplasia and erosion of the glandular stomach were seen at doses of 8000 ppm, equal to 411 mg/kg bw per day, and above. The NOAEL for non-neoplastic effects was 200 ppm, equal to 10 mg/kg bw per day. There was no treatment related increase in the incidence of any tumour type. The NOAEL for neoplastic effects was 20 000 ppm, equal to 1045 mg/kg bw per day. The Meeting concluded that methoxyfenozide was not carcinogenic in rats.

Methoxyfenozide (99% pure material) has been investigated in an adequate range of in vitro and in vivo studies of genotoxicity and found to give negative results. The Meeting noted that the purity of the material tested was greater than that of the proposed technical specification, but that the impurity profile (qualitative and quantitative) of the technical material (97%) did not give rise to any significant concerns regarding genotoxicity. The Meeting concluded that methoxyfenozide (technical material) was unlikely to be genotoxic.

In view of the lack of genotoxicity and the absence of carcinogenicity observed in studies in rats and mice, the Meeting concluded that methoxyfenozide is not likely to pose a carcinogenic risk to humans.

A two-generation study of reproductive toxicity in rats treated with methoxyfenozide showed that there were no adverse effects on oestrus cycling, sperm parameters, mating performance, litter size, pup body weight, pup viability or pup gross pathology at doses of up to 20 000 ppm, equal to 1474 mg/kg bw per day. A significant increase in absolute and relative liver weights and altered liver histopathology were seen in parental animals exposed to 20 000 ppm methoxyfenozide. The only compound related effect observed in pups was a slight delay in attainment of vaginal patency, noted in both generations at a dose of 20 000 ppm, the values being outside the range of historical data for the test facility. The developmental delay in attainment of vaginal patency did not have any impact on reproduction at the second mating. There was no evidence that developing pups or second-generation parents were especially sensitive to methoxyfenozide. The NOAEL for reproductive effects was 20 000 ppm, equal to 1474 mg/kg bw per day, the highest dose tested. The NOAEL for pup development was 2000 ppm, equal to 143 mg/kg bw per day, based on delayed vaginal patency at 20 000 ppm. The NOAEL for parental toxicity was 2000 ppm, based on increased liver weights and histopathological changes at 20 000 ppm.

The developmental toxicity of methoxyfenozide was investigated in rats and rabbits. Some marginal increases in fetal alterations were noted, but these were within the range of historical control values and not of toxicological concern. There was no evidence of maternal toxicity at the limit dose of 1000 mg/kg bw per day used in both studies. The overall NOAEL was 1000 mg/kg bw per day. The Meeting concluded that methoxyfenozide is not teratogenic.

Methoxyfenozide was tested in studies of neurotoxicity, although there were no signs of neurotoxicity induced by methoxyfenozide in routine studies of toxicity. No evidence of neurotoxicity or neuropathy was seen at 2000 mg/kg bw, the highest dose tested in a study of acute neurotoxicity in rats, or at 20 000 ppm, equal to 1318 mg/kg bw per day, the highest dose in a 90-day study of neurotoxicity in rats receiving repeated doses of methoxyfenozide. No haematological investigations were performed in these studies.

The animal, soil and plant metabolite, N-2,3-hydroxybenzoyl-N'-3,5-dimethylbenzoyl-N'-*tert*-butylhydrazine (M14) has low acute oral toxicity in mice (LD₅₀ of > 5000 mg/kg bw), and was not mutagenic in an Ames test. It is expected that the metabolites of methoxyfenozide identified in rats will be of no greater toxicity than the parent compound.

Methoxyfenozide is a new compound and there has been only limited exposure of humans to this pesticide. No adverse findings have been identified during routine medical monitoring of workers and operators.

The Meeting concluded that the existing database on methoxyfenozide was adequate to characterize the potential hazards to fetuses, infants and children.

Toxicological evaluation

The Meeting established an ADI for methoxyfenozide of 0–0.1 mg/kg bw based on the NOAELs of 200 ppm, equal to 10 mg/kg bw per day, for effects on erythrocytes plus liver and thyroid hypertrophy in the long-term study in rats, and 300 ppm, equal to 9.8 mg/kg bw per day, for haematological effects in the 1-year study in dogs, and a 100-fold safety factor.

The Meeting concluded that the toxicological profile of methoxyfenozide required the derivation of an acute RfD. The most appropriate end-point was considered to be haematotoxicity, for which the dog is the most sensitive species. In view of the fact that a 1-day study in dogs was available for the closely related compound, tebufenozide, which has a similar toxicity profile on repeated dosing, the Meeting decided to use this study to establish the acute RfD for methoxyfenozide. An acute RfD of 0.9 mg/kg bw was established, on the basis of the lack of haematological effects at 4300 ppm, equal to 89.4 mg/kg bw, and using a safety factor of 100 (see general item 2.2) the Meeting noted that this value was likely to be conservative since tebufenozide was more potent than methoxyfenozide in producing effects on erythrocytes.

A toxicological monograph was prepared.

Levels relevant to risk assessment

Species	Study ^a	Effect	NOAEL	LOAEL
Mouse	78-week study of chronic toxicity and carcinogenicity	Toxicity and carcinogenicity	7000 ppm ^b , equal to 1020 mg/kg bw per day	—
Rat	2-year study of chronic toxicity and carcinogenicity	Toxicity	200 ppm, equal to 10 mg/kg bw per day	8000 ppm, equal to 411 mg/kg bw per day
		Carcinogenicity	20 000 ppm ^b , equal to 1945 mg/kg bw per day	—
	Two-generation study of reproductive toxicity	Parental and offspring toxicity	2000 ppm, equal to 143 mg/kg bw per day	20 000 ppm, equal to 1474 mg/kg bw per day
Dog	1-year study of toxicity	Toxicity	300 ppm, equal to 9.8 mg/kg bw per day	3000 ppm, equal to 106 mg/kg bw per day
	Single dose study with tebufenozide	Toxicity	4300 ppm ^b , equal to 89.4 mg/kg bw	—

^aAll studies investigated dietary administration of methoxyfenozide

^bHighest dose tested

Estimate of acceptable daily intake for humans

0–0.1 mg/kg bw

Estimate of acute reference dose

0.9 mg/kg bw

Studies which would provide information useful for continued evaluation of the compound

Observations in humans

Summary of critical end-points for methoxyfenozide

Absorption, distribution, excretion and metabolism in mammals

Rate and extent of absorption: About 60–70% within 72 h in the rat (including biliary excretion of 40–65%) at a dose of 10 mg/kg bw

Distribution: Widely distributed; highest absorbed concentrations after 15 min–2 h in the liver

Potential for accumulation: Low potential: < 0.1% in liver after 5 days

Rate and extent of excretion: Rapid: 60–80% in 24 h, mainly in the faeces

Metabolism in animals Extensive (no parent found in urine or bile)

Little cleavage of parent

Toxicologically significant compounds: Methoxyfenozide

Acute toxicity

Rat, LD₅₀, oral: > 5000 mg/kg bw

Rat, LD₅₀, dermal: > 5000 mg/kg bw

Rat, LC₅₀, inhalation: > 4.3 mg/l (4-h exposure, nose only, maximum achievable concentration)

Skin sensitization: Not sensitizing (Magnusson and Kligman test)

Short term studies of toxicity

Target/critical effect: Liver (hypertrophy), erythrocytes (methaemoglobin and haemolysis)

Lowest relevant oral NOAEL: 10 mg/kg bw per day (1-year study in dogs)

Lowest relevant dermal NOAEL: 1000 mg/kg bw per day (28-day study in rats)

Lowest relevant inhalation NOAEC: No data

Genotoxicity: No genotoxic potential

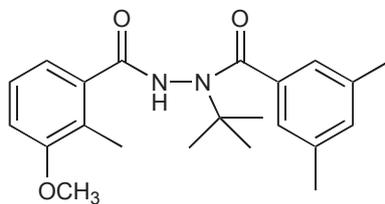
Long term studies of toxicity and carcinogenicity

Target/critical effect	Erythrocytes (reduced parameters), liver (hypertrophy), thyroid (hypertrophy)
Lowest relevant NOAEL	10 mg/kg bw per day (80–90 week study in rats)
Carcinogenicity	No carcinogenic potential
<i>Reproductive toxicity</i>	
Reproduction target/critical effect	Delayed attainment of vaginal patency Parental hepatotoxicity
Lowest relevant NOAEL for reproductive toxicity	143 mg/kg bw per day
Developmental target/critical effect	No embryotoxicity or fetotoxicity Not teratogenic
Lowest relevant NOAEL for developmental toxicity	1000 mg/kg bw per day (highest dose tested in rats and rabbits)
<i>Neurotoxicity/delayed neurotoxicity</i>	
Acute neurotoxicity	NOAEL: > 2000 mg/kg bw; no neuropathy (rat)
90-day study of neurotoxicity	NOAEL: 1318 mg/kg bw per day (highest dose tested); no neuropathy (rat)
<i>Other toxicological studies</i>	
Tebufenozide single dose study in dogs	No effects at 89.4 mg/kg bw (highest dose tested)
Metabolite: N-2,3-hydroxybenzoyl-N'-3,5-dimethylbenzoyl-N'-tert-butylhydrazine (M14)	Acute LD ₅₀ > 5000 mg/kg bw in mice treated orally; not mutagenic in an Ames test
<i>Medical data</i>	No adverse effects reported but data limited (new compound)

Summary	Value	Study	Safety factor
ADI	0–0.1 mg/kg bw	Rat, long-term study; and dog, 1-year study	100
Acute RfD	0.9 mg/kg bw	Dog, single dose of tebufenozide	100

RESIDUE AND ANALYTICAL ASPECTS

Methoxyfenozide, *N-tert-butyl-N'-(3-methoxy-*o*-toluoyl)-3,5-xylodrazide* or 3-methoxy-2-methylbenzoic acid 2-(3,5-dimethylbenzoyl)-2-(1,1-dimethylethyl)hydrazide, is a substituted dibenzohydrazide and an insecticide that functions by accelerating the moulting process. It was considered for the first time by the present Meeting.



Animal metabolism

The Meeting received information of the metabolism of methoxyfenozide in rats, goats, and hens.

Goats. The metabolism, distribution, and elimination of [¹⁴C]methoxyfenozide, labelled in the methoxyphenyl (A) ring, the dimethylphenyl (B) ring, or the *tert*-butyl group, were studied in lactating dairy goats. The methoxyfenozide was administered orally in gelatin capsules to lactating goats once a day at dietary equivalents of 45, 32, or 61 ppm, for 7 consecutive days. Over the treatment period 81-88% of the administered dose was eliminated in the faeces (74-84%) and urine (5-7%). The major accumulation was in liver, where up to 0.14% of the total dose was found. The total radioactive residue (TRR) was <0.010-0.037 mg/kg in milk, 0.26-1.2 mg/kg in liver, 0.045-0.20 mg/kg in kidney, <0.010-0.017 mg/kg in leg muscle, <0.010-0.023 mg/kg in loin muscle, and 0.018-0.053 mg/kg in fat, expressed as methoxyfenozide. In general, residues were highest in the *tert*-butyl-labelled samples and lowest in dimethylphenyl-labelled samples.

About 85% of the TRR was extracted from milk, and 28-72% of the TRR was identified. Extraction was 98% from liver, 87-94% from kidney, and 68-98% from muscle. Identification was 22-68% from muscle, 68-84% from fat, 44-76% from kidney, and 40-56% from liver. An additional 50% was characterized in kidney and liver extracts from the *tert*-butyl labelled residue as lactose and triglycerides (*see below*).

The milk from the last day of dosing contained methoxyfenozide as the major component (14%-35% of the TRR), the only significant metabolite(s) being a B-ring alcohol-carboxylic acid and/or an A-ring phenol-B-ring alcohol (<10% of the TRR).

Methoxyfenozide was the major component of the radioactive residue in fat (68-81% of the TRR) and muscle (20%) and constituted 2-3% of the TRR in liver and kidney. The major component of the radioactive residue in liver (23-30% of the TRR, 0.075-0.27 mg/kg equivalents) and kidney (25-42% of the TRR, 0.015-0.049 mg/kg) was the glucuronide conjugate of the A-ring phenol formed by the demethylation of the methoxy group of the parent compound. It was present at low levels in the other samples (0.54%-8.1% of the TRR, <0.001-0.004 mg/kg).

The other metabolites identified in milk and most tissues from various labels at low levels were the A-ring phenol or demethylated parent, 0.72-7.4% of the TRR, <0.001-0.069 mg/kg, the B-ring carboxylic acid, 0.25-4.2% of the TRR, <0.001-0.013 mg/kg, the glucuronide conjugate of the A-ring phenol with an additional OH group ortho or para to glucuronide moiety, 0.32-18.2% of the TRR, <0.001-0.024 mg/kg, and the A-ring phenol glucuronide, B-ring monoalcohol, 0.16-14.1% of the TRR, <0.001-0.12 mg/kg.

The metabolite profiles were broadly similar from the three labels, with radioactivity from the *tert*-butyl group prominent in the fat-soluble fraction. The hexane extracts of *tert*-butyl-labelled liver and kidney were hydrolysed, and additional analytical procedures demonstrated the incorporation of radioactivity into triglycerides. From the results of HPLC, TLC, LC/MS, and LC/MS/MS analyses, triglyceride structures were proposed for several major molecular ions. Triglycerides accounted for 18% of the TRR (0.21 mg/kg as methoxyfenozide) and 22% of the TRR (0.043 mg/kg) in *tert*-butyl-labelled liver and kidney respectively. The incorporation of radioactivity into lactose in *tert*-butyl-labelled milk (23-31% of the TRR, 0.007-0.011 mg/kg) was also demonstrated.

Hens. After oral doses of [methoxyphenyl-¹⁴C]methoxyfenozide (A-ring), [dimethylphenyl-¹⁴C]methoxyfenozide (B-ring), or [*tert*-butyl-¹⁴C]methoxyfenozide to laying hens for 7 consecutive days at the equivalent of 58-68 ppm in the diet, the TRRs were 0.005-0.10 mg/kg in eggs, 0.28-1.57 mg/kg in liver, 0.009-0.027 mg/kg in dark muscle, 0.007-0.014 mg/kg in light muscle, 0.042-0.072 mg/kg in fat, and 0.042-0.052 mg/kg in skin with fat. Total recovery of the administered dose ranged from 84 to 93%. In general, ¹⁴C residues were highest in *tert*-butyl-labelled samples and lowest in dimethylphenyl-labelled samples, as in the ruminant study.

Approximately 81-98% of the TRR was characterized or identified in eggs and tissues from all labels except *tert*-butyl-labelled light muscle (TRR = 0.014 mg/kg, 48% characterized or identified). Methoxyfenozide was identified in eggs and tissues with all labels except the dimethylphenyl label in liver. It was the major residue in methoxyphenyl- and dimethylphenyl-labelled dark muscle, fat, and skin with fat, and in *tert*-butyl-labelled fat and skin with fat (11-55% of the TRR, 0.001-0.032 mg/kg), and was a minor residue in eggs, methoxyphenyl- and *tert*-butyl-labelled liver, and *tert*-butyl-labelled dark and light muscle (0.26-8.1% of the TRR, <0.001-0.006 mg/kg). The glucuronide conjugate of the A-ring phenol was identified in eggs and tissues with all labels except methoxyphenyl- and dimethylphenyl-labelled dark muscle. It was a major metabolite in eggs, methoxyphenyl- and dimethylphenyl-labelled liver, and *tert*-butyl-labelled light muscle and skin with fat (10-30% of the TRR, 0.001-0.054 mg/kg), and was present at low levels in the other samples (1.8-9.7% of the TRR, 0.001-0.007 mg/kg). The A-ring phenol or demethylated parent was identified in eggs and tissues with all labels at levels of 1.5-11% of the TRR (<0.001-0.044 mg/kg). Two other metabolites were identified at significant levels: the glucuronide conjugate of the A-ring phenol with an additional -OH group ortho or para to glucuronide moiety (1.1-9.5% of the TRR, <0.001-0.009 mg/kg), and the A-ring phenol glucuronide-B-ring monoalcohol 2.2-28% of the TRR, <0.001-0.047 mg/kg). The B-ring carboxylic acid was also identified at <6% of the TRR in eggs and various tissues.

As in goats the metabolite profiles were broadly similar from the three labels, and the incorporation of radioactivity into triglycerides in *tert*-butyl-labelled liver ($\leq 56\%$ of the TRR, ≤ 0.89 mg/kg) and kidney ($\leq 32\%$ of the TRR, ≤ 0.18 mg/kg) was demonstrated.

The Meeting concluded that the metabolism of methoxyfenozide is similar in poultry and ruminants. The major component in muscle, fat, and milk was the parent, which was present at low levels (<5% of the TRR) in eggs, liver, and kidney. The main metabolite in eggs, liver, and kidney is the glucuronide conjugate of the A-ring phenol. The residues were concentrated in the fat relative to the muscle by factors of about 2-5. This is consistent with the partition coefficient whose log value of 3.7 suggests slightly greater solubility in fat than muscle.

The metabolites found in rats were qualitatively the same as those in the goat and hens.

Plant metabolism

Studies on cotton, apples, grapes and rice were reported.

Cotton. The total radioactive residues were 0.072, 0.054, and 0.057 mg/kg in hulled kernels and 0.089, 0.107, and 0.162 mg/kg in hulls and lint 21 days after two applications each of A-ring-, *tert*-butyl- and B-ring-labelled [^{14}C]methoxyfenozide at 1 kg ai/ha. The TRRs in the whole cotton seed calculated from the total weight of kernels, hulls and lint were 0.081 mg/kg (methoxyphenyl label), 0.080 mg/kg (*tert*-butyl label), and 0.11 mg/kg (dimethylphenyl label). In whole cotton plants, the TRR decreased from 72 mg/kg (methoxyphenyl label), 60 mg/kg (*tert*-butyl label), and 86 mg/kg (dimethylphenyl label) in immature plants harvested after 7 days to 17 mg/kg (methoxyphenyl label), 13 mg/kg (*tert*-butyl label), and 17 mg/kg (dimethylphenyl label) in mature plants harvested after 21 days.

Solvent extractions released $\geq 75\%$ of the TRR, and about 65-86% of the TRR was characterized or identified in whole cotton seed. Methoxyfenozide was the only residue identified, accounting for 46% of the TRR (0.038 mg/kg) in methoxyphenyl-labelled, 67% (0.054 mg/kg) in *tert*-butyl labelled, and 57% (0.063 mg/kg) in dimethylphenyl-labelled whole cotton seed.

Apples. The total radioactive residues were 0.23 and 0.28 mg/kg in or on apples collected 14 and 36 days (normal harvest) after two applications of [methoxyphenyl- ^{14}C]methoxyfenozide at 1 kg ai/ha.

Over 93% of the TRR was characterized or identified in apples. Methoxyfenozide was the major residue identified, accounting for 91% of the TRR (0.26-0.27 mg/kg) in apples collected after 14 and 36 days. Two other metabolites identified in 14- and 36-day apples were the B-ring monoalcohol at 1.4% of the TRR (0.004 mg/kg) and the B-ring dialcohol at 0.08% of the TRR and 0.11% of the TRR (both 0.003 mg/kg). The half-life of methoxyfenozide on apple foliage and fruit was estimated at 23 ± 8 days and 12 ± 9 days respectively.

Grapes. The total radioactive residues were 0.75 mg/kg in grapes collected 27 days (normal harvest) after two applications of [*tert*-butyl-¹⁴C]methoxyfenozide at 1 kg ai/ha. The TRR was 110 mg/kg in grape foliage at harvest.

Approximately 93% of the TRR were characterized or identified. Methoxyfenozide was the major residue identified, accounting for 81% of the TRR (0.60 mg/kg). Two metabolites identified were the B-ring monoalcohol at <2.3% of the TRR (<0.017 mg/kg), and the glucose conjugate of the A-ring phenol at 3.6% of the TRR (0.027 mg/kg).

The TRRs in grapes and grape foliage sampled between the first and second applications and after the second application to harvest and beyond (for foliage) were monitored. The half-lives of methoxyfenozide were determined to be 13-21 days on grapes and 11-26 days on foliage.

Rice. Radiolabelled methoxyfenozide (A-ring, B-ring, and *tert*-butyl) was applied to rice 70 and 107 days after planting. The B-ring- and *tert*-butyl-labelled compounds were applied at 0.6 kg ai/ha in both applications. The A-ring material was applied first at 0.62 kg ai/ha, then at 0.31 kg ai/ha. Samples of grain (panicles) and foliage were collected 62 days after the second treatment. The panicles were separated into chaff and brown rice. The radioactive residue in plants ranged from 6.6 to 10 mg/kg, in grain 0.52 to 0.71 mg/kg, and in straw 21-44 mg/kg.

Solvent extraction released 88-91% of the TRR from rice straw. The major component was methoxyfenozide, 65-69% of the TRR. Identified metabolites were the B-ring-monoalcohol, 0.9-1.4% of the TRR, the A-ring phenol or demethylated methoxyfenozide, 2.7-2.9% of the TRR, the A-ring phenol B-ring monoalcohol 2.1-2.3%, the B-ring carboxylic acid 1.2-1.6%, and the glucose conjugate of the A-ring phenol 1.5-2.4%. A total of 75-78% of the TRR was identified.

The main component of the residue in the grain was again methoxyfenozide, 52-59% of the TRR. Identified metabolites were the B-ring monoalcohol (1.1-4.1% of the TRR), the A-ring phenol (3.2-7.5%), the B-ring carboxylic acid (1.6-2.9%), the B-ring dialcohol (0.4-0.7%), and the glucose conjugate of the A-ring alcohol (1.8-2.3%).

Summary. The Meeting concluded that the metabolism studies on apples, rice, grapes, and cotton adequately elucidate the nature of the residue from the foliar application of methoxyfenozide to various types of crop. The major component of the residue is methoxyfenozide, typically 50-90%. The metabolism of methoxyfenozide in plants is slow but occurs via the same pathways as in animals. The primary routes of metabolism involve demethylation of the A-ring methoxy group to produce a phenol which is then conjugated with sugars, and the oxidation of the methyl groups on the B-ring to produce alcohols, acids, and combinations of alcohol and acids. B-ring alcohols and acids also form glucose conjugates.

Environmental fate in soil

The aerobic degradation of radiolabelled methoxyfenozide was studied in four soils at a concentration of 0.75 kg ai/ha over a one-year period. The results demonstrate that methoxyfenozide is very persistent in soil, with 59-75% of the applied dose remaining after one year. Calculated first-order half-lives ranged from 340 to 1100 days, depending on the soil. The major degradation pathway of methoxyfenozide in soil leads to incorporation into soil natural products, mainly humic and fulvic acids and to a lesser extent humins. Degradation also proceeds by oxidation of a methyl substituent of

the B-ring to the acid (up to 3.2% of the applied dose), followed by mineralization to carbon dioxide (5.5% of the applied dose). No other degradation product exceeding 2% of the applied radioactivity was identified. Total recoveries during the test period ranged from 90 to 123%.

Confined rotational crop studies were conducted with methoxyfenozide labelled in the A-ring, B-ring, and *tert*-butyl group. Three applications of each, formulated as an emulsifiable concentrate, were made to bare soil at a total application rate of 2.2 kg ai/ha, equivalent to the maximum registered rate in the USA. Mustard, white radish and wheat were planted in the treated soil at three different plant-back intervals, 30, 90 and 365 days (nominal) after the last application. Crops were harvested at an intermediate stage and at maturity.

Total radioactive residue levels were <0.05-0.3 mg/kg in all crops except wheat forage and straw, 1-3 mg/kg. Residue levels were similar in immature and mature crops harvested from the same plant-back intervals, except in wheat. In general, the total residues found in mature and immature crop samples decreased significantly with increasing plant-back time. The highest TRRs, averaging about 3 mg/kg, were found in wheat straw samples at 30 days plant-back. Wheat forage residues averaged only about one-third those found in wheat straw. Wheat grain residues, at <0.05 mg/kg, were the lowest in any of the crops investigated. In general, most of the residue in all crops was readily extractable, but wheat straw and grain contained a large amount of bound residue.

In mustard leaves at 30 days plant-back, the parent methoxyfenozide was present up to 0.027 mg/kg (about 21% of the TRR) and individual metabolites were all below 0.01 mg/kg.

In radish leaves at 30 days plant-back, individual residues (up to 21 components were characterized) were all <0.05 mg/kg. The parent compound was found at up to 0.013 mg/kg (about 18% of the TRR). The *N*-glycosyl conjugate of the B-ring monoalcohol was detected at up to 0.035 mg/kg (about 13%) while the glucose conjugate of the A-ring phenol was detected at up to 0.028 mg/kg, (12~13% of the TRR). Radish roots contained the highest levels of unmetabolized parent of any of the crops investigated. Methoxyfenozide was the main residue in mature roots of radishes planted 30 days after treatment, from 0.022 to 0.033 mg/kg (up to 41% of the TRR).

Residues in wheat forage ranged from 0.72 to 1.5 mg/kg at a 30-day plant-back. The parent compound was a very minor component, less than 1% of the TRR (maximum 0.009 mg/kg). The two major components of the extracted residue were the malonylglycosyl conjugate of the A-ring phenol (up to 0.70 mg/kg, 48% of the TRR) and the glucose conjugate of the A-ring phenol (up to 0.36 mg/kg, 24% of the TRR).

Wheat straw contained the highest residues of any crop, 2-4 mg/kg at 30 days plant-back. Only about 45-50% of the straw residue was extractable. The main residue in the extract was the A-ring phenol (demethylated methoxyfenozide), which was present at up to 1.4 mg/kg and up to about 37% of the TRR.

Wheat grain contained the lowest residue levels, about 0.05 mg/kg. Only 11-23% of the grain residue was extractable. The main component of the extractable residue was the A-ring phenol, at a concentration of 0.006 mg/kg (about 15% of the TRR).

Potentially quantifiable residues of methoxyfenozide transformation products were found in wheat forage and straw at a 365-day plant-back interval. These included the A-ring phenol and its glucose and malonylglycosyl conjugates.

Residues of methoxyfenozide were determined in rotational crops at two trial locations (Texas and California) in the USA. Leaf lettuce, used as the cover crop, was planted in plots at each location for subsequent planting of rotational crops. Five applications of methoxyfenozide 80W were made at 7-10 days intervals to the lettuce crop at 0.45 kg ai/ha per application with a season total of 2.2 kg ai/ha. The leaf lettuce cover crop was harvested and removed from the plot 1-3 days after the last

application. Rotational crops representative of leafy crops (mustard greens), fruiting vegetables (tomatoes), cucurbits (cucumbers), root vegetables (turnips), cereal grains (wheat), legumes (soya beans), and bulb crops (onions) were planted 6-7 days after the last application.

The methoxyfenozide contents of the rotational crops harvested at maturity were mustard greens 0.12 mg/kg, turnip tops 0.004 mg/kg, turnip roots 0.021 mg/kg, onions 0.055 mg/kg, wheat hay 0.031 mg/kg, wheat straw 0.057 mg/kg, soya beans 0.02 mg/kg, soya forage 1.2 mg/kg, soya hay 1.1 mg/kg, tomatoes <0.02 mg/kg, wheat grain <0.02 mg/kg. The wheat and soya samples were also analysed for the A-ring phenol and its glucose conjugate. Neither was detected in wheat grain or soya beans (<0.05 mg/kg), but both were found in the animal feed commodities at levels as high as 4.1 mg/kg of the conjugate and 2.2 mg/kg of the phenol.

The Meeting concluded that methoxyfenozide persists in the soil. The major pathways of transformation are incorporation into soil natural products and slow oxidation of the methyl substituent of the B-ring to form the acid. The Meeting also concluded that methoxyfenozide and/or its degradation products may accumulate in rotational crops, particularly in forages and fodders.

Environmental fate in water

The hydrolytic stability of methoxyfenozide was evaluated in sterile buffer solutions at pH 5, 7, and 9. The concentration of combined unlabelled and *tert*-butyl-labelled material was 1 µg/ml. Samples were incubated in the dark at 25°C for 30 days. Methoxyfenozide was found to be stable for the 30-day test period. The calculated half-life values were 600 days at pH 5, 1600 days at pH 7 and 700 days at pH 9.

Methods of analysis

Numerous methods were presented for the determination of methoxyfenozide in plant commodities, both for data collection in field trials and processing studies and for monitoring and enforcement of national MRLs. Enforcement methods included independent laboratory validations. Methods that determine both methoxyfenozide and the glucuronide conjugate of the A-ring phenol were reported for meat, milk, fat, poultry, and eggs.

In all methods, an extraction suitable for the sample is followed by a standard clean-up, such as solid-phase extraction and Florisil chromatography, and analysis by HPLC. Detection is by UV (240 nm), MS (367.3 ion) or MS/MS (369 → 149). HPLC-MS and HPLC-MS/MS are used for metabolites. The methods typically have limits of quantification of 0.01- 0.05 mg/kg for methoxyfenozide in plant commodities, 0.01 mg/kg for methoxyfenozide in milk, eggs, and meat, and 0.01-0.02 mg/kg for the glucuronide conjugate of the A-ring phenol.

Enforcement methods based on the above procedures were developed with HPLC and UV detection as the primary analytical method for many plant commodities (apples, pears, grapes, peppers, tomatoes, leafy vegetables, brassica vegetables, pecans, almonds, almond hulls, sweet corn, corn forage and fodder, cotton seed, cotton gin trash) and some animal commodities (milk, fat, bovine muscle, chicken liver, eggs) and HPLC-MS and/or HPLC-MS/MS as the confirmatory method and the primary method for the glucuronide conjugate of the A-ring phenol in animal commodities and for methoxyfenozide in bovine liver and kidney and chicken muscle. The methods underwent successful independent laboratory validations. Methods were also radio-validated using samples from the goat metabolism and confined rotational crop studies.

Neither the parent nor metabolites are determined by multiresidue methods.

The Meeting concluded that adequate methods exist for the determination of methoxyfenozide in a variety of plant commodities with a limit of quantification of 0.01 or 0.02 mg/kg in most instances, and for the determination of methoxyfenozide in poultry and bovine

commodities at LOQs of 0.01 mg/kg. It was noted that the method for methoxyfenozide in bovine liver and kidney and chicken muscle for methoxyfenozide is HPLC-MS and/or HPLC-MS/MS and may not be practicable for some laboratories.

Stability of residues in stored analytical samples

The stability of methoxyfenozide in numerous plant commodities and of methoxyfenozide and the glucuronide conjugate of the A-ring phenol in bovine and poultry commodities stored frozen at about -20°C was reported. Methoxyfenozide was stable for at least the indicated periods in the following commodities: apples 365 days, apple juice 283 days, wet apple pomace 302 days, tomatoes 372 days, head lettuce 365 days, cotton seed 9 months, refined cotton seed oil 12 months, cotton gin trash 6 months, maize grain 397 days, maize meal 127 days, maize oil 184 days, milk 106 days, bovine muscle 165 days, bovine liver 261 days, bovine kidney 265 days, eggs 93 days.

The Meeting concluded that methoxyfenozide is stable for 6-12 months in various plant commodities and for about 100 days in animal commodities stored frozen.

Definition of the residue

Studies of metabolism in a variety of crops and of its environmental fate demonstrated that methoxyfenozide did not undergo extensive transformation. The major residue found in soil and plants is the parent compound, methoxyfenozide. The main residue in goat milk and tissues (except liver and kidney) is again methoxyfenozide, as it is in poultry tissues except liver, kidney, and eggs. In goat and poultry liver and kidney as well as in eggs, the A-ring phenol glucuronide is the main residue and the parent residue is about 10% of the metabolite and below the typical level of quantification. The glucuronide conjugate constituted a significant proportion of the total radioactive residues in eggs (30%), goat kidney (42%), goat liver (29%), hen liver (20%), and hen kidney (36%). However, the feeding studies described below revealed approximately equal concentrations of methoxyfenozide and the metabolite in poultry eggs and bovine kidney and liver.

The distribution of methoxyfenozide between fat and muscle in the ruminant and poultry metabolism studies indicate that it is fat-soluble. The methoxyfenozide concentration in fat was approximately 10 times that in muscle in goats and about 3-8 times that in muscle in hens. The log of the partition coefficient, 3.7, also indicates solubility in fat.

The Meeting concluded that the residue should be defined as methoxyfenozide for compliance with MRLs and for dietary intake estimation in both plant and animal commodities.

The compound is fat-soluble in its distribution between meat muscle and fat, but not in its distribution in milk.

Results of supervised trials on crops

Oranges and mandarins. Supervised field trials were conducted on oranges and mandarins in various parts of Europe, but there is no finalized GAP so the trials could not be evaluated.

Apples. Supervised field trials were conducted in the USA and in Europe. GAP in the USA requires WP 800 g/kg or SC 240 g/l, 0.34 or 0.28 kg ai/ha, 1.1 kg ai/ha per season, 14-day PHI. This corresponds to no more than 4 applications per season. All US trials were with 6 applications at 14-day intervals with a total application of 2.0 kg ai/ha. Two of the trials were conducted as residue decline studies. The half-life of the methoxyfenozide residue was about 20 days, and since it was found in the apple metabolism study that the half-life of the total radioactive residue was 12 ± 9 days it can be estimated that the residue contribution from the first two applications would have decreased to $\leq 20\%$ of the initial value by the time of the last application (56-70-day interval). The trials may therefore be considered as being according to maximum GAP. The residues of methoxyfenozide from

trials according to maximum GAP in the USA in ranked order were 0.20, 0.23, 0.25, 0.30, 0.36, 0.37, 0.40, 0.43, 0.52, 0.56, 0.60, 0.62, 0.62, 1.0, 1.0 mg/kg. The HR is 1.0 mg/kg and the STMR is 0.43 mg/kg.

The proposed GAP in northern and southern Europe, Austria, Belgium, France, Germany, Greece, Hungary, Ireland, Italy, Luxembourg, The Netherlands, Portugal, Spain, and Switzerland have not been adopted by the respective national authorities. The recently finalized GAP for the UK specifies a 240 g/l SC formulation applied at 0.6 l product /ha (0.14 kg ai/ha in 1500 l water/ha) for large trees and 0.4 l product/ha (0.096 kg ai/ha in 1000 l water/ha) for smaller trees, 3 applications and a 14-day PHI. The spray concentration is 0.0096 kg ai/hl. The residues found on apples from trials complying with maximum UK GAP in France, Italy, Spain, Belgium, and Germany were <0.05 (3), 0.06, 0.06, 0.10, 0.11, 0.11, 0.13, 0.13, 0.15, 0.15 and 0.23 mg/kg.

The residues in the European trials appear to be from a different population from those in the US trials, which are higher.

Pears. Supervised field trials were conducted in the USA and Europe. GAP in the USA is the same as for apples. In the US trials, as with apples, there were six applications, each at 0.34 mg/kg. Two residue decline studies on pears in Europe indicated a residue half-life of 14-20 days. Assuming a 20-day half-life, the residues from the first two applications would have decreased to $\leq 20\%$ of the initial value by the time of the last application, so the trials may be considered as complying with maximum GAP. The residues of methoxyfenozide on pears from 10 trials at maximum GAP in the USA in ranked order were 0.27, 0.31, 0.35, 0.36, 0.39, 0.50, 0.68, 0.74, 0.74 and 0.92 mg/kg. The HR is 0.92 mg/kg and the STMR is 0.44 mg/kg.

Proposed GAP in northern and southern Europe, Austria, Belgium, France, Germany, Greece, Hungary, Ireland, Italy, Luxembourg, The Netherlands, Portugal, Spain, and Switzerland is SC 240 g/l, 0.0096 kg ai/hl, 3 applications, 14-day PHI. However, this GAP has not been finalized. Maximum GAP for the UK specifies a 240 g/l SC formulation applied at 0.6 l product /ha (0.14 kg ai/ha) in 15 l water/ha, 3 applications, and a 14-day PHI. For small trees (foliar canopy height 2 m or less), the application rate is reduced to 0.096 kg ai/ha in 10 hl water/ha. The spray concentration is 0.0096 kg ai/hl in both cases. The ranked order of residues in pear trials at the maximum UK GAP in Italy (2), France (1), and Germany (1) is 0.07, 0.08, 0.09, 0.14 and 0.15 mg/kg.

The European residues again appear to be from a different population from those in the US trials, which are higher.

The residues from the 25 apple and pear trials in the USA are comparable, and can be combined to give 0.20, 0.23, 0.25, 0.27, 0.30, 0.31, 0.35, 0.36 (3), 0.37, 0.40, 0.43, 0.50, 0.52, 0.56, 0.60, 0.62, 0.62, 0.68, 0.74 (2), 0.92 and 1.0 (2) mg/kg. The Meeting estimated an STMR of 0.43 mg/kg and a maximum residue level of 2 mg/kg for pome fruit. The HR is 1.0 mg/kg.

Stone fruit. Trials were reported from the USA and various countries in Europe for the period 1998-1999. GAP for peaches, cherries, nectarines, and plums in the USA is SC 240 g/l or WP 800 g/kg, 0.28 kg ai/ha, 1.1 kg ai/ha per season, 7-day PHI. GAP for cherries specifies SC 240 g/l, 0.28 kg ai/ha, 0.95 kg ai/ha per season, 7-day PHI. Compliance with the 1.1 kg ai/ha/season rate requires no more than 4 applications per season. All US trials were conducted with 6 applications at 14-day intervals. Several decline studies conducted on peaches, cherries, and plums in the USA and Europe showed residue half-lives of 7 to 21 days, and the half-life of methoxyfenozide in the grape metabolism study was 13-21 days. The residues from the first two applications would therefore have decreased to $\leq 20\%$ of the initial value by the last application. As the fruits would also have been rather small at the time of the first two applications, the first two would have a minimal effect on the residue level compared with the final four applications, and the trials may be considered to accord with maximum GAP.

The ranked order of residues on peaches from 9 trials at maximum GAP is 0.32, 0.50, 0.54, 0.64, 0.78, 0.88 (2), 0.98 and 1.4 mg/kg. The STMR is 0.78 mg/kg and the HR 1.4 mg/kg.

The ranked order of residues on cherries from 7 trials at maximum GAP is 0.19, 0.26, 0.28, 0.34, 0.43, 0.52 and 0.56 mg/kg, with an STMR of 0.34 mg/kg and an HR of 0.56 mg/kg.

The ranked order of residues on plums from 7 trials at maximum GAP is 0.13, 0.14, 0.16, 0.19, 0.29, 0.30 and 0.34 mg/kg, with an STMR of 0.19 mg/kg and an HR of 0.34 mg/kg.

The trials on peaches and nectarines in France, Italy, Spain, and Greece could not be evaluated because there is no finalized relevant GAP.

The Meeting noted the identical use patterns for peaches, cherries, and plums and decided to combine the residues to give 0.13, 0.14, 0.16, 0.19 (2), 0.26, 0.28, 0.29, 0.30, 0.32, 0.34 (2), 0.43, 0.50, 0.52, 0.54, 0.56, 0.64, 0.78, 0.88 (2), 0.98, 1.4 mg/kg.

The Meeting estimated an STMR of 0.34 mg/kg and a maximum residue level of 2 mg/kg for stone fruit. The HR is 1.4 mg/kg.

Grapes. Supervised field trials on grapes were reported from Europe and the USA. Trials on table grapes in Greece, Italy, France, Spain, and Portugal, and on wine grapes in Portugal, France, Spain, Italy and Germany could not be evaluated as there is no finalized GAP. GAP in the USA is WP 800 g/kg or SC 240 g/l, 0.28 kg ai/ha, 0.84 kg ai/ha per season, 30-day PHI. The ranked order of residues in 15 trials at maximum GAP is <0.02, 0.20, 0.20, 0.21, 0.26, 0.26, 0.32, 0.33, 0.34, 0.39, 0.45, 0.46, 0.52, 0.52, 0.84 mg/kg.

Using only the US data with finalized GAP, the Meeting estimated an STMR of 0.33 mg/kg and a maximum residue level of 1 mg/kg. The HR is 0.84 mg/kg.

Broccoli. Eight supervised field trials were reported from the USA. GAP is WP 800 g/kg or SC 240 g/l, 0.28 kg ai/ha, 1.2 kg ai/ha per season, 1-day PHI. The ranked order of residues is 0.52, 0.70, 0.76, 0.89, 0.98, 1.4, 1.6, 1.6 mg/kg. The Meeting estimated an STMR of 0.94 mg/kg and a maximum residue level of 3 mg/kg. The HR is 1.6 mg/kg.

Cabbage. Nine supervised field trials on head cabbage were reported from the USA. The GAP is the same as for broccoli. The ranked order of residues is 0.56, 0.57, 0.67, 0.88, 0.93, 2.2, 3.3, 3.4, 6.2 mg/kg. The Meeting estimated an STMR of 0.93 mg/kg and a maximum residue level of 7 mg/kg. The HR is 6.2 mg/kg.

Tomato. Supervised field trials were reported from Australia, Germany, Belgium, The Netherlands, Spain, Portugal, Italy, France, and the USA. GAP in Australia is SC 240 g/l, 0.03 or 0.04 kg ai/hl, (0.3 or 0.4 kg ai/ha, calculated), 3 applications, 0-day PHI. Nine trials were conducted at maximum GAP (0.04 kg ai/hl and/or 0.4 kg ai/ha), and the ranked order of residues is 0.13, 0.14, 0.21, 0.26, 0.56, 0.57, 0.73, 1.0, 1.6 mg/kg.

Glasshouse trials in Germany, Belgium, The Netherlands, Spain, Portugal, Italy, and France. These trials could not be evaluated for lack of finalized GAP.

GAP in the USA is SC 420 g/l or WP 800 g/kg, 0.28 kg ai/ha, 1.2 kg ai/ha per season, 1-day PHI. Thirteen trials were conducted at maximum GAP, with residues in ranked order of 0.052, 0.088, 0.12, 0.12, 0.13, 0.14, 0.16, 0.19, 0.20, 0.28, 0.33, 0.94, 1.8 mg/kg.

As the residues from Australia and the USA represent similar use patterns and are from the same population the values were combined, giving 0.052, 0.088, 0.12, 0.12, 0.13, 0.13, 0.14, 0.14, 0.16, 0.19, 0.20, 0.21, 0.26, 0.28, 0.33, 0.56, 0.57, 0.73, 0.94, 1.0, 1.6, 1.8 mg/kg.

The Meeting estimated an STMR of 0.20 mg/kg and a maximum residue level of 2 mg/kg for tomatoes. The HR is 1.8 mg/kg.

Peppers. Supervised field trials were reported from the USA on peppers (bell and non-bell) and from Portugal, Spain, Italy, France, and The Netherlands on bell peppers. The 14 glasshouse trials in Europe could not be evaluated as there is no GAP. GAP in the USA is SC 240 g/l or WP 800 g/kg, 0.30 kg ai/ha, 1.1 kg ai/ha per season, 1-day PHI. The ranked order of residues on peppers from 13 trials at maximum GAP is 0.041, 0.049, 0.050, 0.12, 0.14, 0.16, 0.16, 0.20, *0.26*, 0.36, *0.40*, *0.48*, *0.94* mg/kg. The residues in non-bell peppers are in italics.

The Meeting estimated an STMR of 0.16 mg/kg and a maximum residue level of 2 mg/kg for peppers. The HR is 0.94 mg/kg.

Egg plants. Two trials were reported from Malaysia, one within 75% of maximum GAP with a residue value of 0.13 mg/kg.

The Meeting considered one trial insufficient to estimate a maximum residue level.

Sweet corn. Supervised field trials were reported from the USA, where GAP is 0.13 kg ai/ha in a minimum of 94 l/ha (ground and aerial) before tasselling and in a minimum of 190 l/ha after tasselling (ground equipment) for SC 240 g/l, and 0.28 kg ai/ha in 94 l/ha through silking and 0.13 kg ai/ha thereafter for WP 800 g/kg, 1.1 kg ai/ha per season, 3-day PHI. The 14 trials were conducted at 0.28 kg ai/ha. But the residues (kernels + cob with husk removed) were all <0.02 mg/kg.

The Meeting estimated an STMR of 0 mg/kg and a maximum residue level of 0.02 mg/kg (*) for sweet corn (corn-on-the-cob). The HR was estimated as 0.02 mg/kg.

Lettuce (head and leaf). Supervised field trials were reported from the USA on leaf and head lettuce. GAP for leaf and head lettuce is 0.28 kg ai/ha, 1.1 kg ai/ha per season, 1-day PHI. Eight trials on leaf lettuce at maximum GAP gave the ranked order of residues of 3.4, 8.2, 10, 12, 13, 17, 18, 18 mg/kg.

The Meeting estimated an STMR of 12.5 mg/kg and a maximum residue level of 30 mg/kg for leaf lettuce. The HR is 18 mg/kg.

Eight trials on head lettuce at maximum GAP gave the ranked order of residues for head lettuce with wrapper leaves of 1.6, 4.8, 5.4, 6.0, 6.2, 6.5, 7.9, 9.6 mg/kg.

The Meeting estimated an STMR of 6.1 mg/kg and a maximum residue level of 15 mg/kg for head lettuce. The HR is 9.6 mg/kg.

Spinach. Supervised field trials were reported from the USA where GAP is the same as for lettuce. Eight trials at maximum GAP showed the ranked order of residues 9.8, 10, 12, 14, 16, 18, 23, 43 mg/kg.

The Meeting estimated an STMR of 15 mg/kg and a maximum residue level of 50 mg/kg for spinach. The HR is 43 mg/kg.

Mustard greens. Supervised field trials were reported from the USA. GAP is the same as for lettuce. Seven trials at maximum GAP gave the ranked order of residues 10, 12, 14, 16, 17, 17, 18 mg/kg.

The Meeting estimated an STMR of 16 mg/kg and a maximum residue level of 30 mg/kg for mustard greens. The HR is 18 mg/kg.

Soya beans. Two supervised trials on soya beans were reported from Brazil. The residue was 0.03 mg/kg in the one trial according to GAP.

The Meeting considered one trial inadequate to estimate a maximum residue level.

Long beans. Two supervised trials were reported from Malaysia, one within 75% of the maximum GAP with a residue of <0.05 mg/kg.

The Meeting considered one trial inadequate to estimate a maximum residue level.

Celery. Supervised trials for the foliar application of methoxyfenozide to celery were reported from the USA. GAP is SC 240 g/l or WP 800 g/kg, 0.28 kg ai/ha, 1.1 kg ai/ha per season, 1-day PHI. Seven trials were according to GAP. An eighth trial was rejected because of a disease which made the celery unmarketable. The ranked order of residues is 0.48, 0.72, 3.0, 3.4, 5.5, 7.2, 7.8 mg/kg.

The Meeting estimated an STMR of 3.4 mg/kg and a maximum residue level of 15 mg/kg. The HR is 7.8 mg/kg.

Rice. Residues in two supervised trials in Japan at maximum GAP were <0.02 (2) mg/kg.

The Meeting concluded that an STMR and/or maximum residue level could not be estimated from the limited data base.

Maize (field corn). Numerous supervised field trials were reported from the USA, where GAP is SC 240 g/l or WP 800 g/kg, 0.13 kg ai/ha in a 47 l/ha minimum spray volume (ground and aerial), 1.1 kg ai/ha per season, 21-day PHI. Methoxyfenozide residues in maize grain from 24 trials conducted at between 2 and 3 times maximum GAP (0.24-0.36 kg ai/ha) were all <0.02 mg/kg. One additional trial at a similar rate yielded 0.033 mg/kg on one of duplicate samples.

Two supervised trials were reported from Mexico, where GAP is SC 240 g/l, 0.04 kg ai/ha, 4 applications, 30-day PHI. The PHIs were 77 and 156 days.

Two supervised trials were reported from Brazil, where GAP is 0.043 kg ai/ha, 1 application, 7-day PHI. The residues were 0.11 and 0.40 mg/kg.

Although the trials in Brazil produced the highest residues, the Meeting considered two trials inadequate for the estimation of an STMR and/or maximum residue level. Moreover, the description of the plants at the time of the last application (0.7 m high) suggests harvest of an immature commodity.

The Meeting estimated an STMR and HR of 0.02 mg/kg and a maximum residue level of 0.02 mg/kg (*), based on the US trials.

Cotton seed. Supervised trials on cotton were reported from Australia, Mexico, and the USA.

GAP in Australia is SC 240 g/l, 0.6 kg ai/ha, 3 applications at 10-day intervals, 28-day PHI. Eight trials at maximum GAP yielded residues in the seed of <0.05, <0.05, <0.05, <0.05, 1.6, 3.2, 4.8, 4.9 mg/kg. Those values below the LOQ are from delinted cotton seed with little or no boll opening. Those with finite values are for undelinted seed with substantial boll opening at the last application.

GAP in Mexico is SC 240 g/l, 0.12 kg ai/ha, 2 applications, 14-day PHI. Residues in two trials at maximum GAP were 0.02 and 0.11 mg/kg.

GAP in the USA is WP 800 g/kg, 0.45 kg ai/ha in a minimum of 19 l water/ha (aerial) or 47 l water/ha (ground), 1.1 kg ai/ha per season, 14-day PHI. The 1.1 kg ai/ha seasonal rate limits the number of applications at maximum rate to 2, but all US trials were conducted with 5 applications at 14-day intervals for a total seasonal rate of 2.2 kg ai/ha. As the trials in Australia indicate, however, the state of the boll (closed or open) is much more likely to affect the residue level than additional

applications 28-70 days before harvest. Eighteen trials were at maximum GAP, and the ranked order of residues in undelinted seed is 0.013, 0.08, 0.10, 0.14, 0.22, 0.26, 0.26, 0.37, 0.41, 0.50, 0.51, 0.51, 0.52, 0.52, 0.98, 1.1, 1.2, 1.3 mg/kg.

The trials in Australia, Mexico, and the USA were combined to give the ranked order <0.05 (4), 0.013, 0.020, 0.08, 0.10, 0.11, 0.14, 0.22, 0.26, 0.26, 0.37, 0.41, 0.50, 0.51, 0.51, 0.52, 0.52, 0.98, 1.1, 1.2, 1.3, 1.6, 3.2, 4.8, 4.9 mg/kg.

The Meeting estimated an STMR of 0.46 mg/kg and a maximum residue level of 7 mg/kg for cotton seed, with an HR of 4.9 mg/kg.

Tree nuts. Supervised trials on almonds and pecans were reported from the USA. GAP is SC 240 g/l or WP 800 g/kg, 0.43 kg ai/ha, 1.1 kg ai/ha per season, 14-day PHI. The ranked order of residues from trials at maximum GAP is <0.02 (3), 0.024, 0.027, 0.034 mg/kg in pecans and <0.020, 0.020, 0.021 (2), 0.036 0.074 mg/kg in almonds.

The combined ranked order of residues in pecans and almonds is <0.02 (4), 0.020, 0.021 (2), 0.024, 0.027, 0.034, 0.036, 0.074 mg/kg

The Meeting estimated an STMR of 0.021 mg/kg and a maximum residue level of 0.1 mg/kg for tree nuts. The HR is 0.074 mg/kg.

Animal feed items

Almond hulls. In the US trials on almonds described above the ranked order of residues in hulls is 6.4, 10(2), 16, 26, 35 mg/kg.

The Meeting estimated a maximum residue level of 50 mg/kg on a dry weight basis (90% dry matter), and an STMR of 13 mg/kg (not dry weight) for almond hulls.

Maize forage and fodder. Supervised field trials in the USA on maize are described above. The GAP application rate is 0.13 kg ai/ha with a 21-day PHI. As all the trials were at twice this rate (0.24-0.36 kg ai/ha) and showed finite residues at the 21-day PHI they were not evaluated. The evaluation of residues in sweet corn forage and fodder is described below.

Sweet corn forage and fodder. Supervised field trials were reported from the USA for the foliar application of methoxyfenozide to sweet corn according to the following GAP: SC 240 g/l or WP 800 g/kg, 0.13 kg ai/ha in a minimum of 94 l/ha (ground and aerial) before tasselling and in a minimum of 190 l/ha after tasselling for SC, 0.28 kg ai/ha through silking and 0.13 kg ai/ha thereafter for WP in 94 l water/ha (aerial and ground) before tasselling and in 190 l water/ha after tasselling, 1.1 kg ai/ha per season, 3-day PHI for forage and 21-day PHI for fodder. The 14 trials were conducted at 0.28 kg ai/ha/application. The ranked order of residues in forage for the 12 trials with the WP formulation at maximum GAP is 0.20, 0.52, 1.4, 1.5, 3.4, 4.4, 4.6, 6.1, 6.2, 7.2, 15, 22 mg/kg.

The Meeting estimated a maximum residue level of 50 mg/kg on a dry weight basis (48% dry matter), and an STMR of 4.5 mg/kg (not dry weight) for maize forage.

The ranked order of residues in fodder for the 11 trials with the WP formulation at maximum GAP is 1.0, 2.0, 4.9, 5.9, 8.2 (2), 8.4, 9.4, 20 (2), 46 mg/kg.

The Meeting estimated a maximum residue level of 60 mg/kg on a dry weight basis (83% dry matter) and an STMR of 8.2 mg/kg (not dry weight) for maize fodder.

Cotton gin by-products. Eight of the 18 cotton trials in the USA at maximum GAP described above included the determination of methoxyfenozide residues in cotton gin trash. The ranked order of residues in the gin trash is 3.8, 7.1, 9.4, 9.9, 12, 15, 17, 18 mg/kg.

The Meeting estimated an STMR of 11 mg/kg and an HR of 18 mg/kg for cotton gin by-products (trash containing 90% dry matter).

Fates of residue during processing

Processing studies on oranges, apples, grapes, tomatoes, maize (field corn), fresh prunes, and cotton seed were reported.

Two orange processing trials were conducted in Spain and one in Italy. Oranges were converted to marmalade and in two trials juice. The processing factors for juice were 0.3 and 0.2, average 0.25, and for marmalade 0.8, 0.5 and 1.1, average 0.8.

Single processing studies were conducted on apples in Germany, Belgium, France, and the USA. The processing factors were as follows: apple sauce, 0.4, 0.4, 0.4, average 0.4; apple juice, 0.4, 0.4, 0.4, 0.2, average 0.3; apple pomace (wet), 2, 2, 2, 6, average 3; apple pomace (dry), 7, 8, 7, average 7.

From the STMR of 0.43 mg/kg for pome fruit and the average processing factors for apple juice and wet pomace the Meeting estimated STMR-Ps of 0.13 mg/kg for apple juice and 1.3 mg/kg for apple pomace (wet). From the HR of 1 mg/kg for pome fruit and the average processing factor of 7 for dry apple pomace, the Meeting estimated a maximum residue level of 7 mg/kg for apple pomace (dry).

A processing study on the preparation of peach preserves was reported from Italy, but neither the RAC nor the preserves contained a quantifiable residue.

A study on processing plums to dried prunes was reported from the USA. The processing factor was 1.3, which when applied to the HR and STMR for stone fruits (1.4 and 0.34 mg/kg), provides a maximum residue level, an STMR-P and an HR-P of 3, 0.44 and 1.8 mg/kg respectively for prunes (dried plums).

Processing studies were conducted on grapes in France, Italy, Germany, Portugal, Greece, and the USA. The processing factors for grape juice were 0.3 (USA), 0.4 (Portugal), 0.3 (France), 0.2 (Greece), and 0.1 (Italy), average 0.3; for dried grapes (raisins) 1.3 (USA), 2.4 (Greece), 3.1 (Italy), and 2.1 (Italy), average 2.2; for wine 0.4 (USA), 0.3 (USA), 1.3 (Italy), 0.2 (Germany), 0.3 (Germany), 0.4 (Germany), 0.3 (Germany), 0.4 (Portugal), 0.4 (France) and 0.3 (France), average 0.4.

From the processing factors and the STMR for grapes (0.33 mg/kg) the Meeting estimated STMR-Ps for grape juice, raisins, and wine of 0.10 mg/kg, 0.73 mg/kg, and 0.13 mg/kg respectively.

From the processing factor for raisins (2.2) and the STMR and HR for grapes (0.33 and 0.84 mg/kg), the Meeting estimated a maximum residue level of 2 mg/kg, and STMR-P of 0.73 mg/kg and an HR-P of 1.8 mg/kg for dried grapes (raisins).

Tomato processing studies were carried out in the USA, Belgium, Germany, and Italy. The processing factors for juice were 0.2 (USA), 0.3 (Belgium), 0.4 (Germany), 0.4 (Germany) and 0.4 (Italy), average 0.3; for tomato paste 0.7 (USA), 2.2 (Belgium), 1.7 (Germany), 3.0 (Germany) and 3.4 (Italy), average 2.2; and for tomato pomace 3.6 (Belgium). The processing factor for peeling was 0.3 (average of 0.2 (Belgium), 0.4 (Germany), 0.4 (Germany), and 0.2 (Italy)).

Commodity	Codex group	Residue (mg/kg)	Basis	% Dry matter	Residue, dry wt (mg/kg)	Diets (%)			Residue contribution (mg/kg)		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
Almond hulls	AM	50 dry wt	MRL		50						
Apple pomace, wet	AB	1.3	STMR-P	40	3.25	15	5	0	0.49	0.16	
Maize grain	GC	0.02	MRL	88	0.023			80			0.018
Maize forage	AF	50 dry wt	MRL		50	40	50	0	20	25	
Maize fodder	AS	60 dry wt	MRL		60						
Cotton seed	SO	7	MRL	88	8.0	25	25	0	2.0	2.0	
Cotton seed hulls	AM	0.064	STMR-P	90	0.07						
Cotton seed meal	-	0.21	STMR-P	89	0.24			20			0.05
Cotton gin by-products	AM	18	HR	90	20	20	20	0	4.0	4.0	
TOTAL						100	100	100	26	31	0.07

Estimated median dietary burdens of livestock

Commodity	Codex group	Residue (mg/kg)	Basis	% Dry matter	Residue dry wt (mg/kg)	Diets (%)			Residue contribution (mg/kg)		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
Almond hulls	AM	13	STMR	90	14			0			
Apple pomace, wet	AB	1.3	STMR-P	40	3.25	40	20	0	1.3	0.64	
Maize grain	GC	0.02	STMR	88	0.023			80			0.018
Maize forage	AF	4.5	STMR	40	11	40	50	0	4.4	5.5	
Maize fodder	AS	8.2	STMR	83	11			0			
Cotton seed	SO	0.46	STMR	88	0.52		10	0		0.052	

Commodity	Codex group	Residue (mg/kg)	Basis	% Dry matter	Residue dry wt (mg/kg)	Diets (%)			Residue contribution (mg/kg)		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
Cotton seed hulls	AM	0.064	STMR-P	90	0.071			0			
Cotton seed meal	-	0.21	STMR-P	89	0.24			20			0.05
Cotton gin by-products	AM	11	STMR	90	12	20	20	0	2.4	2.4	
TOTAL						100	100	100	8.1	8.6	0.07

The estimated maximum dietary burdens of methoxyfenozide for beef cattle, dairy cattle, and poultry are 26 ppm, 31 ppm, and 0.07 ppm respectively, and the estimated median dietary burdens 7.5 ppm, 7.8 ppm, and 0.07 ppm respectively.

Feeding studies

Three cows at each level were dosed orally with the equivalent of 16, 54, or 180 ppm in the diet for 28 consecutive days. Milk was collected daily and analysed on days 1, 2, 4, 7, 10, 14, 17, 21, 24, and 28. The cows were slaughtered within 24 h of the last dose, and tissues were collected and analysed for methoxyfenozide and the glucuronide conjugate of the A-ring phenol.

All milk samples from the 16 and 54 ppm feeding levels were below the LOQ (0.01 mg/kg) for methoxyfenozide. Methoxyfenozide was detected (>0.003 mg/kg) in some samples, the highest values being 0.0063 mg/kg in day 28 milk at the 16 ppm feeding level and 0.0076 mg/kg in day 7 milk at the 54 ppm level. Quantifiable residues were found in milk from the 180 ppm group. The residue reached a plateau of 0.03-0.05 mg/kg on days 7-10 and an average of 0.027-0.030 mg/kg for days 10-28. The highest residue was 0.10 mg/kg from a single cow on day 7.

Day 28 milk from the 180 ppm level was separated into cream and skimmed milk. The residue in the cream was 0.12 mg/kg, in the skimmed milk 0.0054 mg/kg. The residue in the whole milk was 0.028 mg/kg. The concentration factor for cream relative to whole milk is 4.3. This does not represent a significantly higher solubility in milk fat than in whole milk. No information was provided on the residues in cream from the other feeding levels.

Fat, muscle, liver, and kidney from each of the cows at each of the feeding levels were analysed for methoxyfenozide. The glucuronide conjugate of the A-ring phenol was also determined in liver and kidney.

In fat, methoxyfenozide was quantifiable at all feeding levels: 0.011 mg/kg maximum (<0.01 mg/kg average) at 16 ppm; 0.082 mg/kg maximum (0.041 mg/kg average) at 54 mg/kg; 0.44 mg/kg maximum (0.28 mg/kg average) at 180 ppm.

Methoxyfenozide was not detected in muscle at the 16 and 54 ppm feeding levels (limit of detection, 0.003 mg/kg). At the 180 ppm level, the maximum residue was 0.10 mg/kg and the average was estimated at 0.0073 mg/kg (LOQ 0.01 mg/kg).

Methoxyfenozide residues were not quantifiable in liver (<0.01 mg/kg) at the 16 ppm feeding level. The highest residue was 0.0094 mg/kg. At the 54 ppm feeding level the highest methoxyfenozide residue was 0.030 mg/kg, average 0.028 mg/kg, while the highest and average residues of the glucuronide conjugate of the A-ring phenol were 0.035 mg/kg and 0.026 mg/kg respectively. At the 180 ppm feeding level, the highest and average residues of methoxyfenozide were 0.15 mg/kg and 0.13 mg/kg, and of the glucuronide conjugate of the A-ring phenol 0.12 mg/kg and 0.10 mg/kg.

In kidneys, methoxyfenozide was not detected at the 16 ppm feeding level, and was below the limit of quantification at the 54 ppm feeding level. At the 180 ppm level, the highest and average methoxyfenozide residues were 0.034 mg/kg and 0.026 mg/kg, and those of the glucuronide conjugate of the A-ring phenol 0.046 mg/kg and 0.029 mg/kg.

The Meeting noted that the methoxyfenozide and glucuronide conjugate residues were approximately equal in kidney and liver in the feeding studies, whereas in the metabolism study the metabolite concentration was about 10 times that of the parent.

In a poultry feeding study 10 or 12 hens in each of three feeding groups were dosed orally at the equivalent of 2.4, 7.6, and 24 ppm methoxyfenozide for 28 consecutive days. Eggs were collected each day by group, and the hens were killed within 24 h of the last dose. Tissues were analysed for methoxyfenozide.

At the 2.4 ppm feeding level, residues in eggs were below the limit of detection on days 1, 3, and 7, as they were at the 7.6 ppm level except in one of three samples (0.0032 mg/kg) on day 1. The estimated limit of detection for methoxyfenozide was 0.003 mg/kg.

At the 24 ppm feeding level, residues of methoxyfenozide in eggs were below the limit of detection over the entire 28 days, except in one sample on day 10 (0.0054 mg/kg) and one sample on day 17 (0.0030 mg/kg). Residues of the glucuronide conjugate of the A-ring phenol became detectable on day 7 but never reached the limit of quantification (0.01 mg/kg).

Residues of methoxyfenozide never reached the limit of detection (0.003 mg/kg) in fat, muscle, or liver at any feeding level. At the 7.6 and 24 ppm feeding levels the glucuronide conjugate of the A-ring phenol in liver averaged 0.013 and 0.021 mg/kg respectively.

Maximum residue levels in animal commodities

The Meeting agreed that the residues in cows from the 54 ppm feeding level could be extrapolated to the 31 ppm maximum dietary burden for dairy cattle to estimate maximum residue levels for ruminant commodities. The 16 ppm feeding level could not be used as the residues were undetectable or unquantifiable.

The Meeting further agreed that the residues from the 16 mg/kg feeding level, all below the LOQ, could be used without extrapolation as the residues at the 8.1 and 8.6 median feeding levels for beef and dairy cattle respectively.

Dietary burden (ppm) Feeding level [ppm]	Methoxyfenozide residue ¹ (mg/kg)								
	Milk ²	Muscle		Liver		Kidney		Fat	
	Mean	Highest	Mean	Highest	Mean	Highest	Mean	Highest	Mean
MRL dairy/beef cattle (31)	0.0027	0.0017		0.017		0.0022		0.047	
[54] ³	0.0047	<0.003		0.0305		0.0038		0.0820	

Dietary burden (ppm) Feeding level [ppm]	Methoxyfenozide residue ¹ (mg/kg)								
	Milk ²	Muscle		Liver		Kidney		Fat	
	Mean	Highest	Mean	Highest	Mean	Highest	Mean	Highest	Mean
STMR dairy cattle (7.8)	0.0041		0.003		0.0075		0.003		0.0082
[16] ⁴	0.0041		<0.003		0.0075		<0.003		0.0082

¹ Methoxyfenozide only

² Day 28

³ Extrapolation

⁴ Direct application of the 16 ppm level, owing to high uncertainty in the values (undetectable or below the LOQ)

The Meeting estimated a maximum residue level for milk of 0.01 mg/kg and an STMR of 0.0041 mg/kg. Although methoxyfenozide distributed preferentially in the fat of muscle, the concentration factor from whole milk to cream at the 180 ppm feeding level was only 4.3 to 1. No measurements were made on cream at the feeding level of relevance, 54 ppm. The Meeting estimated maximum residue levels for mammalian meat (fat) of 0.05 mg/kg and for mammalian offal of 0.02 mg/kg, and STMRs for mammalian muscle at 0.003 mg/kg, for offal at 0.0075 mg/kg, and for mammalian fat (trimmable) at 0.0082 mg/kg. The HRs are 0.017 mg/kg for mammalian offal, 0.0017 mg/kg for mammalian meat muscle, and 0.047 mg/kg for mammalian meat fat.

The Meeting concluded that residues of methoxyfenozide are unlikely in poultry commodities at the maximum and median dietary burden levels of 0.07 ppm. At the lowest feeding level, 2.4 ppm, methoxyfenozide and the glucuronide conjugate of the A-ring phenol were generally undetectable in eggs (<0.003 mg/kg). Methoxyfenozide was detected in one sample at the 2.4 ppm feeding level and in several samples at higher feeding levels, so the estimated maximum residue level is 0.01 mg/kg and the STMR 0.000 mg/kg in eggs. At all feeding levels, residues were undetectable (<0.003 mg/kg) in muscle and fat, so the estimated maximum residue level is 0.01 (*) mg/kg for poultry meat, and the STMR 0.000 mg/kg for poultry muscle and fat. In liver, residues were undetectable at all feeding levels (<0.003 mg/kg). The maximum residue level for poultry offal is therefore 0.01(*) mg/kg and the STMR 0.000 mg/kg. The HRs are 0.003 mg/kg for eggs and 0.000 mg/kg for poultry offal and meat.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes of methoxyfenozide based on the STMRs estimated for 42 commodities for the five GEMS/Food regional diets were in the range of 0-9% of the maximum ADI (Annex 3). The ADI is 0-0.1 mg/kg bw. The Meeting concluded that the long-term dietary intake of residues of methoxyfenozide is unlikely to present a public health concern.

Short-term intake

The acute RfD for methoxyfenozide is 0.9 mg/kg body weight. The international estimate of short term intake (IESTI) for methoxyfenozide was calculated for food commodities for which maximum residue levels, STMRs and/or HR values were established at this Meeting. The results are shown in Annex 4.

The IESTI for spinach is 310% of the acute RfD for the children. The information provided to the Meeting precludes an estimate that the short-term dietary intake of spinach by children would be below the acute reference dose. The Meeting noted that a conservative acute RfD was established and that a refinement is possible.

For all the other commodities considered, the percentage of the acute RfD varied from 0% to 100%. The Meeting concluded that short-term intake of residues of methoxyfenozide in these commodities, when used in ways that have been considered by the JMPR, is unlikely to present a public health concern.

4.15 PARAQUAT

TOXICOLOGY

Paraquat is a bipyridilium herbicide that was evaluated by the JMPR in 1970, 1972, 1976, 1985 and 1986, in order to establish an ADI. A toxicological monograph was published after the 1970 JMPR and addenda to the monograph were published after the 1972, 1976 and 1982 Meetings. A toxicological monograph was published after the 1986 JMPR. At the 1970 JMPR, an ADI of 0–0.001 mg/kg bw, as paraquat dichloride, was established. The 1972 JMPR assigned an ADI of 0–0.002 mg/kg bw, while the 1982 JMPR reduced the ADI to 0–0.001 mg/kg bw. The 1986 JMPR established an ADI of 0–0.004 mg/kg bw as paraquat ion (equal to 0–0.006 mg/kg bw as the dichloride).

Paraquat was re-evaluated by the present Meeting within the periodic review programme of the Codex Committee on Pesticide Residues. A considerable amount of data has been generated since 1986 and was submitted for evaluation; these data include studies on the absorption, distribution, metabolism and excretion of paraquat and numerous studies of toxicity (acute, reproductive and developmental). Furthermore, a substantial number of papers in the open literature on, *inter alia*, the genotoxicity and neurotoxicity of paraquat have been reviewed. In all studies relevant to risk assessment, doses and intakes are expressed as paraquat ion.

The pharmacokinetics and metabolism of paraquat have been the subject of many studies. Paraquat is not well-absorbed when administered orally. After oral administration of radiolabelled paraquat to rats, more than half the dose (60–70%) appeared in the faeces and a small proportion (10–20%) in the urine. In studies involving single or repeated doses, excretion of the radiolabel was rapid; about 90% was excreted within 72 h. Residual radioactivity was primarily found in the lungs, liver and kidneys. Some studies have found small amounts in the brain, but only in structures outside the blood–brain barrier or in structures without a blood–brain barrier (the pineal gland and linings of the cerebral ventricles, the anterior portion of the olfactory bulb, hypothalamus and area postrema). Paraquat is taken up into the lungs by an active process, whose normal substrate is endogenous diamines, e.g. putrescine and polyamines such as spermine and spermidine. In rats, dogs and monkeys, there are indications that paraquat is actively secreted in the kidneys.

Paraquat is largely eliminated unchanged; in rats, approximately 90–95% of radiolabelled paraquat in urine was excreted as the parent compound. Some studies have failed to show the presence of any metabolites after oral administration of paraquat, while others have shown a small degree of metabolism probably occurring in the gut as a result of microbial metabolism. Paraquat was not found in the bile.

The acute LD₅₀ after oral administration was 290–360 mg/kg bw in mice and 112–350 mg/kg bw in rats, while the guinea-pig was more sensitive (LD₅₀ of 22–30 mg/kg bw). The LD₅₀ in cynomolgus monkeys was 50–70 mg/kg bw. Paraquat was considered to be a mild skin irritant and a moderate eye irritant and was not a skin sensitizer in the Magnusson and Kligman test.

The predominant feature of exposure to repeated doses of paraquat was lung toxicity. Renal toxicity (proximal tubular damage) and toxicity to the liver (jaundice and elevations of enzyme activity) were also found. In some studies, lens opacities were seen. At higher doses, decreased body-weight gain, clinical signs (dyspnoea, increased respiratory sounds, swellings and sores in the genital area), haematological changes and effects on organ weight were reported, as well as increased mortality.

Lung abnormalities observed in mice, rats and dogs consisted of increased lung weight and gross pathological changes. Associated histopathological changes included cell necrosis, alveolar cell proliferation and hypertrophy, oedema, infiltration of macrophages and mononuclear cells and exudate. Dogs were most sensitive to paraquat-induced lung toxicity, followed by rats and mice; a NOAEL of 0.45 mg paraquat ion/kg bw per day was found in a 1-year study in dogs, on the basis of signs of respiratory dysfunction and histopathological changes at higher doses. This finding was supported by the NOAEL of 0.55 mg paraquat ion/kg bw per day from a 13-week study in dogs.

Ophthalmoscopy in-life and histopathological examination of eyes at necropsy revealed corneal opacity and cataracts in animals receiving doses of 3.75 mg and 7.5 mg paraquat ion/kg bw per day in a lifetime study in Fischer rats. Other ocular effects included lenticular degeneration, lens capsular fibrosis and/or lens ruptures, peripheral retinal degeneration, and proteinaceous vitreous humour. At time-points after 2 years (i.e. after the study would have ended according to current guidelines), rats receiving the lowest dose exhibited age-related peripheral morgagnian corpuscles and slight peripheral and moderate mid-zonal lenticular degeneration. Histopathological evidence of cataracts was also found at the highest dose (7.67 mg paraquat ion/kg bw per day) in a 2-year study in Fischer rats, but not at lower doses. In another 2-year study in Wistar rats, no intergroup differences in the prevalence of cataracts were seen. These differences between effects on the lens in the three long-term studies in rats may be indicative of a difference between Wistar and Fischer rats.

Paraquat elicited renal toxicity, which comprised changes in the proximal tubules of the kidneys (hydropic degeneration, eosinophilia and dilatation) in mice fed with 15.0 mg paraquat ion/kg bw per day in a lifetime study. Some very mild changes were also observed in males at 5.62 mg paraquat ion/kg bw per day, however, there was a clear NOAEL at 1.88 mg paraquat ion/kg bw per day. There were some histopathological effects on renal distal tubular cells at 1.75 mg and 3.52 mg paraquat ion/kg bw per day in a 13-week study in dogs, the NOAEL being 0.55 mg paraquat ion/kg bw per day.

The frequency of pulmonary adenoma was increased in females in a 2-year study in rats receiving a dose of 8.47 mg paraquat ion/kg bw per day; however, there was a clear NOAEL at 3.13 mg paraquat ion/kg bw per day. In males, adenocarcinoma was found in three animals (out of 80) receiving a dose of 10.6 mg paraquat ion/kg bw per day, one animal (out of 80) receiving 3.52 mg paraquat ion/kg bw per day and two animals (out of 80) receiving 1.34 mg paraquat ion/kg bw per day. The NOAEL for males in this study was 0.77 mg paraquat ion/kg bw per day, on the basis of histopathology of the lungs. In a second 2-year study in rats, no intergroup differences in tumour incidence were seen at any site. After review of the histopathological findings in the lifetime study in rats, it was concluded that the incidence of lung neoplasms in the test groups was comparable to that in the control groups. Thus tumours were seen in only one out of three long-term studies in rats. The Meeting concluded that the weight of evidence suggested that paraquat was not carcinogenic in the rat. Paraquat was not considered to be tumorigenic in two studies in mice.

Paraquat has been tested extensively in a broad range of in vitro and in vivo assays for genotoxicity, with mixed results. Studies more commonly gave positive results when DNA damage or clastogenicity were the end-points. Paraquat is known to produce active oxygen species and the available evidence indicates that it is probably this property that is responsible for its genotoxicity. Consequently, there is a threshold below which genotoxic activity will not be evident, provided that normally functioning antioxidant defence mechanisms have not been overwhelmed. The Meeting concluded that paraquat is unlikely to pose a genotoxic risk to humans.

Because of the nature of the genotoxicity observed and the lack of carcinogenicity in rats and

mice, the Meeting concluded that paraquat was unlikely to pose a carcinogenic risk to humans.

Three studies of reproductive toxicity in rats were reported. The overall NOAEL for parental toxicity was 1.67 mg paraquat ion/kg bw per day, and the NOAEL for pup toxicity was 5.0 mg paraquat ion/kg bw per day. Impaired fertility was not seen in these studies. Two studies of developmental toxicity in rats and two in mice were available for evaluation. The lowest NOAELs observed for both maternal and developmental toxicity in rats were 1 mg paraquat ion/kg bw per day, on the basis of clinical signs, and reduced body-weight gain in the dams and reduced mean fetal weights and retarded ossification in the fetuses. Higher NOAELs for maternal and developmental toxicity were seen in mice. Teratogenicity was not seen at any dose in any study in either rats or mice.

Paraquat is structurally similar to the known dopaminergic neurotoxicant 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). As a result, paraquat has been considered as a possible etiologic factor in Parkinson's disease. However, paraquat is a quaternary nitrogen compound and therefore crosses biological membranes poorly, unlike MPTP, the precursor of the neurotoxicant methylphenylpyridinium ion (MPP⁺). Data made available to the Meeting suggested that paraquat was not taken up by the dopamine transporter. Studies on the effects of paraquat on the central nervous system have used a variety of routes, including subcutaneous or intraperitoneal injection and direct injection into the central nervous system, and end-points observed have been behavioural, morphological and neurochemical. Behavioural effects and loss of neurones in the substantia nigra were observed and, neurochemically, depletion of dopamine was reported in many, but not all of these studies. However, the design of these studies renders the relevance of these data questionable for the risk assessment of dietary exposure to paraquat residues.

Persistent hypoactivity was observed in mice given paraquat by mouth on post-natal days 10 and 11. Reduced striatal content of dopamine and its metabolites was seen, but concentrations of serotonin were not affected. In a similar study of which the Meeting was aware, these findings had not been reproduced.

The Meeting concluded that the available mechanistic and other animal studies did not support the hypothesis that paraquat residues in food are a risk factor for Parkinson's disease in humans.

Two studies carried out to assess the potential involvement of combined exposure to the herbicide paraquat and the manganese-containing ethylenebisdithiocarbamate fungicide maneb in the etiology of idiopathic Parkinson's disease were evaluated by the Meeting. Paraquat or maneb, or a combination of the two, was given intraperitoneally to mice. The study was not designed appropriately to investigate potentiation and the results could have reflected dose-additivity.

Intentional and accidental poisoning with paraquat has been a major cause of death in many countries. Most incidents are caused by ingestion of the concentrate intended for agricultural use. Local effects include damage to the skin, nails, mouth, eyes and nose. Sore throat, dysphagia and epigastric pain may occur. Systemic effects, which produce the fatal outcome seen in those who have ingested a sufficient quantity of paraquat, mainly involve the respiratory system. The changes in the lungs that underly the symptoms and clinical signs comprise a proliferative alveolitis similar to that seen in most experimental animals treated with paraquat. In most, but not all, patients who develop the characteristic lung changes, the condition progresses inevitably towards a fatal outcome, death being due to respiratory failure. Numerous therapies have been tested but none has been consistently successful.

A number of epidemiological (case-control) studies have been carried out in humans with Parkinson's disease. In some of these, associations with exposure to chemicals including pesticides (in some cases specifically paraquat) were sought. Some but not all studies have shown a relationship between working in situations which might involve contact with or use of pesticides and Parkinson's disease, but associations with exposure to specific pesticides have not been shown consistently.

The Meeting established an ADI of 0–0.005 mg paraquat ion/kg bw on the basis of a NOAEL

of 0.45 mg paraquat ion/kg bw per day in the 1-year study in dogs and using a safety factor of 100. Although a 1-year study in dogs is not considered to be a long-term study, the nature and time-course of the pathogenesis of the lung lesions were such that the application of an additional safety factor was not considered necessary.

The Meeting established an acute RfD of 0.006 mg paraquat ion/kg bw based on the NOAEL of 0.55 mg paraquat ion/kg bw per day in the 13-week study in dogs, with a safety factor of 100. Histopathological changes in the lungs were present at higher doses in both studies in dogs.

A toxicological monograph was prepared.

Toxicological evaluation

Levels relevant to risk assessment

Species	Study	Effect	NOAEL ^a	LOAEL ^a
Mouse	13-week study	Toxicity	100 ppm, equal to 8.33 mg ion/kg bw per day	300 ppm, equal to 25.9 mg ion/kg bw per day
	97–99-week study	Toxicity	12.5 ppm, equivalent to 1.88 mg ion/kg bw per day	37.5 ppm, equivalent to 5.62 mg ion/kg bw per day
		Carcinogenicity	100 ppm equivalent to 15.0 mg ion/kg bw per day ^b	—
	Study of developmental toxicity	Maternal toxicity	10 mg/kg bw per day ^b	—
Embryo- and fetotoxicity		10 mg/kg bw per day ^b	—	
Rat	13-week study	Toxicity	100 ppm, equal to 4.74 mg/kg bw per day	300 ppm, equal to 14.2 mg/kg bw per day
	104-week study	Toxicity	30 ppm, equal to 0.77 mg/kg bw per day	100 ppm, equal to 2.55 mg/kg bw per day
		Carcinogenicity	300 ppm, equal to 7.67 mg ion/kg bw per day ^b	—
	Multigeneration study of reproductive toxicity	Parental toxicity	25 ppm, equivalent to 1.67 mg/kg bw per day	75 ppm, equivalent to 5.0 mg/kg bw per day
		Pup toxicity	75 ppm, equivalent to 5.0 mg/kg bw per day	150 ppm, equivalent to 10.0 mg/kg bw per day
	Study of developmental toxicity	Maternal toxicity	1 mg/kg bw per day	5 mg/kg bw per day
Embryo- and fetotoxicity		1 mg/kg bw per day	5 mg/kg bw per day	
Dog	13-week study	Toxicity	20 ppm, equal to 0.55 mg/kg bw per day	60 ppm, equal to 1.75 mg/kg bw per day
	1-year	Toxicity	15 ppm, equal to 0.45 mg/kg bw per day	30 ppm, equal to 0.93 mg/kg bw per day

^a Dietary concentrations are expressed as dichloride or ion as in the study report; intakes and doses are expressed as paraquat ion

^b Highest dose tested

Estimate of acceptable daily intake for humans

0–0.005 mg paraquat ion/kg bw

Estimate of acute reference dose

0.006 mg paraquat ion/kg bw

Studies that would provide information useful for continued evaluation of the compound

Further observations in humans

Summary of critical end-points for paraquat

Absorption, distribution, excretion and metabolism in mammals

Rate and extent of oral absorption	Poor
Dermal absorption	Poor; 0.25–0.29% absorbed (humans)
Distribution	Highest concentrations found in the lungs, liver and kidneys
Potential for accumulation	No potential for passive accumulation; active uptake into type II pneumocytes
Rate and extent of excretion	Rapid, about 64% in 24 h; 10% in urine, the remainder in the faeces; none is found in bile
Metabolism	Some metabolism (< 5%) in gut (probably microbial); paraquat is largely excreted unchanged
Toxicologically significant compounds (animals, plants and environment)	Parent compound

Acute toxicity

Rat, LD ₅₀ , oral	100–300 mg paraquat ion/kg bw
Rat, LD ₅₀ , dermal	80→ 660 mg paraquat ion/kg bw
Rat, LC ₅₀ , inhalation	0.0006–0.0014 mg paraquat ion/l (4-h exposure)
Rabbit, skin irritation	Mild
Rabbit, eye irritation	Moderate
Skin sensitization	Not sensitizing (Magnusson and Kligman test)

Short term toxicity

Target organ/critical effect	Lung toxicity
Lowest relevant oral NOAEL	0.55 mg paraquat ion/kg bw per day (13-week study in dogs); 0.45 mg paraquat ion/kg bw per day (1-year study in dogs)
Lowest relevant dermal NOAEL	1.15 mg paraquat ion/kg bw per day (21-day study in rabbits)

		rabbits)	
Lowest relevant inhalation NOAEC		0.00001 mg/l (21-day study in rats)	
<i>Genotoxicity</i>		Paraquat was clastogenic at high concentrations Unlikely to pose a genotoxic risk to humans at dietary concentrations	
<i>Long term studies of toxicity and carcinogenicity</i>			
Target organ/critical effect		Lung toxicity	
Lowest relevant NOAEL		0.77 mg paraquat ion/kg bw per day (2-year study in rats)	
Carcinogenicity		Not carcinogenic; unlikely to pose a carcinogenic risk to humans	
<i>Reproductive toxicity</i>			
Reproduction target/critical effect		Lung toxicity in pups	
Lowest relevant reproductive NOAEL		5 mg paraquat ion/kg bw per day (three- generation study in rats)	
Developmental target/critical effect		Not teratogenic; reduced fetus weight and ossification at maternally toxic dose	
Lowest relevant developmental NOAEL		1 mg paraquat ion/kg bw per day (rats)	
<i>Neurotoxicity/delayed neurotoxicity</i>			
		Not neurotoxic by oral route	
<i>Other toxicological studies</i>			
		Mechanistic studies on lung, liver and kidney toxicity	
<i>Medical data</i>			
		Causes acute poisoning	
<hr/>			
Summary	Value	Study	Safety factor
ADI	0–0.005 mg/kg bw	Dog, 1-year study	100
Acute RfD	0.006 mg/kg bw	Dog, 13-week study	100
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4.16 PARATHION-METHYL (059)

RESIDUE AND ANALYTICAL ASPECTS

The CCPR at its 33rd Session (Paragraph 59, ALINORM 03/24, 2002) requested the JMPR to consider an MRL for nectarine based on extrapolation from peach at the request of the delegation of Australia.

Parathion-methyl is registered in Italy for use on stone fruit. The JMPR (2000) estimated a maximum residue level of 0.3 mg/kg and STMR and HR values of 0.095 and 0.22 mg/kg for parathion-methyl on peaches. The estimates were based on supervised trials in Italy.

The Meeting agreed to extrapolate the proposed MRL of 0.3 mg/kg to nectarines.

DIETARY RISK ASSESSMENT

Long-term intake

Nectarines are included with peaches in the five regional diets, so the long-term intake needs no further assessment.

Short-term intake

The International Estimated Short Term Intake (IESTI) for parathion-methyl was calculated for nectarines. The results are shown in Annex 4.

The IESTI for the general population and for children represented 9% and 20% of the parathion-methyl acute RfD respectively. The Meeting concluded that the short-term intake of residues of parathion-methyl, resulting from its uses on nectarines that have been considered by the JMPR, is unlikely to present a public health concern.

4.17 PHOSMET

TOXICOLOGY

Phosmet (*O,O*-dimethyl S-phthalimidomethyl phosphorodithioate) is an insecticide and acaricide that acts by inhibiting acetylcholinesterase activity. Phosmet was evaluated previously by the JMPR in 1978, 1979, 1994 and 1998. An ADI of 0–0.01 mg/kg bw was set in 1994. In 1998, an acute reference dose (RfD) of 0.02 mg/kg bw was set, based on a NOAEL of 2 mg/kg bw per day in a study of developmental toxicity in rabbits. By request of a WHO Member State and the European Union, the acute RfD for phosmet was reviewed by the present Meeting in 2003, instead of in 2004 as originally scheduled. A recent study in human volunteers and additional information on the study of developmental toxicity in rabbits were reviewed by the current Meeting.

In an acceptable¹ double blind, randomized study, volunteers received a single dose of phosmet (96% pure) or placebo, in a capsule, with water. Six subjects receiving phosmet were paired with three subjects receiving placebo, for each dose group. Males received doses of 1, 2 or 4 mg/kg bw, with females receiving 2 mg/kg bw. A wide range of investigations, including assays for erythrocyte cholinesterase activity, were performed pre- and post-dosing (up to 168 h). There were no

¹ Annex 5, reference 83, page 5

adverse findings in any dose groups. The pattern of clinical signs, results of investigations and cholinesterase activities were similar in groups receiving test substance and placebo. The Meeting noted that females had only been given a dose of 2 mg/kg bw and concluded that the overall NOAEL for both sexes was thus 2 mg/kg bw.

The Meeting considered the study in volunteers together with other data on the toxicity of phosmet. The Meeting paid particular attention to the data on fetotoxicity, from the study of developmental toxicity in rabbits, which had been used to derive the acute RfD in 1998. The skeletal effects (reduced ossification) seen at 5 mg/kg bw per day in this study were not reproduced at a dose of 15 mg/kg bw per day and were mostly within the contemporary historical control ranges for the test facility. The forepaw flexure observed in four (out of 132) fetuses receiving 5 mg/kg bw per day was not present in the contemporary historical control database, but there was no dose-response relationship, this finding being present in a single fetus (out of 118) receiving a dose of 15 mg/kg bw per day. Taking into account the absence of dose-response relationship and of historical control data, the Meeting concluded that there were no clear compound related effects at a dose of 5 mg/kg bw per day. The altered ossification observed at 15 mg/kg bw per day was seen in the presence of cholinergic signs and significantly reduced maternal body-weight gain. The Meeting concluded that the fetal effects were unlikely to occur after a single dose that did not induce significant inhibition of acetylcholinesterase activity.

The Meeting established an acute RfD of 0.2 mg/kg bw on the basis of the NOAEL of 2 mg/kg bw (the highest dose tested) for inhibition of erythrocyte cholinesterase in male and female volunteers, and a safety factor of 10.

The Meeting recognized that it was possible that the acute RfD might be refined after a full evaluation of the complete database on phosmet.

An addendum to the toxicological monograph was prepared.

Dietary risk assessment

International estimated short-term intake (IESTI) for phosmet was calculated for the raw or processed commodities for which appropriate data on residues and consumption were available. The IESTI for the general population represented 0–90% of the acute RfD. The IESTI for children aged ≤6 years represented 0–230% of the acute RfD; the short-term intakes for apples and pears were 150% and 230% of the acute RfD, respectively. The information presented to the Meeting precluded the conclusion that the acute dietary intake for these commodities would be below the acute RfD.

The Meeting concluded that the short-term intake of residues of phosmet from uses that have been considered by the JMPR, with the exception of apples and pears, is unlikely to present a public health concern.

4.18 PIRIMIPHOS-METHYL (086)

RESIDUE AND ANALYTICAL ASPECTS

Pirimiphos-methyl, a broad-spectrum insecticide, was first evaluated in 1974 for toxicology and residues. Subsequently, it was reviewed for toxicology in 1976 and 1992 and for residues in 1976, 1977, 1979, 1983, 1985 and 1994. The current ADI of 0-0.03 mg/kg body weight was established by the 1992 JMPR. Currently there are 44 Codex MRLs for residues resulting from pre- and post-harvest uses of pirimiphos-methyl.

The 30th Session of the CCPR identified pirimiphos-methyl as a priority compound for periodic re-evaluation by the present Meeting.

The Meeting received data on metabolism, analytical methods, storage stability, supervised field trials, processing and farm animal feeding trials. The manufacturer and the governments of Australia, France, Germany and The Netherlands provided information on use patterns.

Animal metabolism

When a single dose of 50 mg/kg [^{14}C]pirimiphos-methyl was administered by gavage to rats fitted with a bile duct cannula, 33-38% of the administered radioactivity was excreted in urine, 17-21% in the bile, and 16-30% in the faeces within 48 h. Uncannulated rats receiving the same dose excreted 61-76% of the administered radioactivity in urine and 15-29% in faeces in 48 h.

After a single dose of 1 mg/kg given to normal rats, the main urinary metabolite was 2-ethylamino-6-methylpyrimidin-4-ol (R35510). At a single dose of 250 mg/kg, the main metabolites were *O*-2-ethylamino-6-methylpyrimidin-4-yl *O*-methyl *O*-hydrogen phosphorothioate (desethyl-R402186) and R35510 in male rats and *O*-2-diethylamino-6-methylpyrimidin-4-yl *O*-methyl *O*-hydrogen phosphorothioate (R402186) and desethyl R402186 in female rats. No parent compound was present in urine or bile. Faeces of bile-cannulated rats contained only pirimiphos-methyl while those of normal rats also contained several metabolites.

These results indicate that pirimiphos-methyl was incorporated, metabolized, and eventually excreted in urine. Re-absorption of pirimiphos-methyl metabolites from bile appeared to occur.

A lactating goat dosed with 50 mg/kg [^{14}C]pirimiphos-methyl in gelatin capsules twice daily for 7 days at a rate equivalent to 45 ppm in the diet excreted 89% of the administered dose in urine and faeces and 0.2% in milk. In fat samples (TRR 0.067 mg/kg pirimiphos-methyl equivalents) the major residues were pirimiphos-methyl (55% of the TRR) and *O*-2-ethylamino-6-methylpyrimidin-4-yl *O,O*-dimethyl phosphorothioate (R36341) (17% of the TRR). In other tissues (TRR 0.042 mg/kg in meat, 0.32 mg/kg in liver and 0.50 mg/kg in kidney as pirimiphos-methyl) and milk (TRR 0.18 mg/kg pirimiphos-methyl equivalents) they were R35510 (12-35% of the TRR), 2-amino-6-methylpyrimidin-4-ol (R4039) (7-20% of the TRR) and 2-diethylamino-6-methylpyrimidin-4-ol (R46382) (3-5% of the TRR). Conjugates of R46382 and R35510 were found in liver and kidney. Up to 32% of the total radioactive residues were unextracted from liver. Refluxing the unextracted material in 4M HCl released 27% of the TRR originally in the liver.

Radioactivity in the milk increased sharply after the first dose and reached a peak in the afternoon of day 2. After some decrease, it stabilized on day 4.

Laying hens were dosed with [^{14}C]pirimiphos-methyl in gelatin capsules twice daily for 14 days at a rate equivalent to 50 ppm in the diet, and 97.5% of the administered radioactivity was recovered from excreta collected over 14 days. Pirimiphos-methyl was the predominant residue in the fat (73% of TRR; 0.056 mg/kg) and was also present in egg yolk (9.5% of TRR; 0.022 mg/kg) but not found in muscle, liver or egg albumen.

R35510 and R4039 were the major residues in liver (12 and 6% of TRR), egg yolk (34 and 11% of TRR) and egg albumen (43 and 22% of TRR). Conjugates of these compounds were present in liver while a conjugate of R4039 was the major component of the leg and breast muscle. Thirty-nine per cent of the TRR in liver was unextracted. After refluxing the unextracted material in acid TLC of the extract showed that the major components were R35510 and R4039.

Radioactivity in eggs reached a plateau after about 6 days.

Pirimiphos-methyl was absorbed and extensively metabolized. Five transformation processes seem to occur: hydrolysis of a methyl ester group, de-ethylation of the *N*-diethyl group, conjugation with glucuronic acid or other biological compounds, hydrolysis of the pyrimidinyl group, and oxidation of phosphorothioate to phosphate.

Plant metabolism

Seventy g of wheat grains, rice grains (with husk) and husked rice were treated with a 2% dust formulation containing [2-¹⁴C]pirimiphos-methyl at 4 or 8 mg/kg (g/t). The treated grains were stored at 25°C for 8 months at low (12-15%) or high (17-20%) moisture content. On wheat grains treated at 4 mg/kg, pirimiphos-methyl decreased from the maximum of 2.7 mg/kg to 2.1 mg/kg at the lower moisture content and to 0.4 mg/kg at the higher moisture content in 32 weeks. The percentage of unextracted radioactivity increased from 0.02 to 0.11 mg/kg (lower moisture content) and to 1.60 mg/kg (higher moisture content) expressed as pirimiphos-methyl in 32 weeks after treatment. The main products were pyrimidinols, R46382, R35510 and R4039, with R46382 representing at least 90% of these. In all samples, the main product was R46382 which increased gradually over 8 months to a maximum of 0.17 mg/kg (lower moisture content) or 0.62 mg/kg (higher moisture content).

The degradation pattern of pirimiphos-methyl and the quantities of degradation products in rice and wheat were similar. The main product was R46382.

Radioautograms showed that radioactivity was concentrated in the pericarp of treated grain, indicating that residues in white flour and bread would be lower than in bran and wholemeal products.

Wheat, rice with husk, and husked rice grains were treated with aqueous formulations containing [2-¹⁴C]pirimiphos-methyl at rates equivalent to 15 mg/kg (g/t) (wheat) or 22.5 mg/kg (rice) and stored in the dark in desiccators to keep them at low (10-14%) or high (19-24%) moisture content for 24 weeks at 20°C. The degradation pattern and the quantities of degradation products were similar in wheat and rice. Pirimiphos-methyl accounted for 50-95% of the radioactive residues and R46382 and an unknown compound which was hydrolysed to it by acid reflux accounted for 70-85% of the remaining radioactivity. Other minor products were R36341, R35510 and R4039.

Duplicate samples of maize grain with 14% of moisture were sprayed three times with an EC formulation containing ¹⁴C-pirimiphos-methyl, each at a rate of approximately 47 mg ai/kg grain. This resulted in a total application rate of 96 mg ai/kg, an exaggerated rate. The treated grain was stored under conditions that maintained the moisture content at about 14%. In the first 12 weeks, a decrease of radioactivity corresponding to 44-63% of that applied occurred for unknown reasons. Most of the radioactivity in the grain was extractable with methanol, with 6% of the total radioactivity remaining unextracted at 0, 12 and 24 weeks after the last application. The predominant residue (no less than 60% of the TRR in week 24) was the parent compound with up to 18% of R46382, R46382 and R35510.

The studies on stored grains showed similar profiles. The predominant residue was the unchanged parent compound which accounted for no less than 60% of the TRR at the end of each experiment. The major components of the remaining residues were the pyrimidinols R46382, R35510 and R4039. These were derived from the parent compound by the same transformation processes as in animals. The main pyrimidinol was R46382 which was present at up to 10% of the TRR under conditions reflecting current GAP. Unknown compound(s) were also present in wheat grain, which were converted to R46382 by hydrolysis. R35510 and R4039 were present only at <5% of the TRR. R36341, resulting from the loss of one *N*-ethyl group from the parent compound, was also detected in small amounts.

Environmental fate in soil and water-sediment systems

No studies on environmental fate in soil or water-sediment systems or on rotational crops were reported. The supervised trial data were only on stored cereal grains, where use is only indoors, with little or no impact on the environment or succeeding crops.

However, pre-harvest uses are registered in many countries. Since pirimiphos-methyl is susceptible to photolysis (the half-life in sterile aqueous buffer solution is 0.46 h at pH 5 and 0.47 h at

pH 7) with the major photolytic degradation product being R46382, it was estimated that the impact on the environment might not be significant.

Methods of analysis

The Meeting received information on gas chromatographic methods for determining pirimiphos-methyl in a variety of fruits and vegetables and wheat, and both pirimiphos-methyl and its metabolites in animal tissues, milk and eggs.

All methods for the determination of pirimiphos-methyl involve extraction with acetone/hexane (2:8), maceration, addition of water, shaking and centrifugation. The resulting hexane layer derived from plant samples was analysed directly by gas chromatography, and that from animal tissues, milk or eggs underwent clean-up in a silica solid-phase extraction column. The hexane layer from fat samples was subjected to an additional hexane/acetonitrile partition procedure before clean-up.

A gas chromatographic method using specific thermionic detection showed linearity between 0.0125 and 2.0 µg/ml in the final extract (3.75-600 pg injected) for all plant samples tested including wheat. The limit of quantification was 0.05 mg/kg and the average recovery within an acceptable range (70-110%) although individual recovery values ranged from 60% to 117%. Gas chromatographic methods using mass-selective detection showed linearity between 0.0125 and 2.0 µg/ml (12.5-2000 pg injected) for all plant samples except cotton seed and olives, and between 0.001 and 1.0 mg/kg (2-2000 pg injected) for animal samples. The limit of quantification was 0.05 mg/kg for plant samples and 0.01 mg/kg for animal samples, and the average recovery within an acceptable range although individual recovery values ranged from 65% to 118% for plant samples. The methods were therefore suitable for analysing both plant and animal samples.

A method for the determination of pyrimidinols in animal samples involves extraction of animal tissues with methanol/2N HCl (1:1), centrifugation, extraction with hexane, evaporation of methanol, hydrolysis of the aqueous extract in acid, butanol partition and clean-up by adsorption chromatography. Milk samples were extracted with concentrated HCl, methanol and hexane, and egg samples with methanol/2N HCl (9:1) to remove protein. No hydrolysis was used for egg or milk samples. The final extract was analysed by gas chromatography with mass spectrometric detection after trimethylsilylation. The method showed a limit of quantification of 0.01 mg/kg and an average recovery within the acceptable range for R46382 and R35510. The recovery of R4039 from animal tissues was lower ($65 \pm 13\%$) than from other samples. Since this was attributed to the inhibition of trimethylsilylation, R31680 was added as an internal standard. The validity of using R31680 was confirmed by the linear calibration for 0.1-1.0 mg/kg and 0.01-0.10 mg/kg of R4039 with the addition of 5 mg/kg and 0.5 mg/kg of R31680 respectively. The modified method was shown to be suitable for determining pyrimidinols in animal tissues, milk and eggs.

Stability of residues in stored analytical samples

The stability of pirimiphos-methyl in barley, carrot, lettuce, olive and tomato stored at $<-16^{\circ}\text{C}$ for 24 months was investigated. No significant loss of pirimiphos-methyl residues occurred during the 24-month storage.

Analytical extracts of plant samples (the final extracts for GC with thermionic or MS detection) retained in vials and stored at a temperature of $5-7^{\circ}\text{C}$ were stable for 7 days, the maximum tested period.

No data on the storage stability of pirimiphos-methyl or its main metabolites in animal tissues or eggs were provided. A storage stability study for 2 months showed that pirimiphos-methyl and R35311 added to milk and milk fat at 0.01 or 0.1 mg/kg were stable for 2 months at -14°C . When

R36341 was added to milk at the same fortification level it was degraded to below the LOQ of 0.005 mg/kg after 2 months but it was shown to be stable for 2 months when added to milk fat.

Definition of the residue

Pirimiphos-methyl is metabolized in plants and animals through two major biotransformation routes: hydrolysis of the phosphorothioate group to produce the pyrimidinol R46382, and successive loss of the two *N*-ethyl groups. In muscle, liver, kidney, milk and eggs, and in plants, the main metabolites were the pyrimidinols R46382, R35510 and R4039.

The present Meeting received supervised data only on stored grains in which the predominant residue was pirimiphos-methyl.

In animal fat, the predominant residue was pirimiphos-methyl. Little or no pirimiphos-methyl was found in animal tissues other than fat, or in milk and eggs, although no storage stability studies were conducted on pirimiphos-methyl or its metabolites in animal commodities except milk. A feeding study on cows indicated that pirimiphos-methyl residues were below the limit of quantification in all tissues analysed including fat. In another study pyrimidinols were also below the limit of quantification or very low. A feeding study on hens showed 0.03-0.96 mg/kg R4039 in the muscle of hens dosed with 3.3-38 mg/kg pirimiphos-methyl. The other two pyrimidinols (R46483 and R35510) were in most cases below the limit of quantification or less than 0.06 mg/kg (R35510 in liver). These pyrimidinols were thought to be of much lower toxicity than the parent and their analysis requires a different method from that for pirimiphos-methyl.

The definition of the residue in the all countries whose national MRLs were reported to the Meeting is pirimiphos-methyl.

Pirimiphos-methyl has a log P_{ow} of 3.90 at 20°C and in animals was found only in fat and egg yolk, indicating that pirimiphos-methyl should be categorized as fat-soluble.

The Meeting agreed that the definition of the residue for plant and animal commodities should be pirimiphos-methyl for compliance with MRLs and for the estimation of dietary intake.

The residue is fat-soluble.

Results of supervised trials on crops

Supervised post-harvest trials on stored cereal grains were conducted in Germany and the UK. Approved application rates for stored cereal grains are in general 4-8 g ai/t. Only three of 20 countries whose information was available approved rates outside this range.

In wheat trials in Germany and the UK, pirimiphos-methyl residues resulting from 12 trials using rates within the range mentioned above were 1.8, 1.9, 2.2, 2.3 (2), 2.6 (2), 3.2 (2), 3.7, 3.8 and 4.5 mg/kg, and those from 16 barley trials within the same range were 0.74, 0.80, 1.0 (2), 1.3 (2), 1.4, 1.5, 1.6, 2.0, 2.4, 2.6, 2.7, 2.8, 3.1 and 3.7 mg/kg.

Trials on oats, rye and maize were conducted in accordance with the GAP of many countries. The residues were 2.9 mg/kg in oats, 1.9 mg/kg in rye and 2.4 mg/kg in maize. Only a single trial on each crop was reported, but in the studies on the fate of pirimiphos-methyl in stored grain it was estimated that the degradation profiles after the application of pirimiphos-methyl were similar qualitatively and quantitatively among the grains analysed, namely wheat, rice and maize. The Meeting therefore agreed to combine the results of these trials to recommend a group MRL for cereal grains.

The combined values are 0.74, 0.80, 1.0 (2), 1.3 (2), 1.4, 1.5, 1.6, 1.8, 1.9 (2), 2.0, 2.2, 2.3 (2), 2.4 (2), 2.6 (3), 2.7, 2.8, 2.9, 3.1, 3.2 (2), 3.7 (2), 3.8 and 4.5 mg/kg.

The Meeting recommended an MRL of 7 mg/kg Po for cereal grains to replace the existing CXL of 10 mg/kg Po. The STMR and HR were 2.3 and 4.5 mg/kg respectively.

No data on supervised trials were provided on the following commodities: apples, Brussels sprouts, head cabbages, carrots, cauliflower, cherries, citrus fruits, common beans, cucumbers, blackcurrants, dates, dried fish, gooseberries, kiwifruit, lettuce, mushrooms, olives, peanuts, peanut oil, pears, peas, peppers, plums, potatoes, raspberries, spinach, spring onions, strawberries, and tomatoes. The Meeting therefore decided to recommend withdrawal of the MRLs for these commodities.

Fate of residues during processing

In a laboratory scale baking of flour treated with radiolabelled pirimiphos-methyl to bread and biscuits there was little degradation of pirimiphos-methyl, with up to 10% of the TRR attributed to R46382 and R4039. R46382 was present at 25% of the TRR in bread crusts and R4039 at 12% in breadcrumbs.

Processing wheat grain treated at 4 g ai/t on a commercial scale resulted in a concentration of pirimiphos-methyl in bran and offal and a reduction in white and wholemeal flours and breads.

The calculated processing factors and STMR-Ps are shown in the Table below. A maximum residue level was calculated for bran, in which the highest concentration of pirimiphos-methyl was found, from the HR for wheat grain, 4.5 mg/kg.

The Meeting recommended an MRL of 15 mg/kg (PoP) for unprocessed wheat bran to replace the existing XL of 20 mg/kg and recommended withdrawal of the existing CXIs for wheat wholemeal, wheat flour, white bread and wholemeal bread as STMR-Ps were calculated for intake estimation.

Processing factors for wheat products

	Bran	Fine offal	Wholemeal flour	White flour	Wholemeal Bread	White bread
Processing factor	2.2	1.3	0.71	0.17	0.36	0.097
MRL, mg/kg	15 (HR 9.9)	-	-	-	-	-
STMR-P, mg/kg	5.1	2.9	1.6	0.39	0.83	0.22

Residues in the grain used for processing were 1.9 mg/kg for preparing bran, offal, white flour and white bread, and 2.9 mg/kg for preparing wholemeal flour and wholemeal bread.

Processing wheat grain to processed fractions and to bran breakfast cereals on a commercial scale showed a concentration of pirimiphos-methyl in fine bran (PF 1.7) and light bran (PF 1.6) but a reduction in heavy bran (PF 0.70). The processing factor from grain to bran breakfast cereals was calculated to be 2.3-4.

Residues of pirimiphos-methyl were extremely low, close to or below the limit of quantification of 0.01 mg/kg, in beer produced from barley grain treated with pirimiphos-methyl at a normal rate. Only two of 22 samples brewed separately in single brews in two experiments contained pirimiphos-methyl above the LOQ, with one showing 0.08 mg/kg. In malt, malt germ, wort and spent

malt, low-level residues were detected showing significant degradation (more than 90%) of pirimiphos-methyl during malting. In 16 beer samples obtained from sequential brews pirimiphos-methyl residues were <0.01-0.04 mg/kg. The Meeting calculated a processing factor from these results of <0.002 and an STMR-P for beer of 0.01 mg/kg.

Less than 4% of the residue in treated oat grain was found in rolled oats, but there were insufficient data to calculate a processing factor.

Studies with barley and oats indicated that no more than 10% (2-9%) of the pirimiphos-methyl residue in grain was found in the kernels of treated grains when the application rate was 4 g ai/t. Most of the residues were associated with the husks. There were too few trials to estimate the ratio of pirimiphos-methyl between the husks and kernels.

Since no processing studies were available for rice or rye, the Meeting decided to recommend withdrawal of the existing CXLs for rice bran, unprocessed; rice, husked; rice, polished and rye wholemeal.

Residues in animal commodities

Farm animal dietary burdens

The Meeting estimated farm animal burdens of pirimiphos-methyl residues with the diets in Appendix IX of the FAO Manual. A plateau was reached rapidly in milk (4 days). In eggs, a metabolism study indicated that a plateau was reached in 6 days and feeding studies indicated 15 days and 6 days. The Meeting agreed that calculation from MRLs would provide the feed levels suitable for recommending animal commodity MRLs, and calculation from feed STMRs would be suitable for the estimation of animal commodity STMRs.

Crop	MRL mg/kg	Group	DM %	MRL/DM mg/kg	Choose diet			Residue contribution, mg/kg		
					Beef	Dairy	Poultry	Beef	Dairy	Poultry
Barley grain	7	GC	88	8.0						
Maize grain	7	GC	88	8.0	80			6.36		
Oat grain	7	GC	89	7.9						
Rice grain	7	GC	88	8.0						
Rye grain	7	GC	88	8.0						
Wheat grain	7	GC	89	7.9			80			6.29
Wheat bran	9.9 ¹	CF	88	11.3		50			5.63	
Total								6.36	5.63	6.29
	STMR mg/kg									
Barley grain	2.3	GC	88	2.6					0.00	
Maize grain	2.3	GC	88	2.6	80			2.09		

Crop	MRL mg/kg	Group	DM %	MRL/DM mg/kg	Choose diet			Residue contribution, mg/kg		
					Beef	Dairy	Poultry	Beef	Dairy	Poultry
Oats grain	2.3	GC	89	2.6						
Rice grain	2.3	GC	88	2.6						
Rye grain	2.3	GC	88	2.6						
Wheat grain	2.3	GC	89	2.6			80			2.07
Wheat bran	5.1	CF	88	5.8		50			2.90	
Total								2.09	2.90	2.07

¹ HR

The pirimiphos-methyl dietary burdens for animal commodity MRL and STMR estimation are beef cattle, 6.4 and 2.1 mg/kg, dairy cattle 5.6 and 2.9 mg/kg, and poultry 6.3 and 2.1 mg/kg.

Farm animal feeding studies

Milk obtained from lactating cows fed diets containing 0, 5, 15 or 50 ppm (dry weight basis) of pirimiphos-methyl for 30 days contained only very low concentrations of pirimiphos-methyl throughout the trial; residue concentrations higher than those found in controls were seen only in milk from cows given 15 ppm (<0.005 to 0.02 mg/kg) and 50 ppm in the diet (<0.005 to 0.03 mg/kg), and were below 0.01 mg/kg (<0.005-0.008 mg/kg) from 5 ppm. No trend of accumulation in milk was observed. Pirimiphos-methyl residues were below the limit of quantification in all tissues analysed (heart, liver, kidney, fat, cardiac muscle, adductor and pectoral muscle) from all the cows.

Lactating cows were fed twice a day for 30 days with feed containing 0, 8.3, 31 and 94 ppm of pirimiphos-methyl. Residues of the pyrimidinols R46382, R35510 and R4039 were extremely low in milk, even from animals that received the highest dose; residues above the LOQ of 0.01 mg/kg were found only in isolated cases. At 94 ppm up to 0.03 mg/kg of these hydroxypyrimidines were found in the liver, and slightly higher concentrations in the kidneys, especially of R46382 (up to 0.16 mg/kg) and R35510 (up to 0.14 mg/kg).

Laying hens given single oral doses of [2-¹⁴C]pirimiphos-methyl excreted only 0.16-0.33% of the administered radioactivity in eggs. With unlabelled doses of 1-8 mg/kg 12% of the collected eggs contained pirimiphos-methyl above 0.001 mg/kg, the highest residue being 0.008 mg/kg. Radioactivity in egg albumen and yolk from hens given daily doses of [2-¹⁴C]pirimiphos-methyl for 28 days at 4 mg/kg reached a maximum (0.04 mg/kg) 15 days after the start of dosing, and remained fairly constant thereafter. In egg yolks pirimiphos-methyl did not exceed 0.001 mg/kg. Egg white from hens receiving 32 ppm pirimiphos-methyl for 7 days contained pirimiphos-methyl at 0.001-0.007 mg/kg, which remained constant, while in the yolk the pirimiphos-methyl concentration increased to a maximum of 0.012 mg/kg at day 6. No pirimiphos-methyl was found in any of the muscle samples taken at the end of the study. There was no evidence of accumulation of residues in eggs.

Muscles from laying hens given 3.3-38 ppm pirimiphos-methyl in the diet for 28 days were found to contain 0.03-0.96 mg/kg of R4039. R35510 and R46382 were in most cases below the limit of quantification in muscle, liver and eggs. The highest residue was 0.06 mg/kg R35510 in liver from 38 ppm.

Maximum residue levels for animal commodities

Since no data was reported on the storage stability of pirimiphos-methyl or its metabolites in animal tissues, milk or eggs, the Meeting concluded that it could not exclude the possibility that the low or negligible concentrations of pirimiphos-methyl and metabolites reported were due to the unstable nature of these compounds in the samples.

According to one feeding study pirimiphos-methyl was present at <0.005-0.008 mg/kg (mean 0.0053 mg/kg calculated from 0.005 mg/kg instead of <0.005 mg/kg) in whole milk from cows fed at 5 ppm pirimiphos-methyl, and at <0.005-0.02 mg/kg (mean 0.0064 mg/kg) in whole milk from cows fed at 15 ppm. Pirimiphos-methyl was found to be stable in milk for two months when stored at -14°C. Concentrations of pirimiphos-methyl in butter prepared from the milk of cows fed at 50 ppm were on average twice those in whole milk, indicating that most of the pirimiphos-methyl residue was in the non-fat fraction of the milk.

At the calculated maximum burden of 5.6 mg/kg, it is unlikely that whole milk would contain pirimiphos-methyl above 0.01 mg/kg, and at the STMR burden of 2.9 mg/kg STMR its level was calculated to be less than 0.003 mg/kg.

The Meeting estimated a maximum residue level of 0.01 mg/kg for milks, recommended to replace the existing CXL of 0.05 mg/kg, and an STMR of 0.003 mg/kg. The Meeting concluded that any preferential solubility of pirimiphos-methyl in milk fat was insufficient to attach the suffix "F" to the maximum residue level.

The Meeting decided not to estimate maximum residues levels for animal commodities except milk pending a storage stability study with animal commodities. It therefore recommended withdrawal of the CXLs for eggs at 0.05 mg/kg and meat (from mammals other than marine mammals) at 0.05 mg/kg.

FURTHER WORK OR INFORMATION

Desirable

1. A study on the storage stability of pirimiphos-methyl and metabolites in animal tissues and eggs.
2. Pirimiphos-methyl concentrations in fat in animal feeding studies.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Dietary Intakes (IEDIs) were calculated for the five GEMS/Food regional diets using the STMR for cereal grains and STMR-Ps for milks, beer and processed wheat products estimated by the current Meeting (Annex 3). The current ADI is 0-0.03 mg/kg bw and the calculated IEDIs were 10-50% of the maximum ADI. The Meeting concluded that the intake of residues of pirimiphos-methyl resulting from the uses considered by the current JMPR was unlikely to present a public health concern.

Short-term intake

The International Estimated Short-Term Intakes (IESTI) of pirimiphos-methyl by the general population and by children were calculated for commodities for which STMRS or STMRS-Ps were estimated by the current Meeting (Annex 4). The Meeting considered that it might be necessary to establish an acute reference dose for pirimiphos-methyl, but as one has not been established the short-term risk assessment for pirimiphos-methyl could not be finalized.

4.19 PYRACLOSTROBIN (210)

TOXICOLOGY

Pyraclostrobin is the provisionally approved ISO name for methyl N-{2-[1-(4-chlorophenyl)-1H-pyrazol-3-yl]oxyethyl]phenyl}(N-methoxy)carbamate. Pyraclostrobin is a member of the strobilurin group of fungicides. The strobilurin fungicides act through inhibition of mitochondrial respiration by blocking electron transfer within the respiratory chain, which in turn causes important cellular biochemical processes to be severely disrupted, and results in cessation of fungal growth. Pyraclostrobin has not been evaluated previously by the JMPR.

After oral administration of radiolabelled pyraclostrobin to rats, about 50% of the dose was absorbed. Concentrations of radiolabel in the blood peaked initially after 30 minutes, followed by a secondary peak at 8 or 24 h. The majority (74–91%) of the radiolabelled dose was eliminated in the faeces, with the remainder (10–13%) in the urine. The excretion pattern was not affected by repeated administration. In rats, the metabolism of pyraclostrobin proceeds through three main pathways. The methoxy group on the tolyl-methoxycarbamate moiety is readily lost, with few major metabolites retaining this group. Hydroxylation of the benzene and/or pyrazole rings is followed by conjugation with glucuronide and, to a lesser extent, sulphate. Many metabolites are derived from the chlorophenol-pyrazole or tolyl-methoxycarbamate moieties of pyraclostrobin after cleavage of the ether linkage between these two groups, with subsequent ring hydroxylation and glucuronide or sulphate conjugation. Metabolites were similar in both sexes and across all dose groups. No unchanged parent compound was found in the bile or urine and only small amounts were found in the faeces. The majority of the radiolabel isolated from kidney tissues was in the form of the unchanged parent compound and a demethoxylated derivative.

Pyraclostrobin has low acute toxicity when administered orally or dermally, with LD₅₀s of > 5000 and > 2000 mg/kg bw respectively, and no deaths in either case. The compound has moderate toxicity when administered by inhalation, with an LC₅₀ of 0.31–1.07 mg/l when acetone is used as the solvent, and 4.07–7.3 mg/l when Solvesso is used as the solvent. Pyraclostrobin is a mild skin and eye irritant, but is not a skin sensitizer. Clinical signs after oral administration consisted of dyspnoea, staggering, piloerection, and diarrhoea in all animals, which resolved by day 6. There were no pathology findings.

In short-term studies in mice, rats and dogs, the major toxicological findings after repeated doses of pyraclostrobin involved duodenal mucosal hypertrophy and, in some studies in rodents, erosion/ulceration of the stomach mucosa. These findings are suggestive of a local irritant action, a conclusion supported by the occurrence of vomiting in dogs. However, pyraclostrobin is not a severe skin irritant, although in rabbits the irritation was somewhat prolonged.

Reductions in body-weight gain and food consumption were observed in all species, although the pattern of the response and relationship to treatment varied. To some extent, these effects suggest local disturbance to the gastrointestinal tract and taste aversion, particularly in rabbits, although a systemic effect may also be involved, especially in rodents.

In short-term studies using repeated doses of pyraclostrobin, reduced body-weight gains were

accompanied by reductions in clinical chemistry parameters (including total protein, globulin, glucose, triglycerides and creatinine) and reduced fat storage in the liver. These observations may be secondary to a disturbance of normal metabolic processes following the disruption of mitochondrial respiration, the primary biochemical mechanism by which pyraclostrobin acts. These effects may also reflect a reduced nutritional status caused by reduced food intake or food conversion. Reduced body-weight gain largely determined the minimally toxic dose in lifetime studies in rats and mice, but was not associated with toxicologically relevant alterations in clinical pathology values where these were measured in rats.

Mild anaemia associated with extramedullary haematopoiesis in the spleen was observed in rodents fed with repeated doses of approximately 400 ppm (equal to 120 mg/kg bw per day in mice and 42 mg/kg bw per day in rats) and above in short-term studies. Hepatocellular hypertrophy, in the absence of significant alterations in relevant clinical chemistry parameters or other histological evidence of liver injury, was also observed in rats receiving 120 mg/kg bw per day.

Pyraclostrobin gave negative results in an adequate battery of in vitro studies of genotoxicity and in an in vivo assay for bone marrow micronuclei in mice.

The Meeting concluded that pyraclostrobin was unlikely to be genotoxic.

The carcinogenic potential of pyraclostrobin was studied in rats and mice. While the incidence of hepatocellular adenomas was slightly increased in one study in rats fed with 200 ppm pyraclostrobin (equal to 9 mg/kg bw per day), no increase was observed in a concurrent lifetime study. Moreover, the incidence of liver adenomas in controls was considerably higher (20% versus 8%), suggesting that a low value for controls contributed to the apparent effect in the first study. There was no evidence of carcinogenic potential in mice and rats. This conclusion is supported by the observation that other strobilurin fungicides have not shown carcinogenic activity of relevance to human risk assessment.

On the basis of the above consideration and the absence of genotoxicity, the Meeting concluded that pyraclostrobin is unlikely to pose a carcinogenic risk to humans.

In a two-generation study of reproductive toxicity in rats, body-weight gains and food consumption were reduced in adults and lower body-weight gains and slightly delayed vaginal patency were observed in pups at a dose of 300 ppm (equal to 33 mg/kg bw per day). The NOAEL for general and pup toxicity was 75 ppm (equal to 8.2 mg/kg bw per day). The NOAEL for effects on reproductive performance was 300 ppm, the highest dose tested.

Two studies of developmental toxicity were conducted in rabbits and one in rats. Maternal toxicity consisting of reduced body-weight gains and food consumption was observed at 25 mg/kg bw per day and above in rats, and at 5 mg/kg bw per day and above in rabbits. In rats, the reduction in food consumption persisted beyond the treatment period and the corrected body-weight gains at termination were also reduced. In rabbits, a transient but marked reduction in food intake (and consequently in body-weight gain) after initiation of dosing was observed which resolved within 3–5 days, despite continued dosing. The pattern of the reduced body-weight gains and food consumption in rabbits indicates that they are likely to be caused by local effects on the gastrointestinal tract related to high concentrations of pyraclostrobin or taste disturbance resulting from regurgitation or leakage of the gavaging solution. Consequently, the Meeting concluded that these effects did not reflect systemic toxicity caused by pyraclostrobin. Nonetheless, the reduced nutritional status of dams, which was caused by lower food intakes at a critical time in gestation at and immediately after implantation, must be taken into account when considering the significance of the observed fetal effects at doses that were not otherwise maternally toxic. The NOAEL for maternal toxicity was 10 mg/kg bw per day in the rat and 3 mg/kg bw per day in the rabbit.

Pyraclostrobin was not teratogenic in rats, but fetal effects consisting primarily of developmental delay (incomplete ossification of sternebra and rudimentary cervical ribs) and an increased incidence of dilated renal pelves, were observed at a dose of 50 mg/kg bw per day. In

rabbits, fetal effects consisting of increased post-implantation losses were observed at and above 10 mg/kg bw per day. A slight, non-significant increase in the incidence of skeletal malformations observed at 20 mg/kg bw per day was driven by an increase in the incidence of absent lumbar vertebrae at this dose. Although the incidence was not statistically significant, it exceeded the mean of historical control values and the upper bound of the range, and the Meeting could not exclude the possibility that the effect was potentially treatment related. The effects seen in rabbit fetuses were likely to be secondary to the marked nutritional deficit in the dams at a critical time in gestation. The Meeting concluded, however, that the available data did not provide a sufficient basis on which to confidently exclude other potential mechanisms, and consequently set the NOAEL for developmental toxicity in the study in rabbits at 5 mg/kg bw per day, on the basis of these fetal effects. The developmental NOAEL for rats was 25 mg/kg bw per day.

Pyraclostrobin was investigated for neurotoxicity in rats in a study in which a single dose was administered by gavage and in a 90-day study of pyraclostrobin in the diet. The NOAELs for neurotoxicity were 2000 mg/kg bw and 750 ppm (equal to 50 mg/kg bw per day) respectively, the highest doses tested. Pyraclostrobin was not neurotoxic.

The Meeting concluded that the existing database was adequate to characterize the potential hazard of pyraclostrobin to fetuses, infants and children.

Toxicological evaluation

The Meeting established an ADI of 0–0.03 mg/kg bw based on a NOAEL of 3.4 mg/kg bw per day identified in two 2-year studies in rats, on the basis of reduced body-weight gain and altered liver and stomach histology at 200 ppm and using a 100-fold safety factor.

Pyraclostrobin is not acutely toxic and short-term dosing produced no significant general toxicity, however, fetal resorptions were increased at a dose of 10 mg/kg bw per day in a study of developmental toxicity in rabbits. Although a transient but marked reduction in food intake, and consequently in body-weight gain, was observed at doses of 5 mg/kg bw per day and above after initiation of dosing in studies of developmental toxicity in rabbits, this effect resolved within 3–5 days, despite continued dosing. The pattern of the observations indicates they are likely to be caused by local gastrointestinal tract effects related to high concentrations of pyraclostrobin, or to taste disturbance resulting from regurgitation or leakage of the gavaging solution. Consequently, the Meeting concluded that these observations did not reflect systemic toxicity caused by pyraclostrobin and were not used to establish the acute RfD. The Meeting established an acute RfD of 0.05 mg/kg bw, based on the NOAEL of 5 mg/kg bw per day for fetal toxicity at 10 mg/kg bw per day in the study of developmental toxicity in rabbits and using a 100-fold safety factor. Further information on the relationship between irritation of the gastrointestinal tract and reduced body-weight gains in pregnant rabbits, and the effect of maternal nutritional deficit on fetal resorptions, may allow the acute RfD to be refined.

A toxicological monograph was prepared.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Mouse	18-month study of toxicity and carcinogenicity ^a	Toxicity	30 ppm, equal to 4.1 mg/kg bw per day	120 ppm, equal to 17 mg/kg bw per day
		Carcinogenicity	120 ppm, equal to 17 mg/kg bw per day ^b	—
Rat	2-year study of toxicity and carcinogenicity ^a	Toxicity	75 ppm, equal to 3.4 mg/kg bw per day	200 ppm, equal to 9 mg/kg bw per day

	carcinogenicity ^a		3.4 mg/kg bw per day	mg/kg bw per day
		Carcinogenicity	200 ppm, equal to 9 mg/kg bw per day ^b	—
	3-month study of neurotoxicity ^a	Neurotoxicity	750 ppm, equal to 50 mg/kg bw per day ^b	—
		Toxicity	250 ppm equal to 17 mg/kg bw per day	750 ppm, equal to 50 mg/kg bw per day
	Two-generation study of reproductive toxicity ^a	Parental and offspring toxicity	75 ppm, equal to 8.2 mg/kg bw per day	300 ppm, equal to 33 mg/kg bw per day
	Study of developmental toxicity ^c	Maternal toxicity	10 mg/kg bw per day	25 mg/kg bw per day
		Embryo- and fetotoxicity	25 mg/kg bw per day	50 mg/kg bw per day
Rabbit	Study of developmental toxicity ^c	Maternal toxicity	3 mg/kg bw per day	5 mg/kg bw per day ^d
		Embryo- and fetotoxicity	5 mg/kg bw per day	10 mg/kg bw per day
Dog	1-year study of toxicity ^a	Toxicity	200 ppm, equal to 5.4 mg/kg bw per day	400 ppm, equal to 11 mg/kg bw per day

^a Diet

^b Highest dose tested

^c Gavage

^d A marked but transient reduction in maternal food intake occurred immediately after initiation of dosing at higher concentrations

Estimate of acceptable daily intake for humans

0–0.03 mg/kg bw

Estimate of acute reference dose

0.05 mg/kg bw

Studies that would provide information useful for continued evaluation of the compound

— Observations in humans

— Studies in rabbits to explore the relationship between a marked reduction in food intake at the start of pregnancy and fetal survival and development

Summary of critical end-points for pyraclostrobin

Absorption, distribution, excretion and metabolism in animals

Rate and extent of oral absorption

Rapid, approximately 50%

Dermal absorption

1.6–2.6% in rats in vivo, 3–8% across human skin in vitro (from an unspecified formulation)

Distribution	Rapidly and widely distributed with highest concentrations in the gastrointestinal tract, liver and kidneys
Rate and extent of excretion	Largely complete within 48 h; approximately 15% in urine and 85% in the faeces; 35–40% of the dose was excreted in the bile
Potential for accumulation	No evidence of significant accumulation
Metabolism in mammals	Extensively metabolized with subsequent glucuronide and sulphate conjugation; the metabolites are unlikely to be toxicologically significant
	No unchanged parent compound in the bile or urine and only small amounts in the faeces.
Toxicologically significant compounds (animals, plants and the environment)	Parent compound
<i>Acute toxicity</i>	
Rat, LD ₅₀ , oral	> 5000 mg/kg bw (no deaths)
Rat, LD ₅₀ , dermal	> 2000 mg/kg bw (no deaths)
Rat, LC ₅₀ inhalation	0.310–1.070 mg/l (4-h exposure, head and nose only) in acetone 4.07–7.3 mg/l (4-h exposure, head and nose only) in Solvesso solvent
Rabbit, dermal irritation	Slight but prolonged
Rabbit, eye irritation	Slight
Skin sensitization	Not sensitizing (Magnusson and Kligman)
<i>Short-term studies of toxicity</i>	
Target/critical effect	Ulceration of the glandular stomach in mice, hypertrophy of the duodenal mucosa in mice, rats and dogs, vomiting and diarrhoea in dogs, anaemia in mice and rats, decreased body-weight gains in mice, rats and dogs, hepatocellular hypertrophy in rats
Lowest relevant oral NOAEL	4 mg/kg bw per day (mice)
Lowest relevant dermal NOAEL	100 mg/kg bw per day (rats)
Lowest relevant inhalational NOAEC	No data
<i>Genotoxicity</i>	No genotoxic potential
<i>Long-term toxicity and carcinogenicity</i>	
Target/critical effect	Reduced body-weight gains in rats and mice, elevated liver weights in mice, altered liver and stomach histology in rats
Lowest relevant NOAEL	3.4 mg/kg bw per day (two 2-year studies in rats)
Carcinogenicity	Not carcinogenic in rats or mice
<i>Reproductive toxicity</i>	
Reproductive target/critical effect	None

Lowest relevant reproductive NOAEL	> 33 mg/kg bw per day (two-generation study in rats)
Developmental target/critical effect	Increased post-implantation losses and reduced fetal weight
Lowest relevant developmental NOAEL	5 mg/kg bw per day (rabbits)
<i>Neurotoxicity/delayed neurotoxicity</i>	No evidence of neurotoxicity in a 3-month study in rats at doses of up to 50 mg/kg bw per day
<i>Medical data</i>	No adverse effects have been reported but the data are limited as pyraclostrobin is a new substance

Summary	Value	Study	Safety factor
ADI	0–0.03 mg/kg bw	Rat, 2-year	100
Acute RfD	0.05 mg/kg bw	Rabbit, developmental	100

4.20 PYRETHRINS (063)

TOXICOLOGY

Pyrethrins (pyrethrum extracts) derived from chrysanthemum flowers of the genus *Chrysanthemum* have been used as insecticides for a long time. Pyrethrum, the active principle containing pyrethrin isomers, was evaluated toxicologically by the JMPR in 1965, 1966, 1967, 1968, 1969, 1970 and 1972. In 1999, the compound was re-evaluated on the basis of new studies that used a blend of refined pyrethrum extracts from plants in four major growing areas, with a total pyrethrin content of 57.6%. The 1999 JMPR established an ADI of 0–0.04 mg/kg bw on the basis of the NOAEL for liver effects in a new 2-year study in rats, and a safety factor of 100. At the same Meeting, an acute RfD of 0.2 mg/kg bw was established on the basis of the NOAEL in a study of acute neurotoxicity in rats, and a safety factor of 100.

The 1999 JMPR concluded that the increased incidences of liver and thyroid tumours observed in rats are threshold phenomena of negligible relevance to the low doses of pyrethrins to which humans are exposed. In order to confirm this, the Meeting recommended that additional studies be performed to investigate the mechanism by which pyrethrins cause tumorigenesis in the liver and thyroid. The 1999 Meeting also suggested that a test for gene mutation in mammalian cells and more detailed information on case reports of adverse health effects in humans, for which only an abstract was available, should be submitted for evaluation.

The following information was made available to the present Meeting: a new test for gene mutation in mammalian cells, the full report of the mechanistic studies on liver and thyroid tumorigenesis in rats; and the full report of the analysis of case reports of human exposures to consumer products containing pyrethrins and/or pyrethroids.

In the gene mutation test evaluated by the present Meeting, pyrethrins did not induce mutations at the thymidine kinase (TK) locus in mouse lymphoma L5178Y cells. The Meeting reaffirmed the conclusion of the 1999 JMPR that pyrethrins are not genotoxic.

In mechanistic studies of liver and thyroid tumorigenesis, treatment of rats with pyrethrins at doses of 3000 and 8000 ppm for 7, 14 and 42 days resulted in significant induction of a number of

hepatic microsomal cytochrome P-450 enzyme activities, thyroxine UDPglucuronosyltransferase activity, decreased T3 and T4 and increased thyroid-stimulating hormone (TSH) activity. Additionally, increased liver and thyroid weights in association with increased BrdU labelling indices in the liver and thyroid, and liver cell and thyroid follicular cell hypertrophy were observed. The studies were somewhat limited in that the choice of doses used did not thoroughly assess the dose concordance of the mechanistic events with the induction of tumours (e.g. a dose of 1000 ppm, which produced thyroid follicular adenoma in the long-term study of carcinogenicity in rats, was not tested). Nonetheless, the Meeting concluded that pyrethrins induce the formation of liver and thyroid tumours by mechanisms that appear to be similar to those used by other non-genotoxic, mitogenic substances, e.g. phenobarbital, which produce tumours in rodents that are not predictive of hazard in humans at relevant exposures. The Meeting thus concluded that the increased tumour incidences caused by pyrethrins are threshold phenomena of negligible toxicological relevance to humans.

Although the data on human exposure (based on case reports of 81 838 patients exposed by a variety of routes to consumer products containing pyrethrins and/or pyrethroids) did not permit ready distinction between exposure to natural pyrethrins and synthetic pyrethroids, important inferences can be made about the safety of pyrethrins. Of 49 331 cases with known medical outcomes, > 90% of patients had symptoms that were unrelated to exposure, were asymptomatic, or reported symptoms of minor severity. Major effects of exposure were reported in 114 cases, but only in 28 cases (including 7 cases of people exposed to pyrethrins) could these be confirmed as major outcomes after thorough review of the case reports. Among these 28 cases, respiratory and neurological symptoms were reported most frequently (18 and 15 cases, respectively). There was no evidence that having a history of asthma was disproportionately associated with major adverse outcomes after exposure to pyrethrins.

Toxicological evaluation

The Meeting concluded that the ADI of 0–0.04 mg/kg bw established by the 1972 JMPR and reaffirmed by the 1999 JMPR, and the acute RfD of 0.2 mg/kg bw established by the 1999 JMPR are supported by the new data.

An addendum to the toxicological monograph was prepared.

RESIDUE AND ANALYTICAL ASPECTS

Pyrethrins were evaluated for residues in a periodic review by the JMPR in 2000. The JMPR recommended withdrawal of the CXL of 3 mg/kg Po for cereal grains because no residue data were available. The 34th Session of the CCPR in 2002 decided to retain the CXL for cereal grains under the periodic review procedure since it was informed by the delegation of Germany that data would be made available. The 2003 JMPR received information on GAP for cereals from the government of Germany. New supervised residue trials for the post-harvest use of pyrethrins on wheat and maize were reported by the manufacturer.

Results of supervised trials on crops

Cereal grains. The current German label indicates that pyrethrins may be applied to stored cereal grains by cold fogging in mills and warehouses either 3 times at 2.4 g ai/100 m³ or 10 times at 0.4 g ai/100 m³. Four supervised trials each were available for stored wheat and maize grains according to maximum German GAP (3 x 2.4 g ai/100 m³). The residues of pyrethrins were <0.05 (3) and 0.19 mg/kg in wheat and <0.05 (3) and 0.05 mg/kg in maize. The combined residues of wheat and maize in rank order (median underlined) were <0.05 (6), 0.05 and 0.19 mg/kg.

The Meeting estimated a maximum residue level of 0.3 mg/kg, an STMR of 0.05 mg/kg and an HR of 0.19 mg/kg for the post-harvest use of pyrethrins on cereal grains, and recommended withdrawal of the existing CXL for cereal grains of 3 mg/kg Po.

Residues in animal commodities

The 2000 JMPR considered that an estimate of maximum residue levels for pyrethrins in animal commodities was impossible because of the lack of adequate animal feeding studies. As cereal grains are feed items, residue concentrations in cereals must be considered in the animal dietary burden calculations when feeding studies with ruminants and poultry become available in the future.

FURTHER WORK OR INFORMATION

Desirable

1. Feeding studies with ruminants (from 2000 JMPR)
2. Feeding studies with laying hens

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes (IEDI) of pyrethrins, based on the STMRs estimated by the 2000 and 2003 JMPR for 11 commodities, for the five GEMS/Food regional diets were 1% of the maximum ADI of 0.04 mg/kg bw/day (Annex 3). The Meeting concluded that the long-term intake of residues of pyrethrins resulting from the uses considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The International Estimated Short Term Intake (IESTI) for pyrethrins was calculated for 9 food commodities for which maximum residue levels were estimated by the JMPR in 2000 and 2003 and for which consumption data were available. These results are shown in Annex 4.

The IESTI represented 0-2% of the acute RfD (0.2 mg/kg bw) for the general population and 0-5% of the acute RfD for children. The Meeting concluded that the short term intake of residues of pyrethrins resulting from the uses considered by the JMPR is unlikely to present a public health concern.

4.21 TEBUFENOZIDE (196)

TOXICOLOGY

Tebufenozide was first evaluated by the 1996 JMPR, which established an ADI of 0–0.02 mg/kg on the basis of NOAELs for haematotoxicity of 50 ppm, (equal to 1.8 mg/kg bw per day) in a 1-year study in dogs, and 25 ppm (equal to 1.6 mg/kg bw per day) in a two-generation study of reproductive toxicity in rats. At the 1999 JMPR, it was recommended that the acute toxicity of tebufenozide be

evaluated as soon as possible. The 2001 JMPR evaluated the acute toxicity of tebufenozide on the basis of the available data. The Meeting established an acute reference dose (RfD) of 0.05 mg/kg bw, on the basis of a NOAEL of 5 mg/kg bw per day for haematotoxicity in a 2-week study in dogs. The Meeting noted that it might be possible to refine this estimate using the results of a study designed specifically for this purpose. After submission of data from such a study, the present Meeting reconsidered the acute RfD for tebufenozide.

Tebufenozide has low acute toxicity in rats and mice after oral ($LD_{50} > 5000$ mg/kg bw) or dermal ($LD_{50} > 5000$ mg/kg bw) exposure, and in rats after exposure by inhalation ($LC_{50} > 4.3$ mg/l air). In short-term studies of toxicity in mice, rats and dogs, the main effect was haematotoxicity, with signs of regenerative haemolytic anaemia and compensatory responses in haematopoietic tissues, accompanied by the formation of methaemoglobin. The dog was the most sensitive species, males showing slightly greater changes in several parameters than females (methaemoglobin, reticulocytes and Heinz bodies).

In the study evaluated by the present Meeting, male beagle dogs received tebufenozide in the diet such that intakes of 21.9 and 89 mg/kg bw were achieved. Animals were permitted 9 h to consume the test meal. The diet was not tested for homogeneity, stability or concentration of the test substance, but given the duration of the treatment period, this was not considered to be a serious limitation of the study. No necropsy or histopathology was undertaken but the study design was adequate for the evaluation of the acute haematotoxicity of tebufenozide (see general item 2.2 above). Blood samples were taken before, and 2, 8 and 15 days after exposure to tebufenozide. Treatment with tebufenozide had no significant effect on clinical signs or haematological parameters, including reticulocyte numbers or concentrations of serum total bilirubin. The NOAEL was 89.4 mg/kg bw, the highest dose tested.

In studies evaluated previously by the Meeting, it had been concluded that tebufenozide and its metabolites are not genotoxic. It was also concluded that tebufenozide is not embryo- or fetotoxic, or teratogenic in rats or rabbits at doses of up to 1000 mg/kg bw per day.

Toxicological evaluation

The Meeting considered that the above study in dogs was adequate for the establishment of an acute RfD for tebufenozide. Accordingly, an acute RfD of 0.9 mg/kg bw was established, based on a NOAEL of 89.4 mg/kg bw (the highest dose tested) and a safety factor of 100.

An addendum to the toxicological monograph was prepared.

RESIDUE AND ANALYTICAL ASPECTS

At the 35th Session of the CCPR, the Delegation of Australia requested the JMPR to consider the extrapolation of recommendations for MRLs for tebufenozide in cattle commodities to all mammalian species.

The Meeting recalled that tebufenozide was evaluated by the JMPR in 2001, while in 2002 the Meeting decided that it would generally use cattle feeding studies to estimate maximum residue levels for mammalian commodities to cover the potential exposure of an animal to a pesticide in the diet (Item 2.11, Report 2002). With hindsight, the case of tebufenozide was not consistent with this approach.

The Meeting recommended the withdrawal of the draft MRLs for cattle kidney (0.02* mg/kg), cattle liver (0.02* mg/kg), cattle meat (fat) (0.05 mg/kg) and cattle milk (0.01* mg/kg), to be replaced by recommendations of 0.02* mg/kg for edible offal (mammalian), 0.05 mg/kg (fat) for meat (from mammals other than marine mammals) and 0.01* mg/kg for milks.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes of tebufenozide for the five GEMS/Food regional diets, based on the STMRs estimated for 43 commodities by the 1996, 1997, 1999, 2001 and present Meeting, were in the range of 1 to 20% of the ADI (Annex 3). The Meeting concluded that the long-term intake of residues of tebufenozide resulting from its uses that have been considered by JMPR is unlikely to present a public health concern.

Short-term intake

In the 2001 Meeting, International Estimated Short Term Intake (IESTI) calculations showed an exceedence of the acute RfD for leafy vegetables, cabbage, pomefruit and grapes. In the present Meeting, based on a study better suited to assess acute toxic affects, the acute RfD of 0.05 mg/kg bw was refined to 0.9 mg/kg bw (see Toxicology comments). Therefore the IESTIs for tebufenozide were recalculated for the food commodities for which maximum residue levels were estimated and for which consumption data were available. The results are shown in Annex 4.

The IESTI represented 0-10% of the acute RfD for the general population and 0-40% of the acute RfD for children. The Meeting concluded that the short-term intake of residues of tebufenozide resulting from its uses that have been considered by JMPR is unlikely to present a public health concern.

4.22 TERBUFOS (167)

TOXICOLOGY

Terbufos is an organophosphorus compound classified as a systemic insecticide and nematocide which was last evaluated by the JMPR in 1989 when an ADI of 0–0.0002 mg/kg bw was established. Terbufos was considered by the present Meeting within the periodic review programme of the Codex Committee on Pesticide Residues.

In rats, absorption of single doses of [¹⁴C]terbufos was rapid and fairly complete. Most of the radiolabel was excreted within 24–48 h. Excretion was primarily by the urinary route (about 70–80% of the administered dose). Terbufos was extensively metabolized and little radioactivity was found in the tissues. There were no significant sex-specific differences in the toxicokinetics of terbufos.

Sulfoxidation and desulfuration of terbufos is followed by hydrolysis of the thiolo phosphorus bond (S-P), enzymatic S-methylation and then additional S-oxidation. On the basis of a 14-day study of repeated doses, terbufos showed little potential for bioaccumulation.

By analogy with other phosphorodithioate compounds, it is likely that terbufos is metabolically activated to terbufos oxon and other oxons, which cause inhibition of acetylcholinesterase activity.

Terbufos is of very high acute toxicity when administered by oral, dermal, and inhalation routes. Acute LD₅₀ values in rodents and dogs were similar, ranging from 1.4 to 9.2 mg/kg bw when administered orally. Clinical signs observed were those typical of cholinergic toxicity.

The acute LD₅₀ for terbufos administered dermally was about 1 mg/kg bw in rabbits. A single application of undiluted terbufos to the shaved skin (0.25–0.5 ml) or into the conjunctival sac (0.1 ml) of rabbits killed all animals within 24 h. The acute LC₅₀ for terbufos administered by inhalation ranged from 0.0012 to 0.0061 mg/l in rats.

In studies in rats and dogs, the critical effects of repeated doses of terbufos were inhibition of brain cholinesterase activity and associated clinical signs. NOAELs for inhibition of brain cholinesterase activity in these studies ranged from about 0.04 to 0.11 mg/kg bw per day and LOAELs ranged from about 0.085 to 0.55 mg/kg bw per day. Inhibition of brain cholinesterase activity of 7–12%, in the absence of clinical signs, was not considered toxicologically relevant. NOAELs and LOAELs for inhibition of erythrocyte cholinesterase activity were not substantially different from those for inhibition of brain cholinesterase activity.

In a 1-year study in dogs given terbufos in capsule form, the NOAEL was 0.060 mg/kg bw per day on the basis of inhibition of brain acetylcholinesterase activity at 0.090 mg/kg bw per day. The NOAELs for inhibition of brain acetylcholinesterase activity in other short-term studies in dogs were consistent with that of the 1-year study.

In an 18-month study in mice fed with terbufos, there was no evidence of carcinogenicity at doses considered relevant for risk assessment. Cholinesterase activities were not measured. The NOAEL was 3 ppm (equivalent to 0.45 mg/kg bw per day) on the basis of significant decreases in body weights at the next higher dose of 6 ppm (equivalent to 0.9 mg/kg bw per day).

A 2-year study of toxicity and carcinogenicity in rats had limitations which included outstanding questions involving the etiology and/or relationship to treatment of certain non-neoplastic findings, confounding by non-treatment related illness in test animals and the lack of supporting data to adequately quantify dietary intake, stability, and homogeneity. However, on the basis of inhibition of brain cholinesterase activity in animals receiving the highest dose, this study was considered to be adequate for testing for carcinogenicity. No increase in tumour incidence was observed after a histopathological re-evaluation of tissues for the assessment of carcinogenic potential. The NOAEL was 1 ppm (equivalent to 0.05 mg/kg bw per day) on the basis of inhibition of brain acetylcholinesterase activity at 4 ppm (equivalent to 0.2 mg/kg bw per day).

This conclusion was supported by a subsequently conducted 1-year study of toxicity in rats, in which no significant systemic or neoplastic effects were observed. The NOAEL was 1 ppm (equal to 0.055 mg/kg bw per day) on the basis of the absence of significant inhibition of brain acetylcholinesterase activity at all doses.

The Meeting concluded that terbufos was not carcinogenic in mice or rats.

The genotoxic potential of terbufos was assessed in an adequate range of in vitro and in vivo tests. Based on the overall weight of evidence from the studies of genotoxicity, the Meeting concluded that terbufos is unlikely to pose a genotoxic risk to humans.

In view of the lack of significant genotoxicity and the absence of carcinogenicity observed, the Meeting concluded that terbufos is unlikely to pose a carcinogenic risk to humans.

In a study of reproductive toxicity study in rats, mortality and clinical signs of toxicity in females, some occurrences of excess salivation in males and decreases in body weight and food consumption in both sexes were observed at 5 ppm (equal to 0.42 mg/kg bw per day), a treatment that was terminated prematurely. At a dose of 2.5 ppm, an increase in soft stools and body-weight loss was noted in lactating females. Also observed were decreases in pregnancy rate, male fertility and significant decreases in the mean body weight of viable pups on days 14 and 21 of lactation in P₁ and F₁ litters. The NOAEL for these effects on reproduction and offspring was 1.0 ppm (equal to 0.086 mg/kg bw per day). Inhibition of brain cholinesterase activity was observed in both sexes, with a NOAEL of 0.5 ppm (equal to 0.043 mg/kg bw per day).

In a study of developmental toxicity in rats, the NOAEL for maternal and developmental effects was 0.2 mg/kg bw per day, the highest dose tested. Mortality was seen at a dose of 0.4 mg/kg bw per day in a preliminary study.

In a study of developmental toxicity in rabbits, the NOAEL for maternal and developmental effects was 0.25 mg/kg bw per day on the basis of clinical and systemic findings in does, an increased

number of does with resorption sites and decreased fetal body weights at the next highest dose of 0.50 mg/kg bw per day.

The potential of terbufos to induce delayed polyneuropathy in hens when given as a single dose by gavage was assessed. The activity of neuropathy target esterase was not measured in this study. No significant changes in spinal cord and peripheral nerves were apparent in the group treated with terbufos. The Meeting concluded that at doses relevant to dietary exposure in humans, there was no concern for the induction of delayed polyneuropathy by terbufos.

In a study of neurotoxicity in which terbufos was given as a single dose by gavage to rats, mortality, clinical signs of toxicity, including miosis, and inhibition of brain and erythrocyte cholinesterase activities were noted at the highest dose tested of 0.90 mg/kg bw. The only finding at the intermediate dose (0.30 mg/kg bw) was miosis, which was observed in the absence of inhibition of concurrently measured brain and erythrocyte cholinesterase activities. No neurohistopathological lesions were found at any dose. The NOAEL was 0.15 mg/kg bw on the basis of findings of miosis in both sexes at the next highest dose of 0.30 mg/kg bw.

A 13-week study of neurotoxicity was conducted in rats. Other than a slight decrease in body weight and inhibition of brain and erythrocyte cholinesterase activities at the high dose of 3.0 ppm (equal to 0.25 mg/kg bw per day), no effects (including miosis) were observed. The NOAEL was 0.8 ppm (equal to 0.059 mg/kg bw per day) on the basis of inhibition of brain acetylcholinesterase activity at 0.25 mg/kg bw per day.

The acute oral toxicity of a number of metabolites of terbufos was evaluated in female mice. LD₅₀s were as follows: 1.1 mg/kg bw (terbufosoxon sulfoxide), 3.4 mg/kg bw (terbufos sulfoxide), 3.4 mg/kg bw (terbufosoxon sulfone), 14 mg/kg bw (terbufos sulfone), 2.2 mg/kg bw (terbufosoxon), 3670 mg/kg bw (methane, bis (*tert*-butylsulfonyl) and > 2500 mg/kg bw (methane, (*tert*-butylsulfinyl)(methylsulfinyl)).

In a comparative 14-day study in dogs, terbufos given in capsules was found to be more toxic than either terbufos sulfoxide or terbufos sulfone.

There have been a number of reports of occupational and non-occupational poisoning incidents associated with exposure to terbufos. No information was available regarding possible effects from terbufos manufacturing facilities.

The Meeting concluded that the existing database on terbufos was adequate to characterize the potential for hazard to fetuses, infants and children.

Toxicological evaluation

The Meeting established an ADI of 0-0.0006 mg/kg bw based on an overall NOAEL of 0.06 mg/kg bw per day and a safety factor of 100 for inhibition of brain cholinesterase activity, in the 1-year toxicity study, the 13-week study of neurotoxicity and the two-generation study of reproduction in rats, and the 1-year study in dogs.

The Meeting established an acute RfD of 0.002 mg/kg bw based on a NOAEL of 0.15 mg/kg bw per day for miosis in the study of neurotoxicity in rats given a single dose of terbufos, and a 100-fold safety factor. Since only in this study miosis was observed in the absence of inhibition of cholinesterase activity, it may be possible to refine the acute RfD after better characterization of this effect.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
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Mouse	18-month study of toxicity and carcinogenicity ^a	Toxicity	3 ppm, equivalent to 0.45 mg/kg bw per day	6 ppm, equivalent to 0.90 mg/kg bw per day
		Carcinogenicity	12 ppm, equivalent to 1.8 mg/kg bw per day ^d	—
Rat	2-year study of toxicity and carcinogenicity ^a	Carcinogenicity	4 ppm, nominally equivalent to 0.2 mg/kg bw per day ^d	—
		1-year study of toxicity ^a	Toxicity	1 ppm, equal to 0.055 mg/kg bw per day ^d
	13-week study of neurotoxicity ^a	Toxicity	0.8 ppm, equal to 0.059 mg/kg bw per day	3.0 ppm, equal to 0.25 mg/kg bw per day
	Single-dose study of neurotoxicity ^b	Toxicity	0.15 mg/kg bw per day	0.30 mg/kg bw per day
	Multi-generation study of reproductive toxicity ^a	Parental toxicity	0.5 ppm, equal to 0.043 mg/kg bw per day	1.0 ppm, equal to 0.086 mg/kg bw per day
		Offspring toxicity	1.0 ppm, equal to 0.086 mg/kg bw per day	2.5 ppm, equal to 0.21 mg/kg bw per day
Study of developmental toxicity ^b	Maternal toxicity	0.20 mg/kg bw per day ^d	—	
	Embryo- and fetotoxicity	0.20 mg/kg bw per day ^d	—	
Rabbit	Study of developmental toxicity ^b	Maternal toxicity	0.25 mg/kg bw per day	0.50 mg/kg bw per day
		Embryo- and fetotoxicity	0.25 mg/kg bw per day	0.50 mg/kg bw per day
Dog	1-year study of toxicity ^c	Toxicity	0.06 mg/kg bw per day	0.09 mg/kg bw per day

^a Diet^b Gavage^c Capsule^d Highest dose tested*Estimate of acceptable daily intake for humans*

0–0.0006 mg/kg bw

Estimate of acute reference dose

0.002 mg/kg bw

Studies that would provide information useful for the continued evaluation of the compound

- A study of delayed neurotoxicity with neuropathy target esterase measurements (known to be ongoing)

- Further observations in humans
- Characterization of miosis

Summary of critical end-points for terbufos

Absorption, distribution, excretion and metabolism in mammals

Rate and extent of oral absorption	Rapid and fairly complete
Dermal absorption	No specific study; rapidly penetrating following dermal or ocular application
Distribution	Relatively rapid and fairly complete
Potential for accumulation	Little
Rate and extent of excretion	Relatively rapid and complete; most eliminated in 24 to 48 h; elimination in urine predominates
Metabolism in animals	Sulfoxidation and desulfuration of terbufos is followed by hydrolysis of the thiolo-phosphorus bond (S-P), enzymatic S-methylation and then additional S-oxidation

Toxicologically significant compounds

Terbufos

Terbufos oxon

Terbufos sulfoxide

Terbufos sulfone

Terbuoxon sulfoxide

Terbuoxon sulfone

*Acute toxicity*Rat, LD₅₀, oral

1.4–9.0 mg/kg bw

Rabbit, LD₅₀, dermal

0.81–0.93 mg/kg bw

Rat, LC₅₀, inhalation

Vapour, 4-h whole body exposure: 0.0012–0.0061 mg/l

Rabbit, skin irritation

Could not be determined due to lethality

Rabbit, eye irritation

Could not be determined due to lethality

Skin sensitization

Not determined owing to potential for severe toxicity

Short-term studies of toxicity

Target/critical effect

Inhibition of brain cholinesterase activity

Lowest relevant oral NOAEL

0.059 mg/kg bw per day (13-week study of neurotoxicity in rats)

Lowest relevant dermal NOAEL

Data not available

Lowest relevant inhalation NOAEL

No appropriate data available

Genotoxicity

Unlikely to be genotoxic

Long-term studies of toxicity and carcinogenicity

Target/critical effect

Inhibition of brain cholinesterase activity

Lowest relevant NOAEL

0.055 mg/kg bw per day (1-year study in rats)

Carcinogenicity

No evidence of carcinogenicity;

Unlikely to pose a risk to humans

Reproductive toxicity

Reproduction target/critical effect

Decreases in male fertility and female pregnancy rate

Lowest relevant reproductive NOAEL

0.086 mg/kg bw per day (rats)

Developmental target/critical effect

Not teratogenic;

Reduced fetal body weight

Lowest relevant developmental NOAEL

0.25 mg/kg bw per day (rabbits)

Neurotoxicity/delayed neurotoxicity

Acute neurotoxicity

Target/critical effect	Miosis
Relevant NOAEL	0.15 mg/kg bw (rats)

13-week study of neurotoxicity

Target/critical Effect	Inhibition of brain cholinesterase activity
Relevant NOAEL	0.059 mg/kg bw per day (rats)

Delayed neuropathy

No evidence to suggest toxicity at dietary exposures

Medical data

There have been a number of reports of occupational and non-occupational poisoning incidents associated with exposure to terbufos. No information was available regarding possible effects from terbufos manufacturing facilities.

Summary	Value	Study	Safety factor
ADI	0–0.0006 mg/kg bw	Rats and dogs, overall NOAEL for studies of repeated doses	100
Acute RfD	0.002 mg/kg bw	Rat, study of acute neurotoxicity	100

Dietary risk assessment*Long-term intake*

The Meeting concluded that the long-term intake of residues of terbufos resulting from uses that have been considered by JMPR is unlikely to present a public health concern.

4.23 TOLYLFLUANID (162)**RESIDUE AND ANALYTICAL ASPECTS**

Tolylfluanid, a fungicide closely related to dichlofluanid, was first evaluated for toxicology and residues by the Meeting in 1988, with a subsequent residue evaluation in 1990. It was evaluated again in 2002 under the Periodic Review Programme where the Meeting recommended a number of MRLs and the definition of the residue as follows:

For compliance with MRLs:

tolylfluanid

For the estimation of dietary intake:

sum of tolyfluanid and *N,N*-dimethyl-*N'*-(4-methylphenyl)sulfamide expressed as tolyfluanid.

Among trials data reported to the 2002 JMPR, the results of supervised trials on lettuce conducted in southern France, Italy, Portugal and Spain could not be evaluated as the closest GAP, Slovenian GAP, requires a PHI of 21 days while the maximum sampling interval in these trials was 10 days. A new registered use on lettuce was approved in Spain which requires a PHI of 7 days. The present Meeting reviewed the results of trials conducted in southern France, Italy, Portugal and Spain taking into consideration the new registered use in Spain.

Results of supervised trials

The results of supervised trials on lettuce reported to the 2002 JMPR were evaluated in the light of the new GAP in Spain.

The sum of tolyfluanid and *N,N*-dimethyl-*N'*-(4-methylphenyl)sulfamide (DMST) was calculated and expressed as tolyfluanid on the basis of the molecular weight of tolyfluanid (347.3 g/mol) and DMST (214.3 g/mol). When tolyfluanid and/or DMST was found to be below the limit of quantification, the sum of tolyfluanid and DMST was calculated as follows and expressed as tolyfluanid:

Tolyfluanid	DMST	Total (expressed as tolyfluanid)
<0.02	<0.02	<0.02
0.10	<0.02	0.10
<0.02	0.10	0.16
0.10	0.10	0.26

Head lettuce. Trials were conducted in Belgium, France, Germany, Greece, Italy, Portugal, Spain and the UK.

The results of trials in Germany in 1987 and 1988 at a rate of 0.1 kg ai/hl (0.6 kg ai/ha, 6 applications) were evaluated against the GAP of Germany (0.1 kg ai/hl, 0.6 kg ai/ha, 6 applications, PHI 21 days). The concentrations of tolyfluanid in 8 trials that matched GAP were <0.05 (7) and 0.17 mg/kg and those of the sum of tolyfluanid and DMST expressed as tolyfluanid were <0.07 (7) and 0.17 mg/kg.

The trials carried out in Belgium, northern France, Germany and the UK in 1997 and 1998 at a rate of 0.19 kg ai/hl were not in compliance with any GAP.

The results of trials carried out in southern France, Italy, Portugal and Spain at a rate of 0.08 or 0.1 kg ai/hl were evaluated against GAP in Spain (0.06-0.1 kg ai/hl, PHI 7 days). The concentrations of tolyfluanid in 15 trials that matched GAP and one trial in Spain with a PHI of 6 days were in ranked order 0.11, 0.26, 0.98, 1.3, 1.9, 2.1, 2.3, 2.4, 2.9, 3.1, 3.2, 3.8, 4.6, 6.0, 8.5 and 9.7 mg/kg and those of the sum of tolyfluanid and DMST expressed as tolyfluanid were 0.21, 0.42, 1.2, 1.5, 2.7, 2.9, 3.5, 3.6, 3.9, 4.3, 4.4, 4.5, 5.3, 7.1, 10 and 12 mg/kg.

The trials following German GAP showed significantly lower residues than those according to Spanish GAP. The Meeting decided to base maximum residue level on the results of trials matching Spanish GAP. The Meeting estimated a maximum residue level of 15 mg/kg to replace the

recommendation by the 2007 Meeting for an MRL of 0.2 mg/kg. It also estimated an STMR of 3.75 mg/kg and an HR of 12 mg/kg.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Dietary Intakes (IEDIs) were calculated for the five GEMS/Food regional diets using STMRs for 12 commodities and STMR-Ps, for dried grapes, tomato juice and tomato paste estimated by the 2002 and the current Meetings (Annex 3). The ADI of 0-0.08 mg/kg bw was established by the 2002 Meeting. The calculated IEDIs were 0-4% of the maximum ADI. The Meeting concluded that the intake of residues of tolyfluanid and DMST resulting from the uses considered by the 2002 and the current JMPR was unlikely to present a public health concern.

Short-term intake

The International Estimated Short-Term Intakes (IESTI) for tolyfluanid and DMST were calculated for lettuce. An acute reference dose of 0.5 mg/kg bw was established by the 2002 JMPR. The IESTI for children was 40% of the acute reference dose and that for general population was 20% (Annex 4). The Meeting concluded that the short-term intake of residues of tolyfluanid and DMST from uses on lettuce was unlikely to present a public health concern.

5. RECOMMENDATIONS

5.1. The Meeting recommended (Section 2.2) that WHO establishes a Working Group, including scientists who have helped develop the concepts of the acute RfD at the JMPR, to develop further guidance on the setting of the acute RfD. In particular to give guidance on specific endpoints, guidance on how to interpret existing databases, including single-dose studies and early data from repeated-dose studies, and how to perform single-dose studies in relation to establishing an acute RfD.

5.2. The Meeting recommended (Section 2.4) that the Project to Update the Principles and Methods for the Risk Assessment of Chemicals in Food should

- give clear general principles for risk assessment procedures;
- include guidance for special toxicological considerations, such as the acute RfD;
- give general guidance for analytical methods, including fitness for purpose, sampling, and quality assurance;
- give clear guidance for exposure assessment, including assessment of acute exposures,
- include clear description, with uncertainties, of the process by which maximum residue limits (MRLs) are recommended;
- for residues of pesticides and veterinary drugs, where harmonization of certain risk assessment approaches may not be possible, give clear, transparent justifications for the differences.

5.3. The Meeting recommended (Section 2.5) selective surveys to provide data for estimating maximum residue levels for spices when adequate monitoring data are unavailable and recommended some guidelines for the selective surveys.

5.4. The Meeting recommended (Section 2.9) steps to improve the estimates of dietary intake. Immediate refinements are:

- introduce the proposed 13 sub-regional diets within the GEMS/Food regional diets project.
- increase the availability of large portion sizes and unit weights data, especially from developing countries.

Additional improvement steps recommended are:

- evaluate processing studies submitted to JMPR over the last decade to ascertain if default processing factors are feasible for some processes and/or if processing data can be extrapolated to related processes.
- refine generic and commodity-specific variability factors used in the short-term intake calculations.
- elaborate procedures for probabilistic modelling at the international level.

5.5. The Meeting recommended (Section 2.12) implementation of a pilot project on worksharing. The test compound will be trifloxystrobin at the 2004 JMPR.

5.6. The Meeting recommended (Section 2.13) implementation of a pilot project to apply the recommendations of the York Workshop and the Zoning Report and recommended that FAO initiate the project and recommend a compound suitable for the pilot project in 2004.

5.7. The Meeting recommended (Section 3) that pirimiphos-methyl, carbendazim and thiophanate-methyl should be evaluated for the establishment of acute RfDs in the near future.

6. FUTURE WORK

The items listed below should be considered by the Meeting in 2004 and 2005. The compounds listed include those recommended as priorities by the CCPR at its 35th, 36th or earlier Sessions and compounds scheduled for re-evaluation within the CCPR Periodic Review Programme.

2004 JMPR

Toxicological evaluations

New compounds

fludioxinil
trifloxystrobin

Periodic re-evaluations

glyphosate (158)
phorate (112)
pirimicarb (101)
Propiconazole (160)
triadimefon (133) {should be evaluated
triadimenol (168) {together

Evaluations

bentazone (172) - acute toxicity
captan (007) – acute toxicity
dimethipin (151) – acute toxicity
fenpropimorph (188) – acute toxicity
fenpyroximate (193) – acute toxicity
folpet (041) – acute toxicity

Residue evaluations

New compounds

fludioxinil
pyraclostrobin
Trifloxystrobin

Periodic re-evaluations

ethoprophos (149)
metalaxyl-M
paraquat (057)
prochloraz (142)
Propineb

Evaluations

chlorpyrifos (017)
dithiocarbamates (105)
Fenitrothion (037)
folpet (041)
malathion (047)
methomyl (094)
oxydemeton-methyl (166)
spinosad (203)

2005 JMPR**Toxicological evaluations***New compounds*

dimethenamid-P
fenhexamid
indoxacarb
novaluron

Periodic re-evaluations

benalaxyl (155)
clofentezine (156)
cyhexatin (067)/azocyclotin (129)
propamocarb (148)

Evaluations

carbendazim (072)-acute toxicity
chlorpropham (201)
ethoxyquin (035)
guazatine (114)
haloxyfop (194)
imazalil (110)-acute toxicity
thiabendazole (065)

Residue evaluations*New compounds*

dimethenamid-P
fenhexamid
indoxacarb
novaluron

Periodic re-evaluations

alpha and zeta cypermethrin
cypermethrin (118)
cyhexatin (067)/azocyclotin (129)
endosulfan (032)
glyphosate (158)
methoprene (147)
phorate (112)
terbufos (167)

Evaluations

ethoxyquin (035)
guazatine (114)
methiocarb (132)

ANNEX 1

ACCEPTABLE DAILY INTAKES, ACUTE REFERENCE DOSES, RECOMMENDED MAXIMUM RESIDUE LIMITS, AND SUPERVISED TRIALS MEDIAN AND HIGHEST RESIDUES RECORDED BY THE 2003 MEETING

The table below lists maximum ADIs, acute RfDs, recommended MRLs, and STMR and HR levels. The application of the HR levels is explained in the report of the 1999 Meeting (Section 2.4). 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 in which the acute RfD of a pesticide might be exceeded if the food commodity were consumed. These distinctions apply only to new compounds and to those re-evaluated within the CCPR Periodic Review Programme.

STMR levels were introduced in 1996 in response to recommendations of a Joint FAO/WHO Consultation on Guidelines for Predicting the Dietary Intake of Pesticide Residues held in York, UK, in 1995. The report of the 1996 Meeting (Section 2.2) explains the reasons for their introduction and gives details of the procedures used in their calculation. The application of the HR levels is explained in the report of the 1999 Meeting (Section 2.4).

Those pesticides for which 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 where the available information indicates that the acute RfD of a pesticide might be exceeded by consumption of the food commodity. It should be noted that these considerations apply only to new compounds and to those compounds re-evaluated within the CCPR Periodic Review Programme.

In general, the MRLs recommended for compounds that have been reviewed previously are additional to, or amend, those recorded in the reports of earlier Meetings. If a recommended MRL is an amendment the previous value is also recorded. All recommendations for compounds re-evaluated within the CCPR Periodic Review Programme are listed, however (even if identical to existing Codex or draft MRLs), because such re-evaluations replace the original evaluation rather than supplement it.

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.

Apart from the abbreviations indicated above, the following qualifications may be used in the table.

* following recommended MRL	At or about the limit of quantification
* following name of pesticide	New compound
** following name of pesticide	Reviewed in CCPR Periodic Review Programme
E (following MRLs)	The MRL is based on extraneous residues
F (following MRLs for milk)	The residue is fat-soluble and MRLs for milk and milk products are derived as explained in the introduction to volume 2 of the <i>Codex Alimentarius</i> . See also section 2 of this Report
HR-P	Highest residue in 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 mean	An STMR value for a processed commodity calculated by applying the concentration or reduction factor for the process to the STMR value calculated for the raw agricultural commodity
W in place of a recommended MRL	The previous recommendation is withdrawn, or withdrawal of the existing Codex or draft MRL is recommended

Pesticide (Codex reference no.)	ADI, mg/kg bw	CCN	Commodity	Recommended MRL, mg/kg		STMR or STMR-P, mg/kg	HR or HR-P mg/kg
				New	Previous		
Acephate** (095)	0–0.01	AL 1021	Alfalfa forage (green)	W	10		
		VS 0620	Artichoke, Globe	0.3	—	0.155	0.5
		VP 0061	Beans, except broad bean and soya bean	5 ¹	—	1.35	5.6
		VB 0400	Broccoli	W	2		
		VB 0041	Cabbages, Head	W	2		
		MF 0812	Cattle fat	W	0.1		
		MM 0812	Cattle meat	W	0.1		
		VB 0404	Cauliflower	W	2		
		SO 0691	Cotton seed	W	0.2		
		MO 0105	Edible offal (Mammalian)	0.05	—	0.022	0.022
		PE 0112	Eggs ³	0.01 (*)	0.1	0	0.01
		VB 0042	Flowerhead brassicas	2 ^{1,2}	—	0.16	2.85
		VL 0482	Lettuce, Head	W	5		
		FC 0003	Mandarins (incl. Mandarin-like hybrids)	7 ^{1,2}	—	1.15	6.5
		MM 0095	Meat (from mammals other than marine mammals)	0.05	-	0.022 (muscle) 0.022 (fat)	0.022 (muscle) 0.022 (fat)
		ML 0106	Milks	0.02	0.1	0.011	0.011
		FS 0245	Nectarine	2 ¹	—	1.35	3.2
		FS 0247	Peach	2 ¹	—	1.35	3.2
		VO 0051	Peppers	5 ^{1,2}	—	1.9	11.7
		MF 0818	Pig fat	W	0.1		
		MM 0818	Pig meat	W	0.1		
		FP 0009	Pome fruits	7 ^{1,2}	—	0.81	5.4
		VR 0587	Potato	W	0.5		
		PM 0110	Poultry meat ³	0.01 (*)	0.1	0 (fat) 0 (muscle)	0.01 (fat) 0.01 (muscle)
		PO 0111	Poultry, Edible offal of ³	0.01 (*)	—	0	0.01
		VD 0541	Soya bean (dry)	0.3	0.5	0.055	0.47
		VR 0596	Sugar beet	W	0.1		
		AV 0596	Sugar beet leaves or tops	W	10		
		VO 0448	Tomato	W	1		
		FT 0312	Tree tomato	W	0.5		

Pesticide (Codex reference no.)	ADI, mg/kg bw	CCN	Commodity	Recommended MRL, mg/kg		STMR or STMR-P, mg/kg	HR or HR-P mg/kg
				New	Previous		
¹ The information provided to the JMPR precludes an estimate that the dietary intake would be below the acute RfD for children aged ≤6 years. ² The information provided to the JMPR precludes an estimate that the dietary intake would be below the acute RfD for the general population. ³ Animal commodity, no residues expected from consumption of feed commodities with acephate residues as evaluated by JMPR <u>Residue</u> For compliance with MRLs for plant and animal commodities: acephate For estimation of dietary intake: acephate and methamidophos Acute RfD: 0.05 mg/kg bw							
Carbendazim (072)	0–0.03	VS 0621	Asparagus	0.2 C	W	0.065	0.09
		FS 0013	Cherries	10 Th	W	1.16	9.1
		VP 0526	Common bean (pods and/or immature seeds)	0.5 Th	W	0.08	0.45
		SO 0697	Peanut	0.1* Th	W	0.08	
		AL 0697	Peanut fodder ¹	3 Th	W	0.94	
		VO 0444	Peppers, Chilli	2 C		0.78	0.98
		FI 0345	Mango	5 C	W	0.4	1.7
		VD 0541	Soya bean (dry)	0.5 Th	W	0.08	
		VC 0431	Squash, Summer	0.5 Th	W	0.095	0.32
		VR 0596	Sugar beet	0.1* Th	W	0.08	0.08
		AV 0596	Sugar beet leaves or tops ¹	10 Th	W	1.4	
C: based on carbendazim use Th: based on thiophanate-methyl use ¹ Expressed on dry weight basis <u>Residue</u> (For compliance with MRLs and estimation of dietary intake): sum of benomyl, carbendazim and thiophanate-methyl, expressed as carbendazim.							
Carbofuran ¹ (096)	0–0.002	GC 0645	Maize	0.05*	W	0	
		AF 0645	Maize forage	0.2 (dry wt)		0.1 (dry wt)	
		VR 0589	Potato	0.2	0.1*	0.05	0.11
		VR 0596	Sugar beet	0.2	W	0.05	
		AV 0596	Sugar beet leaves or tops	0.7	W	0.217	
¹ The estimates for carbofuran result from the use of carbosulfan. <u>Residue</u> (For compliance with MRLs): sum of carbofuran and 3-hydroxycarbofuran expressed as carbofuran For estimation of dietary intake: sum of carbofuran, 3-hydroxycarbofuran and conjugated 3-hydroxy carbofuran expressed as carbofuran. Acute RfD: 0.009 mg/kg bw							
Carbosulfan** (145)	0–0.01	SO 0691	Cotton seed	0.05	—	0.05	
		PE 0112	Eggs	0.05*		0	0
		MO 0105	Edible offal (Mammalian)	0.05*	—	0	0
		GC 0645	Maize	0.05*	—	0	
		AF 0645	Maize forage	0.05*	—	0	
		MM 0095	Meat (from mammals other than marine mammals)	0.05* (fat)	—	0	0
		ML 0106	Milks	0.03*		0	0
		VR 0589	Potato	0.05		0.03	0.02
		PM 0110	Poultry meat	0.05*	—	0	0
		PO 0111	Poultry, Edible offal of	0.05*	—	0	0
		GC 0649	Rice	0.05*	—	0	
		VR 0596	Sugar beet	0.3		0.05	
		AV 0596	Sugar beet leaves or tops	0.05*		0	

Pesticide (Codex reference no.)	ADI, mg/kg bw	CCN	Commodity	Recommended MRL, mg/kg		STMR or STMR-P, mg/kg	HR or HR-P mg/kg
				New	Previous		
<p><u>Residue</u> (For compliance with MRLs and for estimation of dietary intake for plant and animal commodities): carbosulfan Acute RfD: 0.02 mg/kg bw Periodic review was for toxicology only</p>							
Cyprodinil* (207)	0–0.03	AM 0660	Almond hulls	0.05*		0.05	
		TN 0660	Almonds	0.02*		0.02	
		FP 0226	Apple	0.05		0.02	
		GC 0640	Barley	3		0.58	
		VP 0061	Beans, except broad bean and soya bean	0.5		0.12	
		VC 0424	Cucumber	0.2		0.08	
		DF 0269	Dried grapes (= Currants, Raisins and Sultanas)	5		1.7	
		MO 0095	Edible offal (Mammalian)	0.01*		0.01	
		VO 0440	Egg plant	0.2		0.07	
		PE 0112	Eggs ¹	0.01*		0	
		FB 0269	Grapes	3		0.79	
		VL 0482	Lettuce, Head	10		2.75	
		VL 0483	Lettuce, Leaf	10		2.75	
		MM 0095	Meat (from mammals other than marine mammals) ¹	0.01* (fat)		0 (fat) 0 (muscle)	
		ML 0106	Milks ¹	0.0004* F ²		0	
		VA 0385	Onion, bulb	0.3		0.065	
		FP 0230	Pear	1		0.26	
		VO 0445	Peppers, Sweet	0.5		0.16	
		PM 0110	Poultry meat ¹	0.01* (fat)		0 (fat) 0 (muscle)	
		PO 0111	Poultry, Edible offal of ¹	0.01*		0	
		DF 0014	Prunes	5		1.2	
		FB 0272	Raspberries, red, black	0.5		0.26	
		FS 0012	Stone fruits	2		0.68	
		AS 0081	Straw and fodder (dry) of cereal grains	10		0.395	
		FB 0275	Strawberry	2		0.31	
		VC 0431	Squash, Summer	0.2		0.08	
		VO 0448	Tomato	0.5		0.13	
		GC 0654	Wheat	0.5		0.07	
		CM 0654	Wheat bran, unprocessed	2		0.21	
			Apple pomace, wet			0.07	
		AB 0269	Grape pomace, dry			42	
<p>¹ Animal commodity, no residues are expected from consumption of feed commodities with cyprodinil residues as evaluated by JMPR. ² For cyprodinil residues in milks, the MRL is calculated as 4% of the LOQ for milk fat (0.01 mg/kg). Milk fat is the fraction of the milk that is analysed. <u>Residue</u> (For compliance with MRLs and for estimation of dietary intake for plant and animal commodities): cyprodinil. The residue is fat-soluble. Acute RfD: unnecessary</p>							
Dicloran (083)	0–0.01	FB 0269	Grapes	7	W	0.89	
		FS 0245	Nectarine	7 Po	—	2.7	
		FS 0247	Peach	7 Po	W	2.7	
<p><u>Residue</u> (For compliance with MRLs and estimation of dietary intake): dicloran The residue is fat-soluble. Acute RfD: unnecessary</p>							
Dimethoate ¹ (027)	0–0.002	VS 0620	Artichoke, Globe	0.05	—	0.1	0.2

Pesticide (Codex reference no.)	ADI, mg/kg bw	CCN	Commodity	Recommended MRL, mg/kg		STMR or STMR-P, mg/kg	HR or HR-P mg/kg
				New	Previous		
		VB 0402	Brussels sprouts	0.2	1	0.35	1.2
		VB 0041	Cabbages, Head	2 ^{2,3,4}	2 ³	0.97	3.26
		VB 0404	Cauliflower	0.2	0.5	0.025	0.13
		VS 0624	Celery	0.5	W	0.2	0.4
		FC 0001	Citrus fruits	5	W	0.27	1.4
		VL 0482	Lettuce, Head	3 ^{2,4}	0.5	0.31	2.7
		FI 0345	Mango	1 Po	—	0.36	0.68
		FT 0305	Olives	0.5	W	2.24	4.3
		VO 0051	Peppers	W	1 Po		
		VO 0445	Peppers, Sweet	5 Po ⁴	—	1.64	3.7
		GC 0654	Wheat	0.05	0.2	0.021	0.05
		AS 0654	Wheat straw and fodder, dry	1	10	0.017	
<p><u>Note:</u> The estimated STMRs and HRs were based on the sum of dimethoate and 10 times omethoate</p> <p>¹The information provided to the JMPR precludes an estimate that the dietary intake would be below the ADI.</p> <p>²The information provided to the JMPR precludes an estimate that the dietary intake would be below the acute RfD for the general population.</p> <p>³Except Cabbage, Savoy.</p> <p>⁴The information provided to the JMPR precludes an estimate that the dietary intake would be below the acute RfD for children aged ≤6 years.</p> <p><u>Residue</u> (For compliance with MRLs): dimethoate For estimation of dietary intake: dimethoate and omethoate Acute RfD: 0.02 mg/kg bw</p>							
Dodine** (084)	0–0.1	FP 0226	Apple	W	5		
		FS 0013	Cherries	3	2	1.21	2.11
		FB 0269	Grapes	W	5		
		FS 0245	Nectarine	5		1.27	3.71
		FS0247	Peach	5	5	1.27	3.71
		FP0230	Pear	W	5		
		FP 0009	Pome fruits	5		1.70	2.43
		FB0275	Strawberry	W	5		
<p><u>Residue</u> (For compliance with MRLs and for estimation of dietary intake): dodine Acute RfD: 0.2 mg/kg bw</p>							
Famoxadone* (208)	0–0.006	GC 0640	Barley	0.2		0.02	
		AS 0640	Barley straw and fodder, dry	5		0.99	
		VC 0424	Cucumber	0.2		0.025	0.10
		FB 0269	Grapes	2		0.54	1.5
		AB 0269	Grape pomace dry	7		1.94	
		DF 0269	Dried grapes (raisins)	5		1.03	2.85
		MO 0105	Edible offal (Mammalian)	0.5		0.046	0.24
		PE 0112	Eggs ¹	0.01*		0	0
		MM 0095	Meat (from mammals other than marine mammals)	0.5 fat		0.005 (muscle) 0.067 (fat)	0.031 (muscle) 0.41 (fat)
		ML 0106	Milks	0.03 (F)		0.009	
		VR 0589	Potato	0.02*		0.0	0.0
		PM 0110	Poultry meat ¹	0.01*		0 (muscle) 0 (fat)	0 (muscle) 0 (fat)
		PM 0111	Poultry, Edible offal of ¹	0.01*		0	0
		VC 431	Squash, Summer	0.2		0.025	0.10
		VO 0448	Tomato	2		0.105	1.1
		GC 0654	Wheat	0.1		0.02	
		CM 0654	Wheat bran, unprocessed	0.2		0.04	
		AS 0654	Wheat straw and fodder, dry	7		2.28	

Pesticide (Codex reference no.)	ADI, mg/kg bw	CCN	Commodity	Recommended MRL, mg/kg		STMR or STMR-P, mg/kg	HR or HR-P mg/kg
				New	Previous		
¹ Animal commodity, no residues expected from consumption of feed commodities with famoxadone residues as evaluated by JMPR. <u>Residue</u> (For compliance with MRLs and for estimation of dietary intake for plant and animal commodities): famoxadone. The compound is fat-soluble Acute RfD: 0.6 mg/kg bw							
Fenitrothion **(037) ¹	0-0.005	FP 0226	Apple	W	0.5 ²		
		VB 0041	Cabbages, head	W	0.5 ²		
		SB 0715	Cacao beans	W	0.1 ²		
		VB 0404	Cauliflower	W	0.1 ²		
		GC 0080	Cereal grains	10 Po ³	10 Po	5	7.6
		FS 0013	Cherries	W	0.5 ²		
		FC 0001	Citrus fruits	W	2 ²		
		VC 0424	Cucumber	W	0.05 (*) ²		
		VO 0440	Eggplant	W	0.1 ²		
		FB 0269	Grapes	W	0.5 ²		
		VA 0384	Leek	W	0.2 ²		
		VL 0482	Lettuce, Head	W	0.5 ²		
		MM 0095	Meat (from mammals other than marine mammals)	W	0.05 (*) (fat) E		
		ML 0812	Milks	W	0.002 (*) E		
		VA 0385	Onion, Bulb	W	0.05 (*) ²		
		FS 0247	Peach	W	1 ²		
		FP 0230	Pear	W	0.5 ²		
		VP 0063	Peas (pods and succulent = immature seeds)	W	0.5 ²		
		VO 0051	Peppers	W	0.1 ²		
		VR 0589	Potato	W	0.05 (*) ²		
		VR 0494	Radish	W	0.2 ²		
		CF 0649	Rice bran, unprocessed	W	20 PoP		
		CM 1205	Rice, polished	W	1 PoP		
VD 0541	Soya beans, dry	W	0.1 ²				
FB 0275	Strawberry	W	0.5 ²				
DT 1114	Tea, Green, Black	W	0.5 ²				
VO 0448	Tomato	W	0.5 ²				
CF 0654	Wheat bran, processed	W	2 PoP				
CM 0654	Wheat bran, unprocessed	30 PoP	20 PoP	19.75	30.02		
CF 1211	Wheat flour	W	2 PoP	1.175			
CF 1212	Wheat wholemeal	W	5 PoP				
CP 1211	White bread	W	0.2 PoP	0.05			
¹ The information provided to the JMPR precludes an estimate that the dietary intake would be below the ADI. ² The CXL was already deleted by the CAC in June 2003. ³ The information provided to the JMPR precludes an estimate that the dietary intake would be below the acute RfD. <u>Residue</u> (For compliance with MRLs and for estimation of dietary intake for plant and animal commodities): fenitrothion. The compound is fat-soluble. Acute RfD: 0.04 mg/kg bw							
Lindane** (048)	0-0.005	GC 0640	Barley	0.01 (*)		0.005	0.005
		VR 0577	Carrot	W	0.2 E		
		MO 0105	Edible offal (Mammalian)	0.01*		0.0002	0.002
		PE 0112	Eggs	0.01*	0.1 E	0.0007	0.002
		GC 0645	Maize	0.01 (*)		0.005	0.005
		MM 0095	Meat (from mammals other than marine mammals)	0.1 (fat)		0.0007 (muscle) 0.008 (fat)	0.005 (muscle) 0.06 (fat)

Pesticide (Codex reference no.)	ADI, mg/kg bw	CCN	Commodity	Recommended MRL, mg/kg		STMR or STMR-P, mg/kg	HR or HR-P mg/kg
				New	Previous		
		ML 0106	Milks	0.01*		0.0003	
		GC 0647	Oats	0.01 (*)		0.005	0.005
		PO 0111	Poultry, Edible offal of	0.01*		0.0004	0.001
		PM 0110	Poultry meat	0.05 (fat)	0.7 (fat) E	0.0006 (muscle) 0.008 (fat)	0.001 (muscle) 0.016 (fat)
		SO 0495	Rape seed	W	0.05 (*)		
		GC 0650	Rye	0.01 (*)		0.005	0.005
		GC 0651	Sorghum	0.01 (*)		0.005	0.005
		AS 0081	Straw and fodder (dry) of cereal grains	0.01 (*)		0.005	0.005
		VR 0596	Sugar beet	W	0.1		
		AV 0596	Sugar beet leaves or tops	W	0.1		
		VO 1275	Sweet corn (kernels)	0.01 (*)		0.005	0.005
		GC 0654	Wheat	0.01 (*)		0.005	0.005
<p><u>Residue</u> (For compliance with MRLs and for estimation of dietary intake for plant and animal commodities): lindane. The residue is fat-soluble Acute RfD: 0.06 mg/kg</p>							
Malathion (049)	0–0.3	Acute RfD: 2 mg/kg bw					
Methamidophos** (100)	0–0.004	AL 1021	Alfalfa forage (green)	W	2		
		VS 0620	Artichoke, Globe	0.2 (Ac)	—	0.03	0.08
		VB 0041	Cabbages, Head ²	1	0.5	0.04	0.62
		MF 0812	Cattle fat	W	0.01 *		
		MM 0812	Cattle meat	W	0.01 *		
		VB 0404	Cauliflower	W	0.5		
		VP 0061	Beans, except broad bean and soya bean	1 (Ac) ³	—	0.17	0.54
		SO 0691	Cotton seed	0.2	0.1	0.01	0.16
		MO 0105	Edible offal (Mammalian)	0.01 *		0.01	0.01
		PE 0112	Eggs ¹	0.01 *		0	0.01
		VB 0042	Flowerhead brassicas	0.5 (Ac) ³	—	0.02	0.33
		AV 1051	Fodder beet	0.02		0.01	0.01
		AM1051	Fodder beet leaves or tops	30		9.1	26.5
		MF 0814	Goat fat	W	0.01 *		
		MM 0814	Goat meat	W	0.01 *		
		VL 0482	Lettuce, Head	W	1		
		FC 0003	Mandarins (including mandarin-like hybrids)	0.5 (Ac) ³	—	0.085	0.26
		MM 0095	Meat (from mammals other than marine mammals)	0.01 *		0.01 (muscle) 0.01 (fat)	0.01 (muscle) 0.01 (fat)
		ML 0106	Milks	0.02	0.01 *	0.01	0.011
		FS 0245	Nectarine	0.5 (Ac) ³		0.19	0.35
FS 0247	Peach	0.5 (Ac) ³	1	0.19	0.35		
VO 0444	Peppers, Chilli	W	2				
VO 0445	Peppers, Sweet	W	1				
VO 0051	Peppers	2 (Ac) ³		0.25	1.6		
MF 0818	Pig fat	W	0.01 *				
MM 0818	Pig meat	W	0.01 *				
FP 0009	Pome fruits	0.5 (Ac) ^{2,3}	0.5	0.06	0.28		
VR 0587	Potato	0.05	0.05	0.01	0.02		
PM 0110	Poultry meat ¹	0.01 *		0 (muscle) 0 (fat)	0.01 (muscle) 0.01 (fat)		
PO 0111	Poultry, Edible offal of ¹	0.01 *		0	0.01		

Pesticide (Codex reference no.)	ADI, mg/kg bw	CCN	Commodity	Recommended MRL, mg/kg		STMR or STMR-P, mg/kg	HR or HR-P mg/kg
				New	Previous		
		MF 0822	Sheep fat	W	0.01 *		
		MM 0822	Sheep meat	W	0.01 *		
		VD 0541	Soya bean (dry)	0.1 (Ac)	0.05	0.01	0.06
		VR 0596	Sugar beet	0.02	0.03	0.01	0.01
		AV 0596	Sugar beet leaves or tops	30	1	9.1	26.5
		VO 0448	Tomato	2 ²	1	0.285	1.5
		FT 0312	Tree tomato	W	0.01	—	—
<p><u>Note:</u> (Ac) residues from use of acephate</p> <p>¹ Animal commodity, no residues expected from consumption of feed commodities with acephate residues as evaluated by JMPR</p> <p>² The information provided to the JMPR precludes an estimate that the dietary intake would be below the acute RfD.</p> <p>³ This recommendation arises from the use of acephate. The information provided to the JMPR precludes an estimate that the dietary intake of acephate (acephate and methamidophos) would be below the acute RfD for acephate, see acephate.</p> <p><u>Residue</u> (For compliance with MRLs and for estimation of dietary intake for plant and animal commodities): methamidophos Acute RfD: 0.01 mg/kg bw</p>							
Methoxyfenozide* (209)	0-0.1	AM 0660	Almond hulls	50		13	
		AB 0226	Apple pomace, dry	7		1.3 (wet)	
		VB 0400	Broccoli	3		0.94	1.6
		VB 0041	Cabbages, head	7		0.93	6.2
		VS 0624	Celery	15		3.4	7.8
		SO 0691	Cotton seed	7		0.46	4.9
		DF 0269	Dried grapes (raisins)	2		0.73	1.8
		MO 0105	Edible offal (Mammalian)	0.02		0.0075	0.017
		PE 0112	Eggs	0.01		0	0.003
		FB 0269	Grapes	1		0.33	0.84
		VL 0482	Lettuce, Head	15		6.1	9.6
		VL 0483	Lettuce, Leaf	30		12	18
		GC 0645	Maize	0.02 (*)		0.02	0.02
		AS 0645	Maize fodder	60 (dry wt)		8.2	
		AF 0645	Maize forage	50 (dry wt)		4.5	
		MM 0095	Meat (from mammals other than marine mammals)	0.05(fat)		0.003 (muscle) 0.0082 (fat)	0.0017 (muscle) 0.046 (fat)
		ML 0106	Milks	0.01		0.0041	
		VL 0485	Mustard greens	30		16	18
		VO 0051	Peppers	2		0.16	0.94
		FP 0009	Pome fruits	2		0.43	1.0
		PM 0110	Poultry meat ¹	0.01 (*)		0 (muscle) 0 (fat)	0 (muscle) 0 (fat)
		PO 0111	Poultry, Edible offal of ¹	0.01 (*)		0	0
		DF 0014	Prunes (dried plums)	3		0.44	1.8
		VL 0502	Spinach	50 ²		15	43
		FS 0012	Stone fruits	2		0.34	1.4
		VO 0447	Sweet corn (corn-on- the-cob)	0.02 (*)		0.0	0.02
		VL 0448	Tomato	2		0.20	1.8
		TN 0085	Tree nuts	0.1		0.012	0.074
			Cotton gin by-products			11	18

Pesticide (Codex reference no.)	ADI, mg/kg bw	CCN	Commodity	Recommended MRL, mg/kg		STMR or STMR-P, mg/kg	HR or HR-P mg/kg
				New	Previous		
¹ Animal commodity, no residues expected from consumption of feed commodities with methoxyfenozide residues as evaluated by the JMPR ² The information provided to the JMPR precludes an estimate that the dietary intake would be below the acute RfD for children. <u>Residue</u> (For compliance with MRLs and for estimation of dietary intake for plant and animal commodities): methoxyfenozide. Acute RfD: 0.9 mg/kg bw The residue is fat-soluble, but is not classed as fat-soluble with respect to its distribution in milk.							
Paraquat ¹ (057)	0–0.005	Previous ADI: 0.004 (1986) Acute RfD: 0.006 mg/kg bw ¹ The information provided to the JMPR precludes an estimate that the dietary intake would be below the ADI. <u>Note:</u> no short-term dietary intake was calculated due to insufficient data.					
Parathion-methyl (059)	0–0.003	FS 0245	Nectarine	0.3		0.095	0.22
<u>Residue</u> For compliance with MRLs: parathion-methyl For estimation of dietary intake: sum of parathion-methyl and paraoxon-methyl expressed as parathion-methyl Acute RfD: 0.03 mg/kg bw							
Phosmet (103)	0–0.01	Acute RfD: 0.2 mg/kg bw Previous acute RfD : 0.02 mg/kg bw (1998)					
Pirimiphos-methyl (086)	0–0.03	FP 0226	Apple	W	2		
		VB 0402	Brussels sprouts	W	2		
		VB 0041	Cabbages, head	W	2		
		VR 0577	Carrot	W	1		
		VB 0404	Cauliflower	W	2		
		GC 0080	Cereal grains	7 Po	10 Po	2.3	4.5
		FS 0013	Cherries	W	2		
		FC 0001	Citrus fruits	W	2		
		VP 0526	Common bean (pods and/or immature seeds)	W	0.5		
		VC 0424	Cucumber	W	1		
		FB 0278	Currant, black	W	1		
		DF 0295	Dates, dried or dried and candied	W	0.5 Po		
		MD 0180	Dried fish	W	8 Po		
		PE 0112	Eggs	W	0.05		
		FB 0268	Gooseberry	W	1		
		FI 0341	Kiwifruit	W	2		
		VL 0482	Lettuce, Head	W	5		
		MM 0095	Meat (from mammals other than marine mammals)	W	0.05		
		ML 0106	Milks	0.01	0.05	0.003	
		VO 0450	Mushrooms	W	5		
FT 0305	Olives	W	5				
SO 0697	Peanut	W	2 Po				
OC 0697	Peanut oil, crude	W	15 PoP				
OR 0697	Peanut oil, edible	W	15 PoP				
SO 0703	Peanut, whole	W	25 Po				
FP 0230	Pear	W	2				
VP 0063	Peas (pods and succulent = immature seeds)	W	0.05				
VO 0051	Peppers	W	1				
FS 0014	Plums (including Prunes)	W	2				
VR 0589	Potato	W	0.05				
FB 0272	Raspberries, Red, Black	W	1				

Pesticide (Codex reference no.)	ADI, mg/kg bw	CCN	Commodity	Recommended MRL, mg/kg		STMR or STMR-P, mg/kg	HR or HR-P mg/kg
				New	Previous		
		CM 1206	Rice bran, unprocessed	W	20 PoP		
		CM 0649	Rice, husked	W	2 PoP		
		CM 1205	Rice, polished	W	1 PoP		
		CF 1251	Rye wholemeal	W	5 PoP		
		VL 0502	Spinach	W	5		
		VA 0389	Spring onion	W	1		
		FB 0275	Strawberry	W	1		
		VO 0448	Tomato	W	1		
		CM 0654	Wheat bran, unprocessed	15 PoP	20 PoP	5.1	
		CF 1211	Wheat flour	W	2 PoP	0.39	
		CF 1212	Wheat wholemeal	W	5 PoP	1.6	
		CP 1211	White bread	W	0.5 PoP	0.22	
		CP 1212	Wholemeal bread	W	1 PoP	0.83	
<p>Residue (For compliance with MRLs and for estimation of dietary intake for plant and animal commodities) : pirimiphos-methyl The residue is fat-soluble.</p>							
Pyraclostrobin * (207)	0-0.03	Acute RfD : 0.05 mg/kg bw					
Pyrethrins (063)	0-0.04	GC 0080	Cereal grains	0.3 Po	3 Po	0.05	0.19
<p>Residue (For compliance with MRLs and estimation of dietary intake for plant and animal commodities): total pyrethrins, calculated as the sum of pyrethrins 1 and 2, cinerins 1 and 2, and jasmolins 1 and 2, determined after calibration with World Standard pyrethrum extract. The residue is fat-soluble. Acute RfD: 0.2 mg/kg bw</p>							
Tebufenozide (196)	0-0.02	MO 1280	Cattle, kidney	W ¹	0.02*	0.006	0.006
		MO 1281	Cattle, liver	W ¹	0.02*	0.02	0.02
		MM 0812	Cattle meat	W	0.05 (fat)	0.006	0.006
		ML 0812	Cattle milk	W	0.01*	0.003	
		MO 0105	Edible offal (Mammalian)	0.02*	—	0.02	0.02
		MM 0095	Meat (from mammals other than marine mammals)	0.05 (fat)	—	0.006 (muscle) 0.015 (fat)	0.006 (muscle) 0.029 (fat)
		ML 0106	Milks	0.01*	—	0.003	
<p>¹Replaced by edible offal (mammalian) Residue (For compliance with MRLs and for estimation of dietary intake) for plant and animal commodities: tebufenozide The residue is fat-soluble. Acute RfD: 0.9 mg/kg Previous acute RfD: 0.05 mg/kg bw (2001 JMPR)</p>							
Terbufos ** (167)	0-0.0006	Previous ADI:0-0.0002 mg/kg bw Acute RfD: 0.002 mg/kg Periodic review was for toxicology only Note: No short-term dietary intake was calculated because of insufficient data.					
Thiophanate- methyl (077)	0-0.08	See recommendations for carbendazim. Acute RfD: unnecessary					
Tolylfluanid (162)	0-0.08	VL 0482	Lettuce, Head	15	0.2	3.75 ^{1/}	12 ¹
<p>¹ Sum of tolylfluanid and <i>N,N</i>-dimethyl-<i>N'</i>-(4-methylphenyl)sulfamide expressed as tolylfluanid Residue (For compliance with MRL for plant commodities): tolylfluanid For the estimation of dietary intake for plant commodities: sum of tolylfluanid and <i>N,N</i>-dimethyl- <i>N'</i>-(4-methylphenyl)-sulfamide expressed as tolylfluanid Acute RfD: 0.5 mg/kg bw</p>							

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)
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)
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)
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)
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)
Azocyclotin (129)	1979 (R), 1981 (T), 1982 (R), 1983 (R), 1985 (R), 1989 (T,R), 1991 (R), 1994 (T)
Benalaxyl (155)	1986 (R), 1987 (T), 1988 (R), 1992 (R), 1993 (R)
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)
BHC (technical-grade)	1965 (T), 1968 (T,R), 1973 (T,R) (see also Lindane)
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)

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)
<i>sec</i> -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)
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)
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)
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)
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)
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	1965 (T), 2000 (T), 2001 (R)
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)
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)
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)	1986 (R), 1987 (T and corr. to 1986 report), 1989 (R), 1990 (R), 1992 (R)
Cyhalothrin (146)	1984 (T,R), 1986 (R), 1988 (R)
Cyhexatin (tricyclohexyltin hydroxide) (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)
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)
Cyprodinil (207)	2003 (T,R)
Cyromazine (169)	1990 (T,R), 1991 (corr. to 1990 R evaluation), 1992 (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- <i>S</i> -methyl (073)	1973 (T,R), 1979 (R), 1982 (T), 1984 (T,R), 1989 (T,R), 1992 (R), 1998 (R)
Demeton- <i>S</i> -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)
1,2-Dibromoethane (023)	1965 (T,R), 1966 (T,R), 1967 (R), 1968 (R), 1971 (R), 1979 (R), 1985 (R)
Dicloran (083)	2003 (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)
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)
Diflubenzuron (130)	1981 (T,R), 1983 (R), 1984 (T,R), 1985 (T,R), 1988 (R), 2001 (T), 2002 (R)
Dimethipin (151)	1985 (T,R), 1987 (T,R), 1988 (T,R), 1999 (T), 2001 (R)
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)
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)
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)
4,6-Dinitro- <i>ortho</i> -cresol (DNOC)	1965 (T)
Dodine (084)	1974 (T,R), 1976 (T,R), 1977 (R), 2000 (T), 2003 (R)
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)
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)
Ethopropophos (149)	1983 (T), 1984 (R), 1987 (T), 1999 (R)
Ethoxyquin (035)	1969 (T,R), 1998 (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)
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)
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)
Fenpropathrin (185)	1993 (T,R)
Fenpropimorph (188)	1994 (T), 1995 (R), 1999 (R), 2001 (T)
Fenpyroximate (193)	1995 (T,R), 1996 (corr. to 1995 report.), 1999 (R)
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	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)
Flumethrin (195)	1996 (T,R)
Flusilazole (165)	1989 (T,R), 1990 (R), 1991 (R), 1993 (R), 1995 (T)
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)
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)
Guazatine (114)	1978 (T,R), 1980 (R), 1997 (T,R)
Haloxyfop (194)	1995 (T,R), 1996 (R and corr. to 1995 report), 2001 (R)
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)
Imidacloprid	2001 (T), 2002 (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)
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,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	2002 (T)
Methacrifos (125)	1980 (T,R), 1982 (T), 1986 (T), 1988 (T), 1990 (T,R), 1992 (R)
Methamidiphos (100)	1976 (T,R), 1979 (R), 1981 (R), 1982 (T,R ²), 1984 (R), 1985 (T), 1989 (R), 1990 (T,R), 1994 (R), 1996 (R), 1997 (R), 2002 (T), 2003 (R)
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)
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)
Methoprene (147)	1984 (T,R), 1986 (R), 1987 (T and corr. to 1986 report), 1988 (R), 1989 (R), 2001 (T)
Methoxychlor	1965 (T), 1977 (T)
Methoxyfenozide (209)	2003 (T,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)
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 (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)
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)
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)
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)
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)
Pirimiphos-methyl (086)	1974 (T,R), 1976 (T,R), 1977 (R), 1979 (R), 1983 (R), 1985 (R), 1992 (T), 1994 (R), 2003 (R)
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)
Procymidone(136)	1981 (R), 1982 (T), 1989 (T,R), 1990 (R), 1991 (corr. to 1990 Annex I), 1993 (R), 1998 (R)
Profenofos (171)	1990 (T,R), 1992 (R), 1994 (R), 1995 (R)
Propamocarb (148)	1984 (T,R), 1986 (T,R), 1987 (R)
Propargite (113)	1977 (T,R), 1978 (R), 1979 (R), 1980 (T,R), 1982 (T,R), 1999 (T), 2002 (R)
Propham (183)	1965 (T), 1992 (T,R)
Propiconazole (160)	1987 (T,R), 1991 (R), 1994 (R)
Propineb	1977 (T,R), 1980 (T), 1983 (T), 1984 (R), 1985 (T,R), 1993 (T,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)
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)
Pyriproxyfen (200)	1999 (R,T), 2000 (R), 2001 (T)
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	2001 (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)
Terbufos (167)	1989 (T,R), 1990 (T,R), 2003 (T)
Thiabendazole (065)	1970 (T,R), 1971 (R), 1972 (R), 1975 (R), 1977 (T,R), 1979 (R), 1981 (R), 1997 (R), 2000 (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)
Thiram (105)	1990 (R), 1994 (R), 1995 (T,E), 1998 (T,R) 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)
Tolyfluanid (162)	1988 (T,R), 1990 (R), 1991 (corr. to 1990 report), 2002 (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)
Triadimenol (168)	1989 (T,R), 1992 (R), 1995 (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)
Trichlorfon (066)	1971 (T,R), 1975 (T,R), 1978 (T,R), 1987 (R)
Trichloronat	1971 (T,R)
Trichloroethylene	1968 (R)
Tricyclohexyltin hydroxide	See Cyhexatin
Triforine (116)	1977 (T), 1978 (T,R), 1997 (T)
Triphenyltin compounds	See Fentin compounds
Vamidotion (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)

ANNEX 3

INTERNATIONAL ESTIMATED DAILY INTAKES OF PESTICIDE RESIDUES

The following tables give details of the International Estimated Daily Intakes of the pesticides evaluated by the Meeting for the five GEMS/ Food Diets, and show the ratios of the estimated intakes to the corresponding ADIs.

(*) at or about the LOQ

The ranges of the intake:ADI ratios for all the compounds evaluated are tabulated in Section 3.

ACEPHATE

ADI= 0 - 0.01 mg/kg bw

International Estimated Daily Intake (IEDI)

Diets: g/person/day. Intake = daily intake: µg/person												
Code	Commodity	STMR or STMR-P	Mid-East		Far-East		African		Latin American		European	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
FP 0226	Apple (note 1)	0.81	7.5	6.1	4.7	3.8	0.3	0.2	5.5	4.5	40.0	32.4
JF 0226	Apple juice	0.81	4.5	3.6	0	0.0	0	0.0	0.3	0.2	3.8	3.1
VS 0620	Artichoke globe	1.55	2.3	3.6	0.0	0.0	0.0	0.0	0.0	0.0	5.5	8.5
VP 0061	Beans except broad bean & soya bean (green pods & immature seeds)	1.35	3.9	5.3	0.9	1.2	0.0	0.0	4.4	5.9	13.2	17.8
VB 0400	Broccoli (note 2)	0.16	0.5	0.1	1.0	0.2	0.0	0.0	1.1	0.2	2.7	0.4
VB 0401	Broccoli, Chinese (note 2)	0.16	-	-	-	-	-	-	-	-	-	-
VB 0404	Cauliflower (note 2)	0.16	1.3	0.2	1.5	0.2	0	0.0	0.3	0.0	13	2.1
MO 0105	Edible offal (mammalian)	0.022	4.2	0.1	1.4	0.0	2.8	0.1	6.1	0.1	12.4	0.3

Diets: g/person/day. Intake = daily intake: µg/person												
Code	Commodity	STMR or STMR-P	Mid-East		Far-East		African		Latin American		European	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
PE 0112	Eggs	0	14.6	0.0	13.1	0.0	3.7	0.0	11.9	0.0	37.6	0.0
FC 0003	Mandarins (incl. Mandarin-like hybrids)	1.15	8.8	10.1	0.2	0.2	0.0	0.0	6.3	7.2	6.0	6.9
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0.022	7.4	0.2	6.6	0.1	4.8	0.1	9.4	0.2	31.1	0.7
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0.022	29.6	0.7	26.2	0.6	19.0	0.4	37.6	0.8	124.4	2.7
ML 0106	Milks	0.011	116.9	1.3	32.1	0.4	41.8	0.5	160.1	1.8	289.3	3.2
-d	Peaches & nectarines	1.35	2.5	3.4	0.5	0.7	0.0	0.0	0.8	1.1	12.5	16.9
FP 0230	Pear (note 1)	0.81	3.3	2.7	2.8	2.3	0.0	0.0	1.0	0.8	11.3	9.2
VO 0051	Peppers	1.9	3.4	6.5	2.1	4.0	5.4	10.3	2.4	4.6	10.4	19.8
PM 0110	Poultry meat: 10% as fat	0	3.1	0.0	1.3	0.0	0.6	0.0	2.5	0.0	5.3	0.0
PM 0110	Poultry meat: 90% as muscle	0	27.9	0.0	11.9	0.0	5.0	0.0	22.8	0.0	47.7	0.0
PO 0111	Poultry, edible offal of	0	0.1	0.0	0.1	0.0	0.1	0.0	0.4	0.0	0.4	0.0
FP 0231	Quince (note 1)	0.81	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
VD 0541	Soya bean (dry)	0.055	4.5	0.2	2.0	0.1	0.5	0.0	0.0	0.0	0.0	0.0
OC 0541	Soya bean oil, crude	0.023	1.3	0.0	1.7	0.0	3.0	0.1	14.5	0.3	4.3	0.1
			Total intake (µg/person)=	44.0		13.9		11.7		27.9		124.1
			Bodyweight per region (kg bw) =	60		55		60		60		60
			ADI (µg/person)=	600		550		600		600		600
			%ADI=	7.3%		2.5%		2.0%		4.7%		20.7%
			Rounded %ADI=	7%		3%		2%		5%		20%

Note 1: Group maximum residue level proposed for pome fruit

Note 2: Group maximum residue level proposed for flowerhead brassicas

CARBENDAZIM (072) ADI= 0 - 0.03 mg/kg bw/day

International Estimated Daily Intake (IEDI)

Diets: g/person/day. Intake = daily intake: µg/person					
	Mid-East	Far-East	African	Latin American	European

Code	Commodity	STMR or STMR-P mg/kg	diet	intake	diet	intake	diet	diet	intake	diet	intake	
VS 0621	Asparagus	0.065	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.5	0.1
FI 0327	Banana	0.03	8.3	0.2	26.2	0.8	21.0	0.6	102.3	3.1	22.8	0.7
GC 0640	Barley (fresh)	0.05	1.0	0.1	3.5	0.2	1.8	0.1	6.5	0.3	19.8	1.0
VD 0071	Beans (dry)	0.165	2.3	0.4	4.8	0.8	0.0	0.0	13.0	2.1	3.5	0.6
VB 0402	Brussels sprouts	0.065	0.5	0.0	1.0	0.1	0.0	0.0	1.1	0.1	2.7	0.2
VR 0577	Carrot	0.04	2.8	0.1	2.5	0.1	0.0	0.0	6.3	0.3	22.0	0.9
MM 0812	Cattle meat	0	14.6	0.0	2.7	0.0	10.4	0.0	30.0	0.0	63.3	0.0
FS 0013	Cherries	1.16	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.0	3.5
VP 0526	Common bean (green pods and/or immature seeds)	0.08	3.5	0.3	0.8	0.1	0.0	0.0	4.0	0.3	12.0	1.0
VC 0424	Cucumber	0.05	2.4	0.1	2.3	0.1	0.0	0.0	4.2	0.2	4.5	0.2
MO 0105	Edible offal (mammalian)	0	4.2	0.0	1.4	0.0	2.8	0.0	6.1	0.0	12.4	0.0
PE 0112	Eggs	0	14.6	0.0	13.1	0.0	3.7	0.0	11.9	0.0	37.6	0.0
VP 0529	Garden pea, shelled (immature seeds)	0.01	4.0	0.0	0.5	0.0	0.0	0.0	0.2	0.0	10.1	0.1
VC 0425	Gherkin	0.05	2.4	0.1	2.3	0.1	0.0	0.0	4.2	0.2	4.5	0.2
FB 0269	Grapes (fresh, wine, excluding dried grapes)	0.87	15.8	13.7	1.0	0.9	0.0	0.0	1.3	1.1	13.8	12.0
FI 0345	Mango	0.4	2.3	0.9	5.3	2.1	3.4	1.4	6.3	2.5	0.0	0.0
ML 0106	Milks	0	116.9	0.0	32.1	0.0	41.8	0.0	160.1	0.0	289.3	0.0
JF 0004	Orange juice	0.13	7.3	0.9	0.0	0.0	0.0	0.0	0.3	0.0	4.5	0.6
FC 0004	Oranges, sweet, sour (incl. Orange-like hybrids)	0.325	31.5	10.2	4.0	1.3	4.8	1.6	31.0	10.1	29.8	9.7
FS 0247	Peach	0.255	1.3	0.3	0.3	0.1	0.0	0.0	0.4	0.1	6.3	1.6
SO 0697	Peanut	0.08	0.3	0.0	0.2	0.0	2.3	0.2	0.3	0.0	3.0	0.2
VO 0444	Peppers, chili	0.78	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
FI 0353	Pineapple (fresh)	0.03	0.0	0.0	9.3	0.3	2.6	0.1	15.5	0.5	1.3	0.0
FS 0014	Plums (fresh, prunes)	0.06	1.8	0.1	0.5	0.0	0.0	0.0	0.0	0.0	4.3	0.3
FP 0009	Pome fruits	0.6	10.8	6.5	7.5	4.5	0.3	0.2	6.5	3.9	51.3	30.8
PM 0110	Poultry meat	0	31.0	0.0	13.2	0.0	5.5	0.0	25.3	0.0	53.0	0.0
SO 0495	Rape seed	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
CM 0649	Rice, husked	0.05	0.0	0.0	1.8	0.1	34.7	1.7	21.0	1.1	2.5	0.1
VD 0541	Soya bean (dry)	0.08	4.5	0.4	2.0	0.2	0.5	0.0	0.0	0.0	0.0	0.0
VC 0431	Squash, summer	0.095	10.5	1.0	2.2	0.2	0.0	0.0	14.0	1.3	3.5	0.3
VR 0596	Sugar beet	0.08	0.5	0.0	0.0	0.0	0.0	0.0	0.3	0.0	2.0	0.2

Diets: g/person/day. Intake = daily intake: µg/person												
			Mid-East		Far-East		African		Latin American		European	
Code	Commodity	STMR or STMR-P mg/kg	diet	intake	diet	intake	diet	diet	intake	diet	intake	
VO 0448	Tomato (fresh, juice, paste, peeled)	0.16	81.5	13.0	7.0	1.1	16.5	2.6	25.5	4.1	66.6	10.7
GC 0654	Wheat	0.03	327.3	9.8	114.8	3.4	28.3	0.8	116.8	3.5	178.0	5.3
Total intake (µg/person) =				58.5	16.5	9.4	34.9	80.3				
Bodyweight per region (kg)				60	55	60	60	60				
ADI (µg/person) =				1800	1650	1800	1800	1800				
%ADI =				3.3%	1.0%	0.5%	1.9%	4.5%				
Rounded %ADI =				3%	1%	1%	2%	4%				

CARBOSULFAN**International Estimated Daily Intake (IEDI)**

ADI=0-..001 m/kg /bw/day

Diets: g/person/day. Intake = daily intake: µg/person														
					Mid-East		Far-East		African		Latin American		European	
Code	Commodity	MRL mg/kg	STMR or STMR-P mg/kg	diet correction factor	diet	Intake	diet	intake	diet	intake	diet	intake	diet	intake
SO 0691	Cotton seed	-	0,05	1	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
PE 0112	Eggs	-	0	1	14,6	0,0	13,1	0,0	3,7	0,0	11,9	0,0	37,6	0,0
MO 0105	Edible offal (mammalian)	-	0	1	4,2	0,0	1,4	0,0	2,8	0,0	6,1	0,0	12,4	0,0
GC 0645	Maize (fresh)	-	0	1	16,5	0,0	0,0	0,0	0,0	0,0	1,5	0,0	0,0	0,0
MM 0095	Meat from mammals other than marine mammals	-	0	1	37,0	0,0	32,8	0,0	23,8	0,0	47,0	0,0	155,5	0,0
FC 0004	Oranges, sweet, sour (incl. Orange-like hybrids)	-	0,01	1	31,5	0,3	4,0	0,0	4,8	0,0	31,0	0,3	29,8	0,3
VR 0589	Potato	-	0,03	1	59,0	1,8	19,2	0,6	20,6	0,6	40,8	1,2	240,8	7,2
PM 0110	Poultry meat	-	0	1	31,0	0,0	13,2	0,0	5,5	0,0	25,3	0,0	53,0	0,0
PO 0111	Poultry, edible offal of	-	0	1	0,1	0,0	0,1	0,0	0,1	0,0	0,4	0,0	0,4	0,0
GC 0649	Rice	-	0	1	48,8	0,0	279,3	0,0	103,4	0,0	86,5	0,0	11,8	0,0
VR 0596	Sugar beet	-	0,05	1	0,5	0,0	0,0	0,0	0,0	0,0	0,3	0,0	2,0	0,1

					Diets: g/person/day. Intake = daily intake: µg/person									
					Mid-East		Far-East		African		Latin American		European	
Code	Commodity	MRL mg/kg	STMR or STMR-P mg/kg	diet correction factor	diet	Intake	diet	intake	diet	intake	diet	intake	diet	intake
				Total intake (µg/person)=	2,1			0,6		0,7		1,5		7,6
				Bodyweight per region (kg bw) =	60			55		60		60		60
				ADI (µg/person)=	600			550		600		600		600
				%ADI=	0,4%			0,1%		0,1%		0,3%		1,3%
				Rounded %ADI=	0%			0%		0%		0%		1%

CYPRODINIL International Estimated Daily Intake (IEDI) ADI=0-0.03 mg/kg bw/day

				Diets: g/person/day. Intake = daily intake: µg/person									
				Mid-East		Far-East		African		Latin American		European	
Code	Commodity	STMR or STMR-P		diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
TN 0660	Almonds	0.02		0.5	0.0	0.0	0.0	0.0	0.0	0.1	0.0	1.8	0.0
FP 0226	Apple	0.02		7.5	0.2	4.7	0.1	0.3	0.0	5.5	0.1	40.0	0.8
JF 0226	Apple juice	0.0006		4.5	0.0	0	0.0	0	0.0	0.3	0.0	3.8	0.0
GC 0640	Barley (fresh)	0.48		1.0	0.5	3.5	1.7	1.8	0.9	6.5	3.1	19.8	9.5
VP 0061	Beans except broad bean & soya bean (green pods & immature seeds)	0.12		3.9	0.5	0.9	0.1	0.0	0.0	4.4	0.5	13.2	1.6
VC 0424	Cucumber	0.08		2.4	0.2	2.3	0.2	0.0	0.0	4.2	0.3	4.5	0.4
MO 0105	Edible offal (mammalian)	0.01		4.2	0.0	1.4	0.0	2.8	0.0	6.1	0.1	12.4	0.1
VO 0440	Egg plant	0.07		6.3	0.4	3.0	0.2	0.7	0.0	6.0	0.4	2.3	0.2
PE 0112	Eggs	0		14.6	0.0	13.1	0.0	3.7	0.0	11.9	0.0	37.6	0.0
FB 0269	Grapes (fresh, wine, excluding dried grapes)	0.79		15.8	12.5	1.0	0.8	0.0	0.0	1.3	1.0	13.8	10.9
DF 0269	Grapes, dried (= currants, raisins and sultanas)	1.7		0.3	0.5	0.0	0.0	0.0	0.0	0.3	0.5	2.3	3.9
VL 0482	Lettuce, head	2.75		2.3	6.3	0.0	0.0	0.0	0.0	5.8	16.0	22.5	61.9
VL 0483	Lettuce, leaf	2.75		2.3	6.3	0.0	0.0	0.0	0.0	5.8	16.0	22.5	61.9

			Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East		Far-East		African		Latin American		European	
Code	Commodity	STMR or STMR-P	diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0	7.4	0.0	6.6	0.0	4.8	0.0	9.4	0.0	31.1	0.0
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0	29.6	0.0	26.2	0.0	19.0	0.0	37.6	0.0	124.4	0.0
ML 0106	Milks	0	116.9	0.0	32.1	0.0	41.8	0.0	160.1	0.0	289.3	0.0
VA 0385	Onion, bulb	0.065	23.0	1.5	11.5	0.7	7.3	0.5	13.8	0.9	27.8	1.8
FP 0230	Pear	0.26	3.3	0.9	2.8	0.7	0.0	0.0	1.0	0.3	11.3	2.9
VO 0445	Peppers, sweet (incl. pim(i)ento)	0.16	3.3	0.5	2.0	0.3	5.3	0.8	2.3	0.4	10.3	1.6
PM 0110	Poultry meat: 10% as fat	0	3.1	0.0	1.3	0.0	0.6	0.0	2.5	0.0	5.3	0.0
PM 0110	Poultry meat: 90% as muscle	0	27.9	0.0	11.9	0.0	5.0	0.0	22.8	0.0	47.7	0.0
PO 0111	Poultry, edible offal of	0	0.1	0.0	0.1	0.0	0.1	0.0	0.4	0.0	0.4	0.0
DF 0014	Prunes	1.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.6
FB 0272	Raspberries, red, black	0.25	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.1
VC 0431	Squash, summer	0.08	10.5	0.8	2.2	0.2	0.0	0.0	14.0	1.1	3.5	0.3
FS 0012	Stone fruits	0.68	7.3	5.0	1.0	0.7	0.0	0.0	0.8	0.5	23.3	15.8
FB 0275	Strawberry	0.31	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.3	1.6
VO 0448	Tomato (fresh)	0.13	44.1	5.7	5.7	0.7	14.6	1.9	25.5	3.3	34.9	4.5
JF 0448	Tomato juice	0.022	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.0	0.0
-d	Tomato paste	0.12	5.8	0.7	0.2	0.0	0.3	0.0	0.0	0.0	4.0	0.5
GC 0654	Wheat	0.07	4.3	0.3	0.8	0.1	0	0	4.8	0.3	2.2	0.2
CM 0654	Wheat bran, unprocessed	0.21	-	-	-	-	-	-	-	-	-	-
CF 1211	Wheat flour	0.019	323.0	6.1	114.0	2.2	28.3	0.5	112.0	2.1	175.8	3.3
CF 1212	Wheat wholemeal	0.064	-	-	-	-	-	-	-	-	-	-
CP 1212	Wholemeal bread	0.036	107.7	3.9	38.0	1.4	9.4	0.3	74.7	2.7	58.6	2.1
-d	Wine only	0.062	0.5	0.0	0.0	0.0	0.8	0.0	19.8	1.2	97.8	6.1
Total intake (µg/person)=			52.9		10.1		5.1		50.9		192.7	
Bodyweight per region (kg bw) =			60		55		60		60		60	
ADI (µg/person)=			1800		1650		1800		1800		1800	
%ADI=			2.9%		0.6%		0.3%		2.8%		10.7%	
Rounded %ADI=			3%		1%		0%		3%		10%	

DICLORAN (83) International estimated daily intake (IEDI) ADI=0-0.01 mg/kg bw/day

Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East diet intake		Far-East diet intake		African diet intake		Latin American diet intake		European diet intake	
VR 0577	Carrot	6.11	2.8	17.1	2.5	15.3	0.0	0.0	6.3	38.5	22.0	134.4
FB 0269	Grapes (fresh, wine, excluding dried grapes)	0.89	15.8	14.1	1.0	0.9	0.0	0.0	1.3	1.2	13.8	12.3
DF 0269	Grapes, dried (= currants, raisins and sultanas)	0	0.3	0.0	0.0	0.0	0.0	0.0	0.3	0.0	2.3	0.0
JF 0269	Grape juice	0.98	-	-	-	-	-	-	-	-	-	-
FS 0245	Nectarine	2.7	1.3	3.4	0.3	0.7	0.0	0.0	0.4	1.1	6.3	16.9
VA 0385	Onion, bulb	0.1	23.0	2.3	11.5	1.2	7.3	0.7	13.8	1.4	27.8	2.8
FS 0247	Peach	2.7	1.3	3.4	0.3	0.7	0.0	0.0	0.4	1.1	6.3	16.9
Total intake (µg/person)=			40.2		18.7		0.7		43.2		183.2	
Bodyweight per region (kg bw) =			60		55		60		60		60	
ADI (µg/person)=			600		550		600		600		600	
%ADI=			6.7%		3.4%		0.1%		7.2%		30.5%	
Rounded %ADI=			7%		3%		0%		7%		30%	

DIMETHOATE (27) International Estimated Daily Intake ADI=0-0.002 mg/kg bw/day

Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East diet intake		Far-East diet intake		African diet intake		Latin American diet intake		European diet intake	
FC 0001	Citrus fruits	0.27	47.1	12.7	6.3	1.7	5.1	1.4	54.6	14.7	44.6	12.0
FP 0009	Pome fruits	0.5	10.8	5.4	7.5	3.8	0.3	0.2	6.5	3.3	51.3	25.7
FS 0013	Cherries	2.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.0	8.1
DF 0014	Prunes	0.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.3
FB 0269	Grapes (fresh, wine, dried)	1.1	16.1	17.7	1.0	1.1	0.0	0.0	1.6	1.8	16.1	17.7
FT 0305	Olives	2.24	1.3	2.9	0.0	0.0	0.0	0.0	0.3	0.7	2.8	6.3
DM 0305	Olives, processed	0.34	-	-	-	-	-	-	-	-	-	-
OC 0305	Olive oil, crude	0.059	1.5	0.1	0.0	0.0	0.0	0.0	0.0	0.0	7.8	0.5

Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East diet intake		Far-East diet intake		African diet intake		Latin American diet intake		European diet intake	
FI 0345	Mango	0.36	2.3	0.8	5.3	1.9	3.4	1.2	6.3	2.3	0.0	0.0
VR 0506	Turnip, Garden	1	0.5	0.5	0.0	0.0	0.0	0.0	0.3	0.3	2.0	2.0
VR 0589	Potato	0.1	59.0	5.9	19.2	1.9	20.6	2.1	40.8	4.1	240.8	24.1
VR 0596	Sugar beet	0.1	0.5	0.1	0.0	0.0	0.0	0.0	0.3	0.0	2.0	0.2
VA 0385	Onion, bulb	0.2	23.0	4.6	11.5	2.3	7.3	1.5	13.8	2.8	27.8	5.6
VO 0448	Tomato (fresh, peeled)	0.5	75.4	37.7	6.8	3.4	16.3	8.2	25.5	12.8	60.6	30.3
JF 0448	Tomato juice	0.09	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.0	0.2
-d	Tomato paste	0.7	5.8	4.1	0.2	0.1	0.3	0.2	0.0	0.0	4.0	2.8
-d	Cabbages (head & leafy brassicas, kohlrabi)	0.97	5.0	4.9	9.7	9.4	0.0	0.0	10.5	10.2	26.8	26.0
VB 0403	Cabbage, Savoy	0.175	0.1	0.0	0.1	0.0	0.1	0.0	0.1	0.0	0.1	0.0
VB 0402	Brussels sprouts	0.35	0.5	0.2	1.0	0.4	0.0	0.0	1.1	0.4	2.7	0.9
VB 0404	Cauliflower	0.025	1.3	0.0	1.5	0.0	0	0.0	0.3	0.0	13	0.3
VL 0482	Lettuce, head	0.31	2.3	0.7	0.0	0.0	0.0	0.0	5.8	1.8	22.5	7.0
VP 0063	Peas (green pods & immature seeds)	0.2	5.5	1.1	2.0	0.4	0.0	0.0	0.8	0.2	14.0	2.8
VS 0620	Artichoke globe	0.1	2.3	0.2	0.0	0.0	0.0	0.0	0.0	0.0	5.5	0.6
VS 0621	Asparagus	0.02	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.5	0.0
VS 0624	Celery	0.2	0.5	0.1	0.0	0.0	0.0	0.0	0.3	0.1	2.0	0.4
GC 0640	Barley (fresh)	0.15	1.0	0.2	3.5	0.5	1.8	0.3	6.5	1.0	19.8	3.0
GC 0651	Sorghum	0.1	2.0	0.2	9.7	1.0	26.6	2.7	0.0	0.0	0.0	0.0
GC 0654	Wheat (excluding flour)	0.021	4.3	0.1	0.8	0.0	0.0	0.0	4.8	0.1	2.2	0.0
CF 1211	Wheat flour	0.014	323.0	4.5	114.0	1.6	28.3	0.4	112.0	1.6	175.8	2.5
CF 1212	Wheat wholemeal	0.027	-	-	-	-	-	-	-	-	-	-
Total intake (µg/person)=			104.7		29.5		18.0		57.9		179.1	
Bodyweight per region (kg bw) =			60		55		60		60		60	
ADI (µg/person)=			120		110		120		120		120	
%ADI=			87.2%		26.9%		15.0%		48.2%		149.3	
Rou-ed %ADI=			90%		30%		10%		50%		150%	

DODINE International Estimated Daily Intake (IEDI). ADI=-0-0.1mg/kg bw/day

Code	Commodity	MRL mg/kg*	STMR or STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
				Mid-East		Far-East		African		Latin American		European	
				diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
JF 0226	Apple juice	-	0.15	4.5	0.7	0	0.0	0	0.0	0.3	0.0	3.8	0.6
FS 0013	Cherries	-	1.21	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.0	3.6
FS 0245	Nectarine	-	1.27	1.3	1.6	0.3	0.3	0.0	0.0	0.4	0.5	6.3	7.9
FS 0247	Peach	-	1.27	1.3	1.6	0.3	0.3	0.0	0.0	0.4	0.5	6.3	7.9
FP 0009	Pome fruits	-	1.74	10.8	18.8	7.5	13.1	0.3	0.5	6.5	11.3	51.3	89.3
Total intake (µg/person)=				22.6		13.7		0.5		12.4		109.3	
Bodyweight per region (kg bw) =				60		55		60		60		60	
ADI (µg/person)=				6000		5500		6000		6000		6000	
%ADI=				0.4%		0.2%		0.0%		0.2%		1.8%	
Rounded %ADI=				0%		0%		0%		0%		2%	

FAMOXADONE International Estimated Daily Intake (IEDI) ADI = 0-0.0060 mg/kg bw/day

Code	Commodity	STMR / STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East		Far-East		African		Latin American		European	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
GC 0640	Barley (fresh)	0.02	1.0	0.0	3.5	0.0	1.8	0.0	6.5	0.1	19.8	0.2
GC 0640	Barley (beer only)	0.008	-	-	-	-	-	-	-	-	-	-
VC 0424	Cucumber	0.025	2.4	0.1	2.3	0.1	0.0	0.0	4.2	0.1	4.5	0.1
MO 0105	Edible offal (mammalian)	0.046	4.2	0.2	1.4	0.1	2.8	0.1	6.1	0.3	12.4	0.6
PE 0112	Eggs	0	14.6	0.0	13.1	0.0	3.7	0.0	11.9	0.0	37.6	0.0
FB 0269	Grapes (fresh, wine, dried)	0.54	16.1	8.7	1.0	0.5	0.0	0.0	1.6	0.9	16.1	8.7
DF 0269	Grapes, dried (= currants, raisins and sultanas)	1.03	0.3	0.3	0.0	0.0	0.0	0.0	0.3	0.3	2.3	2.4
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0.067	7.4	0.5	6.6	0.4	4.8	0.3	9.4	0.6	31.1	2.1

Code	Commodity	STMR / STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East		Far-East		African		Latin American		European	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0.005	29.6	0.1	26.2	0.1	19.0	0.1	37.6	0.2	124.4	0.6
ML 0106	Milks	0.009	116.9	1.1	32.1	0.3	41.8	0.4	160.1	1.4	289.3	2.6
VR 0589	Potato	0	59.0	0.0	19.2	0.0	20.6	0.0	40.8	0.0	240.8	0.0
PM 0110	Poultry meat: 10% as fat	0	3.1	0.0	1.3	0.0	0.6	0.0	2.5	0.0	5.3	0.0
PM 0110	Poultry meat: 90% as muscle	0	27.9	0.0	11.9	0.0	5.0	0.0	22.8	0.0	47.7	0.0
PO 0111	Poultry, edible offal of	0	0.1	0.0	0.1	0.0	0.1	0.0	0.4	0.0	0.4	0.0
VC 0431	Squash, summer	0.025	10.5	0.3	2.2	0.1	0.0	0.0	14.0	0.4	3.5	0.1
VO 0448	Tomato (fresh)	0.1	44.1	4.4	5.7	0.6	14.6	1.5	25.5	2.6	34.9	3.5
JF 0448	Tomato juice	0.022	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.0	0.0
	Tomato paste	0.13	5.8	0.8	0.2	0.0	0.3	0.0	0.0	0.0	4.0	0.5
GC 0654	Wheat	0.02										
CM 0654	Wheat bran, unprocessed	0.04	-	-	-	-	-	-	-	-	-	-
CF 1211	Wheat flour	0.01	323.0	3.2	114.0	1.1	28.3	0.3	112.0	1.1	175.8	1.8
CF 1212	Wheat wholemeal	0.01	-	-	-	-	-	-	-	-	-	-
	Wine only	0.005	0.5	0.0	0.0	0.0	0.8	0.0	19.8	0.1	97.8	0.5
Total intake (µg/person)=				19.6		3.3		2.7		8.0		23.6
Bodyweight per region (kg bw) =				60		55		60		60		60
ADI (µg/person)=				360		330		360		360		360
%ADI=				5.5%		1.0%		0.8%		2.2%		6.6%
Rounded %ADI=				5%		1%		1%		2%		7%

FENITROTHION International Estimated Daily Intake (IEDI) ADI= 0 - 0.005 mg/kg bw

Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East		Far-East		African		Latin American		European	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
GC 0080	Cereal grains (excluding wheat flour) ¹	5	106.9	534.5	336.8	1684.0	290.0	1450.0	140.4	702.0	46.1	230.5

Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East		Far-East		African		Latin American		European	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
CP 1211	White bread	0.05	215.3	10.8	76.0	3.8	18.9	0.9	37.3	1.9	117.2	5.9
CP 1212	Wholemeal bread	1.9	107.7	204.6	38.0	72.2	9.4	17.9	74.7	141.9	58.6	111.3
	Total intake (µg/person)=			749.9		1760.0		1468.8		845.8		347.7
	Bodyweight per region (kg bw) =			60		55		60		60		60
	ADI (µg/person)=			300		275		300		300		300
	%ADI=			250.0%		640.0%		489.6%		281.9%		115.9%
	Rounded %ADI=			250%		640%		490%		280%		120%

¹The consumption value of wheat flour is the sum of the consumption of white bread and that of wholemeal bread. The intake of fenitrothion was calculated using the consumption and STMR-P values of white bread and wholemeal bread.

LINDANE International Estimated Daily Intake (IEDI) ADI=0 - 0.005 mg/kg bw

Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East		Far-East		African		Latin American		European	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
GC 0640	Barley (fresh)	0.005	1.0	0.0	3.5	0.0	1.8	0.0	6.5	0.0	19.8	0.1
MO 0105	Edible offal (mammalian)	0.0002	4.2	0.0	1.4	0.0	2.8	0.0	6.1	0.0	12.4	0.0
PE 0112	Eggs	0.0007	14.6	0.0	13.1	0.0	3.7	0.0	11.9	0.0	37.6	0.0
GC 0645	Maize (fresh)	0.005	16.5	0.1	0.0	0.0	0.0	0.0	1.5	0.0	0.0	0.0
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0.008	7.4	0.1	6.6	0.1	4.8	0.0	9.4	0.1	31.1	0.2
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0.0007	29.6	0.0	26.2	0.0	19.0	0.0	37.6	0.0	124.4	0.1
ML 0106	Milks	0.0003	116.9	0.0	32.1	0.0	41.8	0.0	160.1	0.0	289.3	0.1
GC 0647	Oats	0.005	0.0	0.0	0.0	0.0	0.2	0.0	0.8	0.0	2.0	0.0
PM 0110	Poultry meat: 10% as fat	0.008	3.1	0.0	1.3	0.0	0.6	0.0	2.5	0.0	5.3	0.0
PM 0110	Poultry meat: 90% as muscle	0.0006	27.9	0.0	11.9	0.0	5.0	0.0	22.8	0.0	47.7	0.0
PO 0111	Poultry, edible offal of	0.0004	0.1	0.0	0.1	0.0	0.1	0.0	0.4	0.0	0.4	0.0

Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East		Far-East		African		Latin American		European	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
GC 0650	Rye	0.005	0.0	0.0	1.0	0.0	0.0	0.0	0.0	0.0	1.5	0.0
GC 0651	Sorghum	0.005	2.0	0.0	9.7	0.0	26.6	0.1	0.0	0.0	0.0	0.0
VO 1275	Sweet corn (kernels)	0.005	0.0	0.0	0.0	0.0	3.3	0.0	0.0	0.0	6.2	0.0
GC 0654	Wheat	0.005	327.3	1.6	114.8	0.6	28.3	0.1	116.8	0.6	178.0	0.9
	Total intake (µg/person)=			1.9		0.8		0.4		0.8		1.6
	Bodyweight per region (kg bw) =			60		55		60		60		60
	ADI (µg/person)=			300		275		300		300		300
	%ADI=			0.6%		0.3%		0.1%		0.3%		0.5%
	Rou-ed %ADI=			1%		0%		0%		0%		1%

METHAMIDOPHOS

International Estimated Daily Intake (IEDI) ADI=0 - 0.004 mg/kg bw

Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East		Far-East		African		Latin American		European	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
FP 0226	Apple (note 1)	0.06	7.5	0.5	4.7	0.3	0.3	0.0	5.5	0.3	40.0	2.4
JF 0226	Apple juice	0.06	4.5	0.3	0	0.0	0	0.0	0.3	0.0	3.8	0.2
VS 0620	Artichoke globe	0.03	2.3	0.1	0.0	0.0	0.0	0.0	0.0	0.0	5.5	0.2
VP 0061	Beans except broad bean & soya bean (green pods & immature seeds)	0.17	3.9	0.7	0.9	0.2	0.0	0.0	4.4	0.7	13.2	2.2
VB 0400	Broccoli (note 2)	0.02	0.5	0.0	1.0	0.0	0.0	0.0	1.1	0.0	2.7	0.1
VB 0401	Broccoli, Chinese (note 2)	0.02	-	-	-	-	-	-	-	-	-	-
-d	Cabbages (head & leafy brassicas, kohlrabi)	0.04	5.0	0.2	9.7	0.4	0.0	0.0	10.5	0.4	26.8	1.1
VB 0404	Cauliflower (note 2)	0.02	1.3	0.0	1.5	0.0	0	0.0	0.3	0.0	13	0.3
SO 0691	Cotton seed	0.01	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
OC 0691	Cotton seed oil, crude	0.00014	3.8	0.0	0.5	0.0	0.5	0.0	0.5	0.0	0.0	0.0
MO 0105	Edible offal (mammalian)	0.01	4.2	0.0	1.4	0.0	2.8	0.0	6.1	0.1	12.4	0.1
PE 0112	Eggs	0	14.6	0.0	13.1	0.0	3.7	0.0	11.9	0.0	37.6	0.0
FC 0003	Mandarins (incl. Mandarin-like hybrids)	0.085	8.8	0.7	0.2	0.0	0.0	0.0	6.3	0.5	6.0	0.5

Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East		Far-East		African		Latin American		European	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0.01	7.4	0.1	6.6	0.1	4.8	0.0	9.4	0.1	31.1	0.3
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0.01	29.6	0.3	26.2	0.3	19.0	0.2	37.6	0.4	124.4	1.2
ML 0106	Milks	0.01	116.9	1.2	32.1	0.3	41.8	0.4	160.1	1.6	289.3	2.9
-d	Peaches & nectarines	0.19	2.5	0.5	0.5	0.1	0.0	0.0	0.8	0.2	12.5	2.4
FP 0230	Pear (note 1)	0.06	3.3	0.2	2.8	0.2	0.0	0.0	1.0	0.1	11.3	0.7
VO 0051	Peppers	0.25	3.4	0.9	2.1	0.5	5.4	1.4	2.4	0.6	10.4	2.6
VR 0589	Potato	0.01	59.0	0.6	19.2	0.2	20.6	0.2	40.8	0.4	240.8	2.4
PM 0110	Poultry meat: 10% as fat	0	3.1	0.0	1.3	0.0	0.6	0.0	2.5	0.0	5.3	0.0
PM 0110	Poultry meat: 90% as muscle	0	27.9	0.0	11.9	0.0	5.0	0.0	22.8	0.0	47.7	0.0
PO 0111	Poultry, edible offal of	0	0.1	0.0	0.1	0.0	0.1	0.0	0.4	0.0	0.4	0.0
FP 0231	Quince (note 1)	0.06	0.1	0.0	0.1	0.0	0.1	0.0	0.1	0.0	0.1	0.0
VD 0541	Soya bean (dry)	0.01	4.5	0.0	2.0	0.0	0.5	0.0	0.0	0.0	0.0	0.0
OC 0541	Soya bean oil, crude	0.005	1.3	0.0	1.7	0.0	3.0	0.0	14.5	0.1	4.3	0.0
VR 0596	Sugar beet	0.01	0.5	0.0	0.0	0.0	0.0	0.0	0.3	0.0	2.0	0.0
VO 0448	Tomato (fresh)	0.285	44.1	12.6	5.7	1.6	14.6	4.2	25.5	7.3	34.9	9.9
JF 0448	Tomato juice	0.314	0.3	0.1	0.0	0.0	0.0	0.0	0.0	0.0	2.0	0.6
-d	Tomato paste	1.425	5.8	8.3	0.2	0.3	0.3	0.4	0.0	0.0	4.0	5.7
-d	Tomatoes peeled	0.285	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4.0	1.1
			Total intake (µg/person)=	27.1		4.5		6.9		12.8		37.0
			Bodyweight per region (kg bw) =	60		55		60		60		60
			ADI (µg/person)=	240		220		240		240		240
			%ADI=	11.3%		2.0%		2.9%		5.3%		15.4%
			Rounded %ADI=	10%		2%		3%		5%		20%

Note 1: Group maximum residue level proposed for pome fruit

Note 2: Group maximum residue level proposed for flowerhead brassicas

METHOXYFENOZIDE (209)

International Estimated Daily Intake (IEDI ADI = 0.1 mg/kg bw/day)

Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East diet intake		Far-East diet intake		African diet intake		Latin American diet intake		European diet intake	
JF 0226	Apple juice	0.13	4.5	0.6	0	0.0	0	0.0	0.3	0.0	3.8	0.5
VB 0400	Broccoli	0.94	0.5	0.5	1.0	0.9	0.0	0.0	1.1	1.0	2.7	2.5
VB 0041	Cabbages, head	0.93	ND	-	ND	-	ND	-	ND	-	ND	-
VS 0624	Celery	3.4	0.5	1.7	0.0	0.0	0.0	0.0	0.3	1.0	2.0	6.8
SO 0691	Cotton seed	0.46	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
OC 0691	Cotton seed oil, crude	0.15	3.8	0.6	0.5	0.1	0.5	0.1	0.5	0.1	0.0	0.0
MO 0105	Edible offal (mammalian)	0.0075	4.2	0.0	1.4	0.0	2.8	0.0	6.1	0.0	12.4	0.1
PE 0112	Eggs	0	14.6	0.0	13.1	0.0	3.7	0.0	11.9	0.0	37.6	0
FB 0269	Grapes (fresh, wine, excluding dried grapes)	0.1	15.8	1.6	1.0	0.1	0.0	0.0	1.3	0.1	13.8	1.4
DF 0269	Grapes, dried (= currants, raisins and sultanas)	0.86	0.3	0.3	0.0	0.0	0.0	0.0	0.3	0.3	2.3	2.0
VL 0482	Lettuce, head	6.1	2.3	14.0	0.0	0.0	0.0	0.0	5.8	35.4	22.5	137.3
VL 0483	Lettuce, leaf	12	2.3	27.6	0.0	0.0	0.0	0.0	5.8	69.6	22.5	270.0
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0.0082	7.4	0.1	6.6	0.1	4.8	0.0	9.4	0.1	31.1	0.3
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0.003	29.6	0.1	26.2	0.1	19.0	0.1	37.6	0.1	124.4	0.4
ML 0106	Milks	0.0041	116.9	0.5	32.1	0.1	41.8	0.2	160.1	0.7	289.3	1.2
VL 0485	Mustard greens	16	0.1	1.6	0.1	1.6	0.1	1.6	0.1	1.6	0.1	1.6
VO 0051	Peppers	0.16	3.4	0.5	2.1	0.3	5.4	0.9	2.4	0.4	10.4	1.7
FP 0009	Pome fruits	1	10.8	10.8	7.5	7.5	0.3	0.3	6.5	6.5	51.3	51.3
PM 0110	Poultry meat: 10% as fat	0	3.1	0.0	1.3	0.0	0.6	0.0	2.5	0.0	5.3	0.0
PM 0110	Poultry meat: 90% as muscle	0	27.9	0.0	11.9	0.0	5.0	0.0	22.8	0.0	47.7	0.0
PO 0111	Poultry, edible offal of	0	0.1	0.0	0.1	0.0	0.1	0.0	0.4	0.0	0.4	0.0
DF 0014	Prunes	0.34	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.2
VL 0502	Spinach	15	0.5	7.5	0.0	0.0	0.0	0.0	0.3	4.5	2.0	30.0
FS 0012	Stone fruits	0.34	7.3	2.8	1.0	0.4	0.0	0.0	0.8	0.3	23.3	8.9
VO 0447	Sweet corn (corn-on-the-cob)	0	0.0	0.0	0.0	0.0	4.4	0.0	0.0	0.0	8.3	0.0
VO 0448	Tomato (fresh)	0.2	44.1	8.8	5.7	1.1	14.6	2.9	25.5	5.1	34.9	7.0

Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East diet intake		Far-East diet intake		African diet intake		Latin American diet intake		European diet intake	
JF 0448	Tomato juice	0.06	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.0	0.1
-d	Tomato paste	0.4	5.8	2.3	0.2	0.1	0.3	0.1	0.0	0.0	4.0	1.6
-d	Tomatoes peeled	0.042	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4.0	0.2
TN 0085	Tree nuts	0.012	1.1	0.0	13.5	0.2	4.5	0.1	17.8	0.2	4.6	0.1
Total intake (µg/person)=			81.9		12.6		6.2		127.1		525.0	
Bodyweight per person (kg bw)=			60		55		60		60		60	
ADI (µg/person)=			6000		5500		6000		6000		6000	
%ADI=			1.4%		0.2%		0.1%		2.1%		8.7%	
Rounded %ADI=			1%		0%		0%		2%		9%	

PIRIMIPHOS-METHYL (86) International Estimated Daily Intake (IEDI).

ADI=0-0.03 mg/kg bw/day

Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East diet intake		Far-East diet intake		African diet intake		Latin American diet intake		European diet intake	
GC 0080	Cereal grains (excluding wheat flour)	2.3	106.9	245.9	336.8	774.6	290.0	667.0	140.4	322.9	46.1	106.0
ML 0106	Milks	0.003	116.9	0.4	32.1	0.1	41.8	0.1	160.1	0.5	289.3	0.9
CM 0654	Wheat bran, unprocessed	5.1	-	-	-	-	-	-	-	-	-	-
CF 1212	Wheat wholemeal	1.6	-	-	-	-	-	-	-	-	-	-
CP 1211	White bread	0.22	215.3	47.4	76.0	16.7	18.9	4.2	37.3	8.2	117.2	25.8
CP 1212	Wholemeal bread	0.83	107.7	89.4	38.0	31.5	9.4	7.8	74.7	62.0	58.6	48.6
	Beer	0.01	-	-	-	-	-	-	-	-	-	-
Total intake (µg/person)=			383.0		823.0		679.1		393.6		181.3	
Bodyweight per region (kg bw) =			60		55		60		60		60	

Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East diet intake		Far-East diet Intake		African diet intake		Latin American diet intake		European diet intake	
		ADI (µg/person)=		1800		1650		1800		1800		1800
		%ADI=		21.3%		49.9%		37.7%		21.9%		10.1%
		Rounded %ADI=		20%		50%		40%		20%		10%

NB: As the consumption value of wheat flour is the sum of the consumption value of white bread and that of wholemeal bread, the intake of pirimiphos-methyl was calculated using the consumption and STMR-P values of white bread and wholemeal bread.

PYRETHRINS (63) International Estimated Daily Intake (IEDI) ADI = 0 - 0.04 mg/kg bw/day

Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East		Far-East		African		Latin American		European	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
GC 0080	Cereal grains	0.05	429.9	21.5	450.8	22.5	318.3	15.9	252.4	12.6	221.9	11.1
FC 0001	Citrus fruits	0.04	47.1	1.9	6.3	0.3	5.1	0.2	54.6	2.2	44.6	1.8
DF 0167	Dried fruit	0.05	0.3	0.0	0.2	0.0	0.3	0.0	0.3	0.0	0.0	0.0
VC 0045	Fruiting vegetables, cucurbits	0.04	80.5	3.2	18.2	0.7	0.0	0.0	30.5	1.2	38.5	1.5
SO 0697	Peanut	0.05	0.3	0.0	0.2	0.0	2.3	0.1	0.3	0.0	3.0	0.2
VO 0051	Peppers	0.04	3.4	0.1	2.1	0.1	5.4	0.2	2.4	0.1	10.4	0.4
VD 0070	Pulses	0.05	18.9	0.9	14.5	0.7	17.5	0.9	20.3	1.0	9.4	0.5
VR 0075	Root and tuber vegetables	0	61.8	0.0	108.5	0.0	321.3	0.0	159.3	0.0	242.0	0.0
VO 0448	Tomato	0.04	81.5	3.3	7.0	0.3	16.5	0.7	25.5	1.0	66.6	2.7
JF 0448	Tomato juice	0.018	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.0	0.0
	Tomato paste	0.018	5.8	0.0	0.2	0.0	0.3	0.0	0.0	0.0	4.0	0.0
	Total intake (µg/person) =			31.0		24.6		18.0		18.2		18.1
	Bodyweight per region (kg bw) =			60		55		60		60		60
	ADI (µg/person) =			2400		2200		2400		2400		2400
	%ADI =			1.3%		1.1%		0.8%		0.8%		0.8%
	Rounded %ADI =			1%		1%		1%		1%		1%

TEBUFENOZIDE International Estimated Daily Intake (IEDI) ADI=0 - 0.02 mg/kg bw

Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person										
			Mid-East		Far-East		African		Latin American		European		
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake	
TN 0660	Almonds	0.0205	0.5	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	1.8	0.0
FI 0326	Avocado	0.21	0.0	0.0	0.0	0.0	0.2	0.0	3.3	0.7	1.0	0.2	
FB 0020	Blueberries	0.685	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.3	
VB 0400	Broccoli	0.11	0.5	0.1	1.0	0.1	0.0	0.0	1.1	0.1	2.7	0.3	
	Cabbages (head & leafy brassicas, kohlrabi) ¹	0.34	5.0	1.7	9.7	3.3	0.0	0.0	10.5	3.6	26.8	9.1	
FC 0001	Citrus fruits	0.079	47.1	3.7	6.3	0.5	5.1	0.4	54.6	4.3	44.6	3.5	
FB 0265	Cranberry	0.042	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0	
MO 0105	Edible offal (mammalian)	0.02	4.2	0.1	1.4	0.0	2.8	0.1	6.1	0.1	12.4	0.2	
PE 0112	Eggs	0	14.6	0.0	13.1	0.0	3.7	0.0	11.9	0.0	37.6	0.0	
FB 0269	Grapes (fresh, wine, dried)	0.745	16.1	12.0	1.0	0.7	0.0	0.0	1.6	1.2	16.1	12.0	
DF 0269	Grapes, dried (= currants, raisins and sultanas)	0.551	0.3	0.2	0.0	0.0	0.0	0.0	0.3	0.2	2.3	1.3	
FI 0341	Kiwi fruit	0.14	0.0	0.0	0.0	0.0	1.9	0.3	0.1	0.0	1.5	0.2	
VL 0053	Leafy vegetables	2.45	7.8	19.1	9.7	23.8	0.7	1.7	16.5	40.4	51.7	126.7	
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0.015	7.4	0.1	6.6	0.1	4.8	0.1	9.4	0.1	31.1	0.5	
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0.006	29.6	0.2	26.2	0.2	19.0	0.1	37.6	0.2	124.4	0.7	
ML 0106	Milks	0.003	116.9	0.4	32.1	0.1	41.8	0.1	160.1	0.5	289.3	0.9	
HH 0738	Mints	8.35	-	-	-	-	-	-	-	-	-	-	
FS 0245	Nectarine	0.11	1.3	0.1	0.3	0.0	0.0	0.0	0.4	0.0	6.3	0.7	
JF 0004	Orange juice	0.0077	7.3	0.1	0.0	0.0	0.0	0.0	0.3	0.0	4.5	0.0	
FS 0247	Peach	0.11	1.3	0.1	0.3	0.0	0.0	0.0	0.4	0.0	6.3	0.7	
TN 0672	Pecan	0.01	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0	
VO 0051	Peppers	0.064	3.4	0.2	2.1	0.1	5.4	0.3	2.4	0.2	10.4	0.7	

¹ This is a worst-case calculation. The recommendation is for VB 0041, Cabbage head, only.

Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person										
			Mid-East diet Intake		Far-East diet intake		African diet intake		Latin American diet intake		European diet intake		
	Beer (arising from use on hops)	0.025	-	-	-	-	-	-	-	-	-	-	-
FB 0264	Blackberries	1.95	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
JF 1140	Blackcurrant juice	0.09	-	-	-	-	-	-	-	-	-	-	-
VC 0424	Cucumber	0.37	2.4	0.9	2.3	0.8	0.0	0.0	4.2	1.5	4.5	1.7	
FB 0021	Currants, red, black, white	0.345	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.1	
JF 0269	Grape juice	0.40	-	-	-	-	-	-	-	-	-	-	-
FB 0269	Grapes (fresh, wine, excluding dried grapes)	0.75	15.8	11.9	1.0	0.8	0.0	0.0	1.3	1.0	13.8	10.4	
DF 0269	Grapes, dried (= currants, raisins and sultanas)	2.3	0.3	0.7	0.0	0.0	0.0	0.0	0.3	0.7	2.3	5.3	
DH 1100	Hops, dry	25	0.1	2.5	0.1	2.5	0.1	2.5	0.1	2.5	0.1	2.5	
VA 0384	Leek	0.97	0.5	0.5	0.0	0.0	0.0	0.0	0.3	0.3	2.0	1.9	
VL 0482	Lettuce, head	3.75	2.3	8.6	0.0	0.0	0.0	0.0	5.8	21.8	22.5	2.3	
	Pear juice	0.02	-	-	-	-	-	-	-	-	-	-	-
	Pear, Canned	0.01	-	-	-	-	-	-	-	-	-	-	-
VO 0445	Peppers, sweet (incl. pim(i)ento)	0.67	3.3	2.2	2.0	1.3	5.3	3.6	2.3	1.5	10.3	6.9	
FP 0009	Pome fruits	0.68	10.8	7.3	7.5	5.1	0.3	0.2	6.5	4.4	51.3	34.9	
FB 0272	Raspberries, red, black	1.95	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5	1.0	
FB 0275	Strawberry	0.84	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.3	4.5	
	Strawberry, Canned	0.18	-	-	-	-	-	-	-	-	-	-	-
VO 0448	Tomato (fresh)	0.39	44.1	17.2	5.7	2.2	14.6	5.7	25.5	9.9	34.9	13.6	
JF 0448	Tomato juice	0.2	0.3	0.1	0.0	0.0	0.0	0.0	0.0	0.0	2.0	0.4	
	Tomato puree	0.66	-	-	-	-	-	-	-	-	-	-	-

Total intake (µg/person)=	61.4	13.1	12.4	43.7	174.1
Bodyweight per region (kg bw) =	60	55	60	60	60
ADI (µg/person)=	4800	4400	4800	4800	4800
%ADI=	1.3%	0.3%	0.3%	0.9%	3.6%
Rounded %ADI=	1%	0%	0%	1%	4%

ANNEX 4

INTERNATIONAL ESTIMATES OF SHORT-TERM DIETARY INTAKES OF PESTICIDE RESIDUES

International Estimates of Short-Term Dietary Intakes of the pesticides evaluated by the Meeting and the ratios of the estimates to the corresponding acute RfDs.

ACEPHATE :

International estimate of short term intake (IESTI) for
GENERAL POPULATION

Maximum %acute RfD: 260%
(0.05 mg/kg bw)

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Country	Large portion diet			Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
					Body weight (kg)	Large portion correction factor	Large portion, corrected, g/person							
FP 0226	Apple (note 1)	-	5.4	USA	65.0	1.00	1348	110	FRA	100	3	2a	128.63	260%
JF 0226	Apple juice	0.81	-	-	-	1.00	-	-	-	-	-	3	ND	-
VS 0620	Artichoke globe	-	0.5	FRA	62.3	1.00	534	230	FRA	99	3	2a	5.87	10%
VP 0061	Beans except broad bean & soya bean (green pods & immature seeds)	-	5.6	FRA	62.3	1.00	312	-	-	-	-	1	28.00	60%
VB 0400	Broccoli (note 2)	-	2.85	USA	65.0	1.00	376	608	USA	474	3	2b	49.50	100%
VB 0404	Cauliflower (head) (note 2)	-	2.85	UNK	70.1	1.00	579	1733	UNK	780	3	2b	70.62	140%
PE 0840	Chicken eggs	-	0.01	FRA	62.3	1.00	219	-	-	-	-	1	0.04	0%
MO 0105	Edible offal (mammalian)	-	0.022	FRA	62.3	1.00	277	-	-	-	-	1	0.10	0%
FC 0206	Mandarin	-	6.5	JPN	52.6	1.00	409	70	JPN	70	3	2a	67.81	140%
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.022	AUS	67.0	1.00	104	-	-	-	-	1	0.03	0%
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0.022	AUS	67.0	1.00	417	-	-	-	-	1	0.14	0%
ML 0106	Milks	0.011	-	USA	65.0	1.00	2466	-	-	-	-	3	0.42	1%
FS 0245	Nectarine	-	3.2	USA	65.0	1.00	590	110	FRA	99	3	2a	38.80	80%
FS 0247	Peach	-	3.2	SAF	55.7	1.00	685	110	FRA	99	3	2a	50.74	100%
FP 0230	Pear (note 1)	-	5.4	USA	65.0	1.00	693	100	FRA	89	3	2a	72.35	140%
VO 0444	Peppers, chili (note 3)	-	11.7	USA	65.0	1.00	90	45	USA	43	3	2a	31.82	60%
VO 0445	Peppers, sweet (incl.	-	11.7	FRA	62.3	1.00	207	172	UNK	160	3	2a	99.04	200%

	pim(i)ento (note 3)													
PM 0110	Poultry meat: 10% as fat	-	0.01	AUS	67.0	1.00	43	-	-	-	-	1	0.01	0%
PM 0110	Poultry meat: 90% as muscle	-	0.01	AUS	67.0	1.00	388	-	-	-	-	1	0.06	0%
PO 0111	Poultry, edible offal of	-	0.01	USA	65.0	1.00	248	-	-	-	-	1	0.04	0%
FP 0231	Quince (note 1)	-	5.4	AUS	67.0	1.00	175	92	USA	56	3	2a	23.14	50%
VD 0541	Soya bean (dry)	0.01	-	JPN	52.6	1.00	159	-	-	-	-	3	0.03	0%
OC 0541	Soya bean oil, crude	0.005	-	-	-	-	-	-	-	-	-	3	-	-

Note 1: Group maximum residue level proposed for pome fruit

Note 2: Group maximum residue level proposed for flowerhead brassicas

Note 3: Maximum residue level proposed for peppers includes both peppers, sweet and peppers, chili

ACEPHATE :

CHILDREN UP TO 6 YEARS

Maximum %acute RfD:
(0.05 mg/kg bw)

630%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Country	Large portion diet Body weight (kg)	Large portion correction factor	Large portion, corrected, g/person	Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
FP 0226	Apple (note 1)	-	5.4	USA	15.0	1.00	679	110	FRA	100	3	2a	316.42	630%
JF 0226	Apple juice	0.81	-	-	-	1.00	-	-	-	-	-	3	ND	-
VS 0620	Artichoke globe	-	0.5	FRA	17.8	1.00	89	230	FRA	99	3	2b	7.50	20%
VP 0061	Beans except broad bean & soya bean (green pods & immature seeds)	-	5.6	FRA	17.8	1.00	203	-	-	-	-	1	63.78	130%
VB 0400	Broccoli (note 2)	-	2.85	USA	15.0	1.00	164	608	USA	474	3	2b	93.62	190%
VB 0404	Cauliflower (head) (note 2)	-	2.85	NLD	17.0	1.00	209	1733	UNK	780	3	2b	105.25	210%
PE 0840	Chicken eggs	-	0.01	FRA	17.8	1.00	134	-	-	-	-	1	0.08	0%
MO 0105	Edible offal (mammalian)	-	0.022	FRA	17.8	1.00	203	-	-	-	-	1	0.25	1%
FC 0206	Mandarin	-	6.5	JPN	15.9	1.00	353	70	JPN	70	3	2a	201.66	400%
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.022	AUS	19.0	1.00	52	-	-	-	-	1	0.06	0%
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0.022	AUS	19.0	1.00	208	-	-	-	-	1	0.24	0%
ML 0106	Milks	0.011	-	USA	15.0	1.00	1286	-	-	-	-	3	0.94	2%
FS 0245	Nectarine	-	3.2	AUS	19.0	1.00	302	110	FRA	99	3	2a	84.23	170%
FS 0247	Peach	-	3.2	AUS	19.0	1.00	315	110	FRA	99	3	2a	86.48	170%

FP 0230	Pear (note 1)	-	5.4	UNK	14.5	1.00	279	100	FRA	89	3	2a	170.19	340%
VO 0444	Peppers, chili (note 3)	-	11.7	AUS	19.0	1.00	31	45	USA	43	3	2b	56.34	110%
VO 0445	Peppers, sweet (incl. pim(i)ento) (note 3)	-	11.7	AUS	19.0	1.00	60	172	UNK	160	3	2b	110.92	220%
PM 0110	Poultry meat: 10% as fat	-	0.01	AUS	19.0	1.00	22	-	-	-	-	1	0.01	0%
PM 0110	Poultry meat: 90% as muscle	-	0.01	AUS	19.0	1.00	201	-	-	-	-	1	0.11	0%
PO 0111	Poultry, edible offal of	-	0.01	USA	15.0	1.00	37	-	-	-	-	1	0.02	0%
FP 0231	Quince (note 1)	-	5.4	NLD	17.0	1.00	1	92	USA	56	3	2b	0.97	2%
VD 0541	Soya bean (dry)	0.01	-	JPN	15.9	1.00	88	-	-	-	-	3	0.06	0%
OC 0541	Soya bean oil, crude	0.005	-	-	-	-	-	-	-	-	-	3	-	-

Note 1: Group maximum residue level proposed for pome fruit

Note 2: Group maximum residue level proposed for flowerhead brassicas

Note 3: Maximum residue level proposed for peppers includes both peppers, sweet and peppers, chili

CARBENDAZIM (072) : International estimate of short term intake (IESTI) for **GENERAL POPULATION** ARfD: not established but may be necessary

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Country	Large portion diet		Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
					Body weight (kg)	Large portion, g/person							
VS 0621	Asparagus	-	0.09	NLD	63.0	398	25	FRA	13	3	2a	0.60	-
FI 0327	Banana	-	0.44	SAF	55.7	613	708	USA	481	3	2a	12.45	-
GC 0640	Barley (fresh, flour, beer)	0.05	-	NLD	63.0	378	-	-	-	-	3	0.30	-
VD 0071	Beans (dry)	0.165	-	FRA	62.3	255	-	-	-	-	3	0.68	-
VB 0402	Brussels sprouts	-	0.27	NLD	63.0	394	14	UNK	10	-	1	1.69	-
VR 0577	Carrot	-	0.14	NLD	63.0	335	61	USA	50	3	2a	0.97	-
FS 0013	Cherries	-	9.1	FRA	62.3	375	5	FRA	4	-	1	54.78	-
PE 0112	Eggs (Chicken eggs 1/)	-	0	FRA	62.3	219	-	-	-	-	1	0.00	-
VP 0526	Common bean (green pods and/or immature seeds)	-	0.45	NLD	63.0	431	-	-	-	-	1	3.08	-
VC 0424	Cucumber	-	0.05	NLD	63.0	313	400	FRA	360	3	2b	0.75	-
MO 0105	Edible offal (mammalian)	-	0	FRA	62.3	277	-	-	-	-	1	0.00	-
VP 0529	Garden pea, shelled (immature seeds)	-	0.01	NLD	63.0	301	-	-	-	-	1	0.05	-
VC 0425	Gherkin	-	0.05	NLD	63.0	96	15	FRA	15	-	1	0.08	-
FB 0269	Grapes (fresh, dried, excluding wine)	-	1.9	AUS	67.0	513	125	FRA	118	3	2a	21.21	-

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Country	Large portion diet		Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
					Body weight (kg)	Large portion, g/person							
FI 0345	Mango	-	1.7	FRA	62.3	567	207	USA	139	3	2a	23.04	-
ML 0106	Milks	0	-	USA	65.0	2466	-	-	-	-	3	0.00	-
FC 0004	Oranges, sweet, sour (incl. Orange-like hybrids) 2/	-	0.63	USA	65.0	564	131	USA	96	3	2a	7.32	-
FS 0247	Peach	-	1	SAF	55.7	685	98	USA	85	3	2a	15.36	-
SO 0697	Peanut	0.08	-	FRA	62.3	161	-	-	-	-	3	0.21	-
FP 0009	Pome fruits (Pear 1/)	-	2.4	USA	65.0	693	166	USA	151	3	2a	36.74	-
VO 0444	Peppers, chili	-	0.98	USA	65.0	90	45	USA	43	3	2a	2.66	-
FI 0353	Pineapple (fresh, canned, juice, dried)	-	0.03	JPN	52.6	371	472	USA	245	3	2a	0.49	-
FS 0014	Plums (fresh, prunes)	-	0.34	USA	65.0	413	66	USA	62	3	2a	2.81	-
PM 0110	Poultry meat	-	0	AUS	67.0	431	-	-	-	-	1	0.00	-
SO 0495	Rape seed	0	-	-	-	-	-	-	-	-	3	-	-
CM 0649	Rice, husked	0.05	-	JPN	52.6	319	-	-	-	-	3	0.3	-
VD 0541	Soya bean (dry)	0.08	-	JPN	52.6	159	-	-	-	-	3	0.24	-
VC 0431	Squash, summer	0.095	-	FRA	62.3	343	196	USA	186	3	2a	-	-
VR 0596	Sugar beet	-	0.08	-	-	-	-	-	-	-	-	-	-
VO 0448	Tomato (fresh, juice, paste, peeled)	-	0.22	USA	65.0	391	105	FRA	102	3	2a	2.01	-
GC 0080	Cereal grains (Wheat 1/)	0.03	-	USA	65.0	383	-	-	-	-	3	0.18	-

1/ Highest consumed commodity represents group when consumption is not available

2/ HR for whole orange fruit, no residue data for edible portion available

CARBENDAZIM (072) International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS**

ARfD: not established but may be necessary

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Country	Large portion diet		Unit weight, g	Country	Unit weight, edible portion, g	Variabi lity factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
					Body weight (kg)	Large portion, g/person							
VS 0621	Asparagus	-	0.09	USA	15.0	178	25	FRA	13	3	2a	1.22	-
FI 0327	Banana	-	0.44	JPN	15.9	312	708	USA	481	3	2b	25.89	-
GC 0640	Barley (fresh, flour, beer)	0.05	-	AUS	19.0	14	-	-	-	-	3	0.04	-

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person							
VD 0071	Beans (dry)	0.165	-	FRA	17.8	209	-	-	-	-	3	1.94	-
VB 0402	Brussels sprouts	-	0.27	NLD	17.0	213	14	UNK	10	-	1	3.38	-
VR 0577	Carrot	-	0.14	FRA	17.8	205	61	USA	50	3	2a	2.40	-
FS 0013	Cherries	-	9.1	FRA	17.8	297	5	FRA	4	-	1	151.70	-
PE 0112	Eggs (Chicken eggs 1/)	-	0	FRA	17.8	134	-	-	-	-	1	0.00	-
VP 0526	Common bean (green pods and/or immature seeds)	-	0.45	NLD	17.0	184	-	-	-	-	1	4.87	-
VC 0424	Cucumber	-	0.05	NLD	17.0	162	400	FRA	360	3	2b	1.43	-
MO 0105	Edible offal (mammalian)	-	0	FRA	17.8	203	-	-	-	-	1	0.00	-
VP 0529	Garden pea, shelled (immature seeds)	-	0.01	NLD	17.0	146	-	-	-	-	1	0.09	-
VC 0425	Gherkin	-	0.05	NLD	17.0	56	15	FRA	15	-	1	0.16	-
FB 0269	Grapes (fresh, dried, excluding wine)	-	1.9	AUS	19.0	342	125	FRA	118	3	2a	57.70	-
FI 0345	Mango	-	1.7	AUS	19.0	207	207	USA	139	3	2a	43.35	-
ML 0106	Milks	0	-	USA	15.0	1286	-	-	-	-	3	0.00	-
FC 0004	Oranges, sweet, sour (incl. Orange-like hybrids 2/)	-	0.63	UNK	14.5	495	131	USA	96	3	2a	29.82	-
FS 0247	Peach	-	1	AUS	19.0	315	98	USA	85	3	2a	25.58	-
SO 0697	Peanut	0.08	-	USA	15.0	78	-	-	-	-	3	0.41	-
FP 0009	Pome fruits (Pear 1/)	-	2.4	UNK	14.5	279	166	USA	151	3	2a	96.18	-
VO 0444	Peppers, chili	-	0.98	AUS	19.0	31	45	USA	43	3	2b	4.72	-
FI 0353	Pineapple (fresh, canned, juice, dried)	-	0.03	JPN	15.9	216	472	USA	245	3	2b	1.22	-
FS 0014	Plums (fresh, prunes)	-	0.34	FRA	17.8	254	66	USA	62	3	2a	7.23	-
PM 0110	Poultry meat	-	0	AUS	19.0	224	-	-	-	-	1	0.00	-
SO 0495	Rape seed	0	-	-	-	-	-	-	-	-	3	-	-
CM 0649	Rice, husked	0.05	-	FRA	17.8	223	-	-	-	-	3	0.63	-
VD 0541	Soya bean (dry)	0.08	-	JPN	15.9	88	-	-	-	-	3	0.44	-
VC 0431	Squash, summer	0.095	-	AUS	19.0	219	196	USA	186	3	2a	-	-
VR 0596	Sugar beet	-	0.08	-	-	-	-	-	-	-	-	-	-
VO 0448	Tomato (fresh, juice, paste, peeled)	-	0.22	USA	15.0	159	105	FRA	102	3	2a	5.32	-
GC 0080	Cereal grains (Wheat 1/)	0.03	-	USA	15.0	151	-	-	-	-	3	0.30	-

1/ Highest consumed commodity represents group when consumption is not available

2/ HR for whole orange fruit, no residue data for edible portion available

CARBOFURAN : International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS** Acute RfD= 0.009 mg/kg

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet				Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion correction factor	Large portion, corrected, g/person							
GC 0645	Maize (fresh, flour, oil)	0	-	FRA	17,8	1,00	148	-	-	ND	ND	1	0,00	0%
VR 0589	Potato	0,05	0,11	SAF	14,2	1,00	300	200	FRA	160	3	2a	4,80	50%

CARBOFURAN: International estimate of short term intake (IESTI) for **GENERAL POPULATION** Acute RfD= 0.009 mg/kg (9 µg/kg) maximum% ARfD:20%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	*	Large portion diet				Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
					Country	Body weight (kg)	Large portion correction factor	Large portion, corrected, g/person							
GC 0645	Maize (fresh, flour, oil)	0	-		FRA	62,3	1,00	260	-	-	ND	ND	1	0,00	0%
VR 0589	Potato	0,05	0,11		NLD	63,0	1,00	687	200	FRA	160	3	2a	1,76	20%

CARBOSULFAN: International estimate of short term intake (IESTI) for **GENERAL POPULATION** Acute RfD= 0.020 mg/kg (20 µg/kg) maximum Acute RfD: 2%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	*	Large portion diet				Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
					Country	Body weight (kg)	Large portion correction factor	Large portion, corrected, g/person							
PE 0840	Chicken eggs	0	-		FRA	62,3	1,00	219	-	-	ND	ND	1	0,00	0%
SO 0691	Cotton seed	0,05	-		USA	65,0	1,00	3	-	-	ND	ND	1	ND	-
MO 0105	Edible offal (mammalian)	0	-		FRA	62,3	1,00	277	-	-	ND	ND	1	ND	-
GC 0645	Maize (fresh, flour, oil)	0	-		FRA	62,3	1,00	260	-	-	ND	ND	1	0,00	0%
MM 0095	Meat from mammals other than marine mammals	0	-		AUS	67,0	1,00	521	-	-	ND	ND	1	0,00	0%
ML 0106	Milks	0	-		USA	65,0	1,00	2466	-	-	ND	ND	3	0,00	0%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet				Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion correction factor	Large portion, corrected, g/person							
FC 0004	Oranges, sweet, sour (incl. Orange-like hybrids)	-	0,01	USA	65,0	1,00	564	190	FRA	137	3	2a	0,13	1%
VR 0589	Potato	0,03	0,02	NLD	63,0	1,00	687	200	FRA	160	3	2a	0,32	2%
PM 0110	Poultry meat	0	-	AUS	67,0	1,00	431	-	-	ND	ND	1	0,00	0%
PO 0111	Poultry, edible offal of	0	-	USA	65,0	1,00	248	-	-	ND	ND	1	0,00	0%
GC 0649	Rice	0	-	FRA	62,3	1,00	312	-	-	ND	ND	1	0,00	0%
VR 0596	Sugar beet	0,05	-	-	-	1,00	ND	-	-	ND	ND	ND	ND	-

CARBOSULFAN International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS**

Acute RfD= 0.02 mg/kg (20 µg/kg) Maximum %ARfD: 4%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet				Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion correction factor	Large portion, corrected, g/person							
PE 0840	Chicken eggs	0	-	FRA	17,8	1,00	134	-	-	ND	ND	1	0,00	0%
SO 0691	Cotton seed	0,05	-	USA	15,0	1,00	1	-	-	ND	ND	1	ND	-
MO 0105	Edible offal (mammalian)	0	-	FRA	17,8	1,00	203	-	-	ND	ND	1	ND	-
GC 0645	Maize (fresh, flour, oil)	0	-	FRA	17,8	1,00	148	-	-	ND	ND	1	0,00	0%
MM 0095	Meat from mammals other than marine mammals	0	-	AUS	19,0	1,00	261	-	-	ND	ND	1	0,00	0%
ML 0106	Milks	0	-	USA	15,0	1,00	1286	-	-	ND	ND	3	0,00	0%
FC 0004	Oranges, sweet, sour (incl. Orange-like hybrids)	-	0,01	UNK	14,5	1,00	495	190	FRA	137	3	2a	0,53	3%
VR 0589	Potato	0,03	0,02	SAF	14,2	1,00	300	200	FRA	160	3	2a	0,87	4%
PM 0110	Poultry meat	0	-	AUS	19,0	1,00	224	-	-	ND	ND	1	0,00	0%
PO 0111	Poultry, edible offal of	0	-	USA	15,0	1,00	37	-	-	ND	ND	1	0,00	0%

Codex Code	Commodity	STMR mg/kg	HR or HR-P mg/kg	Country	Large portion diet			Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
					Body weight (kg)	Large portion correc- tion factor	Large portion, correc- ted, g/person							
GC 0649	Rice	0	-	FRA	17,8	1,00	223	-	-	ND	ND	1	0,00	0%
VR 0596	Sugar beet	0,05	-	-	-	1,00	ND	-	-	ND	ND	ND	ND	-
GC 0645	Maize (fresh, flour, oil)	0	-	FRA	17,8	1,00	148	-	-	ND	ND	1	0,00	0%

CHLORMEQUAT (015) International estimate of short term intake (IESTI) for **GENERAL POPULATION**

Acute RfD = 0.05 mg/kg bw

Maximum % ARfD: 170%

Codex Code	Commodity	HR or HR-P mg/kg	Large portion diet			Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
			Country	Body weight (kg)	Large portion, g/person							
FP 0230	Pear	6.3	USA	65.0	693	100	FRA	89	3	2a	84.41	170%

CHLORMEQUAT (015) :

International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS**

Acute RfD = 0.05 mg/kg bw

Maximum %ARfD: 400%

Codex Code	Commodity	HR or HR- P mg/kg	Country	Large portion diet		Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Body weight (kg)	Large portion, g/person							
FP 0230	Pear	6.3	UNK	14.5	279	100	FRA	89	3	2a	198.55	400%

CHLORPROPHAM (201) International estimate of short term intake (IESTI) for **GENERAL POPULATION**
 Acute RfD = 0.03 mg/kg bw Maximum % ARfD: 1080%

Codex Code	Commodity	HR or HR-P mg/kg	Large portion diet			Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
			Country	Body weight (kg)	Large portion, g/person							
VR 0589	Potato	23	NLD	63.0	687	122	USA	99	3	2a	322.85	1080%
	Potato, cooked	7.6	NLD	63.0	687	122	USA	99	3	2a	106.68	360%
	Potato, cooked and peeled	0.2	NLD	63.0	687	122	USA	99	3	2a	2.81	9%

CHLORPROPHAM (201) International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS**
 Acute RfD = 0.03 mg/kg bw Maximum %ARfD: 2680%

Codex Code	Commodity	HR or HR-P mg/kg	Large portion diet			Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
			Country	Body weight (kg)	Large portion, g/person							
VR 0589	Potato	23	SAF	14.2	300	122	USA	99	3	2a	805.42	2680%
	Potato, cooked	7.6	SAF	14.2	300	122	USA	99	3	2a	266.14	890%
	Potato, cooked and peeled	0.2	SAF	14.2	300	122	USA	99	3	2a	7.00	20%

DIMETHOATE (27) International estimate of short term intake (IESTI) for **GENERAL POPULATION**
 Acute RfD= 0.02 mg/kg bw/day (20 µg/kg bw/day) Maximum % acute RfD: 320%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-PP mg/kg	Large portion diet			Unit weight			Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Countr y	Body weight (kg)	Large portion, g/per- son	Unit weight , g	Countr y	Unit weight, edible portion, g				
VS 0620	Artichoke globe	-	0.2	FRA	62.3	534	230	FRA	99	3	2a	2.35	10%
VB 0402	Brussels sprouts	-	1.2	NLD	63.0	394	7	FRA	5	1	1	7.50	40%
VB 0041	Cabbages, head	-	3.26	SAF	55.7	362	771	UNK	540	3	2b	63.57	320%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-PP mg/kg	Large portion diet			Unit weight			Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
VB 0404	Cauliflower (head)	-	0.13	UNK	70.1	579	1500	JPN	1500	3	2b	3.22	20%
VS 0624	Celery (stalk)	-	0.4	FRA	62.3	225	33	UNK	30	3	2a	1.83	9%
FC 0001	Citrus fruits	0.27	-	-	-	-	-	-	-	-	-	-	-
VL 0482	Lettuce, head	-	2.7	USA	65.0	213	450	JPN	450	3	2b	26.49	130%
FI 0345	Mango	-	0.68	FRA	62.3	567	207	USA	139	3	2a	9.22	50%
OC 0305	Olive oil, crude	0.059	-	-	-	ND	-	-	-	-	3	-	-
OR 0305	Olive oil, refined	0.042	-	FRA	62.3	57	-	-	-	-	3	0.04	0%
FT 0305	Olives	2.24	-	NLD	63.0	63	-	-	-	-	-	-	-
DM 0305	Olives, processed	0.34	-	AUS	67.0	80	-	-	-	-	-	-	-
VO 0445	Peppers, sweet (incl. pim(i)ento)	-	3.7	FRA	62.3	207	40	JPN	40	3	2a	17.07	90%
GC 0654	Wheat	0.021	-	USA	65.0	383	-	-	-	-	3	0.12	1%
CF 1211	Wheat flour	0.014	-	USA	65.0	365	-	-	-	-	3	0.08	0%
CF 1212	Wheat wholemeal	0.027	-	USA	65.0	155	-	-	-	-	3	0.06	0%

DIMETHOATE (27) : International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS**
 Acute RfD= 0.020 mg/kg bw/day (20 µg/kg bw/day) Maximum % acute RfD: 760%

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/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, corrected, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
VS 0620	Artichoke globe	-	0.2	FRA	17.8	89	230	FRA	99	3	2b	3.00	20%
VB 0402	Brussels sprouts	-	1.2	NLD	17.0	213	7	FRA	5	1	1	15.00	80%
VB 0041	Cabbages, head	-	3.26	SAF	14.2	220	771	UNK	540	3	2b	151.59	760%

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/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, corrected, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
VB 0404	Cauliflower (head)	-	0.13	NLD	17.0	209	1500	JPN	1500	3	2b	4.80	20%
VS 0624	Celery (stalk)	-	0.4	FRA	17.8	111	33	UNK	30	3	2a	3.85	20%
FC 0001	Citrus fruits	0.27	-	-	-	-	-	-	-	-	-	-	-
VL 0482	Lettuce, head	-	2.7	NLD	17.0	84	450	JPN	450	3	2b	39.85	200%
FI 0345	Mango	-	0.68	AUS	19.0	207	207	USA	139	3	2a	17.34	90%
OC 0305	Olive oil, crude	0.059	-	-	-	-	-	-	-	-	3	-	-
OR 0305	Olive oil, refined	0.042	-	FRA	17.8	63	-	-	-	-	3	0.15	1%
FT 0305	Olives	2.24	-	FRA	17.8	49	-	-	-	-	-	-	-
DM 0305	Olives, processed	0.34	-	FRA	17.8	49	-	-	-	-	-	-	-
VO 0445	Peppers, sweet (incl. pim(i)ento)	-	3.7	AUS	19.0	60	40	JPN	40	3	2a	27.27	140%
GC 0654	Wheat	0.021	-	USA	15.0	151	-	-	-	-	3	0.21	1%
CF 1211	Wheat flour	0.014	-	AUS	19.0	194	-	-	-	-	3	0.14	1%
CF 1212	Wheat wholemeal	0.027	-	USA	15.0	74	-	-	-	-	3	0.13	1%

DODINE : 084 International estimate of short term intake (IESTI) for **GENERAL POPULATION**

Acute RfD= 0.2 mg/kg bw/day (200 µg/kg bw/day) Maximum %acute RfD: 30%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion g/person							
FP 0226	Apple	-	2.43	USA	65.0	1348	138	USA	127	3	2a	59.89	30%
JF 0226	Apple juice	0.15		-	-	-	-	-	-	-	-	-	-
FS 0013	Cherries	-	2.11	FRA	62.3	375	12	UNK	10	-	1	12.70	6%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person							
FS 0245	Nectarine	-	3.71	USA	65.0	590	136	USA	125	3	2a	47.97	20%
FS 0247	Peach	-	3.71	SAF	55.7	685	98	USA	85	3	2a	56.99	30%
FP 0230	Pear	-	2.43	USA	65.0	693	166	USA	151	3	2a	37.20	20%

DODINE : 084 International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS**

Acute RfD= 0.2 mg/kg bw/day (200 µg/kg bw/day) Maximum % Acute RfD: 80%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person							
FP 0226	Apple	-	2.43	USA	15.0	679	138	USA	127	3	2a	151.09	80%
JF 0226	Apple juice	0.15	0.22	-	-	ND	-	-	-	-	-	-	-
FS 0013	Cherries	-	2.11	FRA	17.8	297	12	UNK	10	1-	1	35.17	20%
FS 0245	Nectarine	-	3.71	AUS	19.0	302	136	USA	125	3	2a	107.85	50%
FS 0247	Peach	-	3.71	AUS	19.0	315	98	USA	85	3	2a	94.90	50%
FP 0230	Pear	-	2.43	UNK	14.5	279	166	USA	151	3	2a	97.38	50%

ETHEPHON (106) International estimate of short-term intake (IESTI) for GENERAL POPULATION

Acute RfD= 0.05 mg/kg bw/day (50 µg/kg bw/day)

Maximum %acute RfD: 40%

Codex Code	Commodity	HR or HR-P mg/kg	Unit weight				Unit weight, g	% edible portion, g	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg		% acute RfD rounded	
			Large portion g/kg bw/day	Large portion, g/person	Country	Body weight (kg)						µg/kg bw/day	µg/kg bw/day		
VC 4199	Cantaloupe	-	0.63	USA	65.0	9.32	606	552	USA	50%	276	3	2a	11.22	20%
VO 0445	Peppers, sweet (incl. pim(i)ento)	-	2.4	FRA	62.3	3.33	207	172	UNK	93%	160	3	2a	20.32	40%
FI 0353	Pineapple (fresh, canned, juice, dried)	-	0.97	JPN	52.6	7.06	371	700	FRA	60%	420	3	2b	20.54	40%
VO 0448	Tomato (fresh, juice, paste, peeled)	-	1.7	USA	65.0	6.01	391	123	USA	100%	123	3	2a	16.65	30%

ETHEPHON (106) International estimate of short term intake (IESTI) for CHILDREN UP TO 6 YEARS

Acute RfD= 0.05 mg/kg bw/day (50 µg/kg bw/day) Maximum %acute RfD 90%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Country	Large portion diet			Unit weight			Variability factor	Case	IESTI µg/kg		% acute RfD rounded
					Body weight (kg)	Large portion g/kg bw/day	Large portion, g/person	Unit weight, g	Country	% edible portion			Unit weight, edible portion, g	µg/kg bw/day	
VC 4199	Cantaloupe	-	0.63	USA	15.0	17.98	270	552	USA	50%	276	3	2b	33.98	70%
VO 0445	Peppers, sweet (incl. pim(i)ento)	-	2.4	AUS	19.0	3.16	60	172	UNK	93%	160	3	2b	22.75	50%
FI 0353	Pineapple (fresh, canned, juice, dried)	-	0.97	JPN	15.9	13.61	216	700	FRA	60%	420	3	2b	39.61	80%
VO 0448	Tomato (fresh, juice, paste, peeled)	-	1.7	USA	15.0	10.60	159	123	USA	100%	123	3	2a	45.90	90%

FAMOXADONE

International estimate of short term intake (IESTI)

GENERAL POPULATION

Acute RfD= 0.6 mg/kg bw/day (600 µg/kg bw)

Maximum %ARfD: 3%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion			Unit weight			Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Country	Unit weight , g	Unit weight, edible portion, g				
GC 0640	Barley (beer only)	0.008	-	AUS	67.0	528	-	-	-	-	3	0.06	0%
GC 0640	Barley (fresh, flour, beer)	-	0.11	NLD	63.0	378	-	-	-	-	3	-	-
VC 0424	Cucumber	-	0.1	NLD	63.0	313	FRA	400	360	3	2b	1.49	0%
MO 0105	Edible offal (mammalian)	-	0.24	FRA	62.3	277	-	-	-	-	1	1.07	0%
PE 0112	Eggs	-	0	FRA	17.8	134	-	-	-	-	1	0.0	0%
FB 0269	Grapes (fresh, dried, excluding wine)	-	1.5	AUS	67.0	513	FRA	125	118	3	2a	16.75	3%
DF 0269	Grapes, dried (= currants, raisins and sultanas)	-	2.85	FRA	62.3	135	-	-	-	-	1	6.18	1%
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.41	AUS	67.0	104	-	-	-	-	1	0.64	0%
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0.031	AUS	67.0	417	-	-	-	-	1	0.19	0%
ML 0106	Milks	0.009	-	USA	65.0	2466	-	-	-	-	3	0.34	0%
VR 0589	Potato	-	0	NLD	63.0	687	FRA	200	160	3	2a	0.00	0%
PM 0110	Poultry meat: 10% as fat	-	0	AUS	67.0	43	-	-	-	-	1	0.00	0%
PM 0110	Poultry meat: 90% as muscle	-	0	AUS	67.0	388	-	-	-	-	1	0.00	0%
PO 0111	Poultry, edible offal of	-	0	USA	65.0	248	-	-	-	-	1	0.00	0%
VC 0431	Squash, summer	-	0.1	FRA	62.3	343	FRA	300	270	3	2a	1.42	0%
VO 0448	Tomato (fresh, juice, paste, peeled)	-	1.1	USA	65.0	391	FRA	105	102	3	2a	10.06	2%
JF 0448	Tomato juice	0.022	-	-	-	-	-	-	-	-	3	-	-
	Tomato paste	0.13	-	-	-	-	-	-	-	-	-	-	-
GC 0654	Wheat	0.02	-	USA	65.0	383	-	-	-	-	3	0.12	0%
CF 1211	Wheat flour	0.01	-	USA	65.0	365	-	-	-	-	3	0.06	0%
CF 1212	Wheat wholemeal	0.01	-	USA	65.0	155	-	-	-	-	3	0.02	0%
	Wine only	0.005	-	AUS	67.0	1131	-	-	-	-	3	0.08	0%

FAMOXADONE International estimate of short term intake (IESTI) **CHILDREN UP TO 6 YEARS**

Acute RfD = 0.6 mg/kg bw/day (600 µg/kg bw)

Maximum %acute RfD: 8%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion			Unit weigh			Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Country	Unit weight, g	Unit weight, edible portion, g				
GC 0640	Barley (beer only)	0.008	-	AUS	19.0	12	-	-	-	-	3	0.00	0%
GC 0640	Barley (fresh, flour, beer)	-	0.11	AUS	19.0	14	-	-	-	-	3	-	-
VC 0424	Cucumber	-	0.1	NLD	17.0	162	FRA	400	360	3	2b	2.86	0%
MO 0105	Edible offal (mammalian)	-	0.24	FRA	17.8	203	-	-	-	-	1	2.73	0%
PE 0112	Eggs	-	0	FRA	17.8	134	-	-	-	-	1	0.00	0%
FB 0269	Grapes (fresh, dried, excluding wine)	-	1.5	AUS	19.0	342	FRA	125	118	3	2a	45.55	8%
DF 0269	Grapes, dried (= currants, raisins and sultanas)	-	2.85	USA	15.0	59	-	-	-	-	1	11.26	2%
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.41	AUS	19.0	52	-	-	-	-	1	1.12	0%
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0.031	AUS	19.0	208	-	-	-	-	1	0.34	0%
ML 0106	Milks	0.009	-	USA	15.0	1286	-	-	-	-	3	0.77	0%
VR 0589	Potato	-	0	SAF	14.2	300	FRA	200	160	3	2a	0.00	0%
PM 0110	Poultry meat: 10% as fat	-	0	AUS	19.0	22	-	-	-	-	1	0.00	0%
PM 0110	Poultry meat: 90% as muscle	-	0	AUS	19.0	201	-	-	-	-	1	0.00	0%
PO 0111	Poultry, edible offal of	-	0	USA	15.0	37	-	-	-	-	1	0.00	0%
VC 0431	Squash, summer	-	0.1	AUS	19.0	219	FRA	300	270	3	2b	3.46	1%
VO 0448	Tomato (fresh, juice, paste, peeled)	-	1.1	USA	15.0	159	FRA	105	102	3	2a	26.60	4%
FJ 0448	Tomato juice	0.022	-	-	-	-	-	-	-	-	3	-	-
-d	Tomato paste	0.13	-	-	-	-	-	-	-	-	-	-	-
GC 0654	Wheat	0.02	-	USA	15.0	151	-	-	-	-	3	0.20	0%
CF 1211	Wheat flour	0.01	-	AUS	19.0	194	-	-	-	-	3	0.10	0%
CF 1212	Wheat wholemeal	0.01	-	USA	15.0	74	-	-	-	-	3	0.05	0%
-	Wine only	0.005	-	AUS	19.0	4	-	-	-	-	3	0.00	0%

FENITROTHION : International estimate of short term intake (IESTI) for GENERAL POPULATION

Acute RfD= 0.04 mg/kg bw (40 µg/kg bw) Maximum %ARfD: 150%

Codex Code	Commodity	STMTR or STMTR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight, g	Country	Unit weight		Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, corrected, g/person			Unit weight, edible portion, g	Variabil- ity factor			
GC 0645	Maize (fresh, flour, oil)	-	7.6	FRA	62.3	260	-	-	ND	ND	1	31.69	80%
CM 0649	Rice, husked	-	7.6	JPN	52.6	319	-	-	ND	ND	1	46.13	120%
CM 1205	Rice, polished	-	7.6	JPN	52.6	402	-	-	ND	ND	1	58.06	150%
CF 1211	Wheat flour	1.175	-	USA	65.0	365	-	-	ND	ND	3	6.60	20%
CP 1211	White bread	0.05	-	SAF	55.7	479	-	-	ND	ND	3	0.43	1%
CP 1212	Wholemeal bread	1.9	-	SAF	55.7	395	-	-	ND	ND	3	13.49	30%

FENITROTHION : International estimate of short term intake (IESTI) for CHILDREN UP TO 6 YEARS

Maximum %ARfD: 240%

Codex Code	Commodity	STMTR or STMTR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight, g	Country	Unit weight		Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, corrected, g/person			Unit weight, edible portion, g	Variabil- ity factor			
GC 0645	Maize (fresh, flour, oil)	-	7.6	FRA	17.8	148	-	-	-	-	1	63.31	160%
CM 0649	Rice, husked	-	7.6	FRA	17.8	223	-	-	-	-	1	95.00	240%
CM 1205	Rice, polished	-	7.6	JPN	15.9	199	-	-	-	-	1	94.92	240%
CF 1211	Wheat flour	1.175	-	AUS	19.0	194	-	-	-	-	3	12.02	30%
CP 1211	White bread	0.05	-	SAF	14.2	270	-	-	-	-	3	0.95	2%
CP 1212	Wholemeal bread	1.9	-	SAF	14.2	240	-	-	-	-	3	32.11	80%

LINDANE : International estimate of short term intake (IESTI) for **GENERAL POPULATION**
 Acute RfD= 0.06 mg/kg bw (60 µg/kg bw/day) Maximum %ArfD: 0%

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/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, corrected, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
GC 0640	Barley (fresh)	0.005	-	-	-	-	-	-	-	-	3	-	-
PE 0840 ¹	Chicken eggs	-	0.002	FRA	62.3	219	-	-	-	-	1	0.01	0%
MO 0105	Edible offal (mammalian)	-	0.002	FRA	62.3	277	-	-	-	-	1	0.01	0%
GC 0645	Maize (fresh)	0.005	-	-	-	-	-	-	-	-	3	-	-
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.06	AUS	67.0	104	-	-	-	-	1	0.09	0%
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0.005	AUS	67.0	417	-	-	-	-	1	0.03	0%
ML 0106	Milks	0.0003	-	USA	65.0	2466	-	-	-	-	3	0.01	0%
GC 0647	Oats	0.005	-	FRA	62.3	305	-	-	-	-	3	0.02	0%
PM 0110	Poultry meat: 10% as fat	-	0.016	AUS	67.0	43	-	-	-	-	1	0.01	0%
PM 0110	Poultry meat: 90% as muscle	-	0.001	AUS	67.0	388	-	-	-	-	1	0.01	0%
PO 0111	Poultry, edible offal of	-	0.001	USA	65.0	248	-	-	-	-	1	0.00	0%
GC 0650	Rye	0.005	-	NLD	63.0	77	-	-	-	-	3	0.01	0%
GC 0651	Sorghum	0.005	-	USA	65.0	18	-	-	-	-	3	0.00	0%
VO 1275	Sweet corn (kernels)	0.005	-	-	-	-	-	-	-	-	3	-	-
GC 0654	Wheat	0.005	-	USA	65.0	383	-	-	-	-	3	0.03	0%

¹ Because of lack of information on large portion size of PE 0112 Eggs, the calculation was made for PE 0840 Chicken eggs.

LINDANE

Maximum %ARfD: 0%

International estimate of short term intake (IESTI) for **CHILDREN UP TO 6 YEARS**

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/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, corrected, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
GC 0640	Barley (fresh)	0.005	-	-	-	-	-	-	-	-	3	-	-
PE 0840 ¹	Chicken eggs	-	0.002	FRA	17.8	134	-	-	-	-	1	0.02	0%
MO 0105	Edible offal (mammalian)	-	0.002	FRA	17.8	203	-	-	-	-	1	0.02	0%
GC 0645	Maize (fresh)	0.005	-	-	-	-	-	-	-	-	3	-	-
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.06	AUS	19.0	52	-	-	-	-	1	0.16	0%
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0.005	AUS	19.0	208	-	-	-	-	1	0.05	0%
ML 0106	Milks	0.0003	-	USA	15.0	1286	-	-	-	-	3	0.03	0%
GC 0647	Oats	0.005	-	USA	15.0	62	-	-	-	-	3	0.02	0%
PM 0110	Poultry meat: 10% as fat	-	0.016	AUS	19.0	22	-	-	-	-	1	0.02	0%
PM 0110	Poultry meat: 90% as muscle	-	0.001	AUS	19.0	201	-	-	-	-	1	0.01	0%
PO 0111	Poultry, edible offal of	-	0.001	USA	15.0	37	-	-	-	-	1	0.00	0%
GC 0650	Rye	0.005	-	NLD	17.0	37	-	-	-	-	3	0.01	0%
GC 0651	Sorghum	0.005	-	-	-	-	-	-	-	-	3	-	-
VO 1275	Sweet corn (kernels)	0.005	-	-	-	-	-	-	-	-	3	-	-
GC 0654	Wheat	0.005	-	USA	15.0	151	-	-	-	-	3	0.05	0%

¹ Because of lack of information on large portion size of PE 0112 Eggs, the calculation was made for PE 0840 Chicken eggs.

MALATHION (049) : International estimate of short term intake (IESTI) for **GENERAL POPULATION**
 Acute RfD= 2 mg/kg bw/day (2000 µg/kg bw/day) Maximum %acute RfD: 2%

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/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion g/kg bw/day	Large portion, g/person	Unit weight, g	Country	% edible portion	Unit weight, edible portion, g				
VS 0621	Asparagus	-	0.69	NLD	63.0	6.32	398	16	USA	56%	9	1	1	4.36	0%
VD 0071	Beans (dry)	0.215	-	FRA	62.3	4.10	255	-	-	-	-	-	3	0.88	0%
VP 0061	Beans except broad bean & soya bean (green pods & immature seeds)	-	0.9	FRA	62.3	5.00	312	-	-	-	-	-	1	4.50	0%
FB 0020	Blueberries	-	7.5	AUS	67.0	2.36	158	-	-	-	-	-	1	17.70	1%
SO 0691	Cotton seed	4.8	-	USA	65.0	0.05	3	-	-	-	-	-	3	0.24	0%
OR 0691	Cotton seed oil, edible	3.06	-	USA	65.0	0.14	9	-	-	-	-	-	3	0.43	0%
VC 0424	Cucumber	-	0.1	NLD	63.0	4.97	313	301	USA	95%	286	3	2a	1.40	0%
GC 0645	Maize (fresh, flour, oil)	0.01	-	FRA	62.3	4.17	260	-	-	-	-	-	3	0.04	0%
VL 0485	Mustard greens	-	1.1	USA	65.0	3.50	228	-	-	-	-	-	1	3.85	0%
VA 0385	Onion, bulb	-	1	FRA	62.3	4.91	306	110	USA	91%	100	3	2a	8.12	0%
VO 0445	Peppers, sweet (incl. pim(i)ento)	-	0.08	FRA	62.3	3.33	207	119	USA	82%	98	3	2a	0.52	0%
VL 0502	Spinach (bunch)	-	2.2	NLD	63.0	13.01	820	340	USA	72%	245	3	2a	45.72	2%
VA 0389	Spring onion	-	5	AUS	67.0	0.90	60	-	-	-	-	-	1	4.50	0%
FB 0275	Strawberry	-	0.59	FRA	62.3	5.55	346	14	FRA	96%	13	1	1	3.27	0%
VO 0447	Sweet corn (corn-on-the-cob)	-	0.02	USA	65.0	5.65	367	215	UNK	58%	125	3	2a	0.19	0%
VO 0448	Tomato (fresh, juice, paste, peeled)	-	0.41	USA	65.0	6.01	391	123	USA	100%	123	3	2a	4.02	0%
JF 0448	Tomato juice	0.03	-	-	-	-	-	-	-	-	-	-	3	-	-
VR 0506	Turnip, Garden	-	0.13	USA	65.0	3.61	235	122	USA	86%	105	3	2a	0.89	0%
GC 0654	Wheat	0.702	-	USA	65.0	5.89	383	-	-	-	-	-	3	4.13	0%

MALATHION (049) : International estimate of short term intake (IESTI) for CHILDREN UP TO 6 YEARS

Acute RfD= 2 mg/kg bw/day (2000 µg/kg bw/day Maximum %acute RfD: 7%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Country	Large portion diet			Unit weight, g	Unit weight			Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
					Body weight (kg)	Large portion g/kg bw/day	Large portion, g/person		Country	% edible portion	Unit weight, g/kg bw/day				
VS 0621	Asparagus	-	0.69	USA	15.0	11.88	178	16	USA	56%	9	1	1	8.20	0%
VD 0071	Beans (dry)	0.215	-	FRA	17.8	11.76	209	-	-	-	-	-	3	2.53	0%
VP 0061	Beans except broad bean & soya bean (green pods & immature seeds)	-	0.9	FRA	17.8	11.39	203	-	-	-	-	-	1	10.25	1%
FB 0020	Blueberries	-	7.5	FRA	17.8	7.77	138	-	-	-	-	-	1	58.28	3%
SO 0691	Cotton seed	4.8	-	USA	15.0	0.05	1	-	-	-	-	-	3	0.24	0%
OR 0691	Cotton seed oil, edible	3.06	-	USA	15.0	0.41	6	-	-	-	-	-	3	1.25	0%
VC 0424	Cucumber	-	0.1	NLD	17.0	9.53	162	301	USA	95%	286	3	2b	2.86	0%
GC 0645	Maize (fresh, flour, oil)	0.01	-	FRA	17.8	8.33	148	-	-	-	-	-	3	0.08	0%
VL 0485	Mustard greens	-	1.1	USA	15.0	3.52	53	-	-	-	-	-	1	3.87	0%
VA 0385	Onion, bulb	-	1	FRA	17.8	7.14	127	110	USA	91%	100	3	2a	18.39	1%
VO 0445	Peppers, sweet (incl. pim(i)ento)	-	0.08	AUS	19.0	3.16	60	119	USA	82%	98	3	2b	0.76	0%
VL 0502	Spinach (bunch)	-	2.2	SAF	14.2	29.60	420	340	USA	72%	245	3	2a	140.97	7%
VA 0389	Spring onion	-	5	AUS	19.0	1.52	29	-	-	-	-	-	1	7.59	0%
FB 0275	Strawberry	-	0.59	AUS	19.0	9.28	176	14	FRA	96%	13	1	1	5.48	0%
VO 0447	Sweet corn (corn-on-the-cob)	-	0.02	UNK	14.5	11.09	161	215	UNK	58%	125	3	2a	0.57	0%
VO 0448	Tomato (fresh, juice, paste, peeled)	-	0.41	USA	15.0	10.60	159	123	USA	100%	123	3	2a	11.07	1%
FJ 0448	Tomato juice	0.03	-	-	-	-	-	-	-	-	-	-	3	-	-
VR 0506	Turnip, Garden	-	0.13	JPN	15.9	4.87	77	122	USA	86%	105	3	2b	1.90	0%
GC 0654	Wheat	0.702	-	USA	15.0	10.07	151	-	-	-	-	-	3	7.07	0%

METHAMIDOPHOS : International estimate of short term intake (IESTI) for GENERAL POPULATION

Maximum %acute RfD: 150% (0.01 mg/kg bw)

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Country	Large portion diet		Unit weight, g	Unit weight		Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
					Body weight (kg)	Large portion, g/person		Country	Unit weight, edible portion, g				
FP 0226	Apple (note 1)	-	0.24	USA	65.0	1348	110	FRA	100	3	2a	5.72	60%
JF 0226	Apple juice	-	0.24	-	-	-	-	-	-	-	3	-	-
VS 0620	Artichoke globe	-	0.08	FRA	62.3	534	230	FRA	99	3	2a	0.94	9%
VP 0061	Beans except broad bean & soya bean (green pods & immature seeds)	-	0.54	FRA	62.3	312	-	-	-	-	1	2.70	30%
VB 0400	Broccoli (note 2)	-	0.33	USA	65.0	376	608	USA	474	3	2b	5.73	60%
VB 0041	Cabbages, head	-	0.62	SAF	55.7	362	771	UNK	540	3	2b	12.09	120%
VB 0404	Cauliflower (head) (note 2)	-	0.33	UNK	70.1	579	1733	UNK	780	3	2b	8.18	80%
PE 0840	Chicken eggs	-	0.01	FRA	62.3	219	-	-	-	-	1	0.04	0%
SO 0691	Cotton seed	0.01	-	USA	65.0	3	-	-	-	-	3	0.00	0%
OC 0691	Cotton seed oil, crude	0.00014	-	-	-	-	-	-	-	-	3	-	-
MO 0105	Edible offal (mammalian)	-	0.01	FRA	62.3	277	-	-	-	-	1	0.04	0%
FC 0206	Mandarin	-	0.26	JPN	52.6	409	70	JPN	70	3	2a	2.71	30%
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.01	AUS	67.0	104	-	-	-	-	1	0.02	0%
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0.01	AUS	67.0	417	-	-	-	-	1	0.06	1%
ML 0106	Milks	0.01	-	USA	65.0	2466	-	-	-	-	3	0.38	4%
FS 0245	Nectarine	-	0.35	USA	65.0	590	110	FRA	99	3	2a	4.24	40%
FS 0247	Peach	-	0.35	SAF	55.7	685	110	FRA	99	3	2a	5.55	60%
FP 0230	Pear (note 1)	-	0.24	USA	65.0	693	100	FRA	89	3	2a	3.22	30%
VO 0444	Peppers, chili (note 3)	-	1.6	USA	65.0	90	45	USA	43	3	2a	4.35	40%
VO 0445	Peppers, sweet (incl. pimento) (note 3)	-	1.6	FRA	62.3	207	172	UNK	160	3	2a	13.54	140%
VR 0589	Potato	-	0.02	NLD	63.0	687	216	UNK	216	3	2a	0.36	4%
PM 0110	Poultry meat: 10% as fat	-	0.01	AUS	67.0	43	-	-	-	-	1	0.01	0%
PM 0110	Poultry meat: 90% as muscle	-	0.01	AUS	67.0	388	-	-	-	-	1	0.06	1%
PO 0111	Poultry, edible offal of	-	0.01	USA	65.0	248	-	-	-	-	1	0.04	0%
FP 0231	Quince (note 1)	-	0.24	AUS	67.0	175	92	USA	56	3	2a	1.03	10%
VD 0541	Soya bean (dry)	0.01	-	JPN	52.6	159	-	-	-	-	3	0.03	0%

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/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
OC 0541	Soya bean oil, crude	0.005	-	-	-	-	-	-	-	3	-	-	
VR 0596	Sugar beet	-	0.01	-	-	-	-	-	-	-	-	-	
VO 0448	Tomato (fresh, juice, paste, peeled)	-	1.5	USA	65.0	391	123	USA	123	3	2a	14.69	150%

Note 1: Group maximum residue level proposed for pome fruit

Note 2: Group maximum residue level proposed for flowerhead brassicas

Note 3: Maximum residue level proposed for peppers includes both peppers, sweet and peppers, chili

METHAMIDOPHOS International estimate of short term intake (IESTI) for CHILDREN UP TO 6 YEARS

Maximum %acute RfD: 410% (0.01 mg/kg bw)

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/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
FP 0226	Apple (note 1)	-	0.24	USA	15.0	679	110	FRA	100	3	2a	14.06	140%
JF 0226	Apple juice	-	0.24	-	-	-	-	-	-	-	3	-	-
VS 0620	Artichoke globe	-	0.08	FRA	17.8	89	230	FRA	99	3	2b	1.20	10%
VP 0061	Beans except broad bean & soya bean (green pods & immature seeds)	-	0.54	FRA	17.8	203	-	-	-	-	1	6.15	60%
VB 0400	Broccoli (note 2)	-	0.33	USA	15.0	164	608	USA	474	3	2b	10.84	110%
VB 0041	Cabbages, head	-	0.62	SAF	14.2	220	771	UNK	540	3	2b	28.83	290%
VB 0404	Cauliflower (head) (note 2)	-	0.33	NLD	17.0	209	1733	UNK	780	3	2b	12.19	120%
PE 0840	Chicken eggs	-	0.01	FRA	17.8	134	-	-	-	-	1	0.08	1%
SO 0691	Cotton seed	0.01	-	USA	15.0	1	-	-	-	-	3	0.00	0%
OC 0691	Cotton seed oil, crude	0.00014	-	-	-	-	-	-	-	-	3	-	-
MO 0105	Edible offal (mammalian)	-	0.01	FRA	17.8	203	-	-	-	-	1	0.11	1%
FC 0206	Mandarin	-	0.26	JPN	15.9	353	70	JPN	70	3	2a	8.07	80%
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.01	AUS	19.0	52	-	-	-	-	1	0.03	0%
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0.01	AUS	19.0	208	-	-	-	-	1	0.11	1%
ML 0106	Milks	0.01	-	USA	15.0	1286	-	-	-	-	3	0.86	9%
FS 0245	Nectarine	-	0.35	AUS	19.0	302	110	FRA	99	3	2a	9.21	90%
FS 0247	Peach	-	0.35	AUS	19.0	315	110	FRA	99	3	2a	9.46	90%
FP 0230	Pear (note 1)	-	0.24	UNK	14.5	279	100	FRA	89	3	2a	7.56	80%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Country	Large portion diet		Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
					Body weight (kg)	Large portion, g/person							
VO 0444	Peppers, chili (note 3)	-	1.6	AUS	19.0	31	45	USA	43	3	2b	7.71	80%
VO 0445	Peppers, sweet (incl. pim(i)ento) (note 3)	-	1.6	AUS	19.0	60	172	UNK	160	3	2b	15.17	150%
VR 0589	Potato	-	0.02	SAF	14.2	300	216	UNK	216	3	2a	1.03	10%
PM 0110	Poultry meat: 10% as fat	-	0.01	AUS	19.0	22	-	-	-	-	1	0.01	0%
PM 0110	Poultry meat: 90% as muscle	-	0.01	AUS	19.0	201	-	-	-	-	1	0.11	1%
PO 0111	Poultry, edible offal of	-	0.01	USA	15.0	37	-	-	-	-	1	0.02	0%
FP 0231	Quince (note 1)	-	0.24	NLD	17.0	1	92	USA	56	3	2b	0.04	0%
VD 0541	Soya bean (dry)	0.01	-	JPN	15.9	88	-	-	-	-	3	0.06	1%
OC 0541	Soya bean oil, crude	0.005	-	-	-	-	-	-	-	-	3	-	-
VR 0596	Sugar beet	-	0.01	-	-	-	-	-	-	-	-	-	-
VO 0448	Tomato (fresh, juice, paste, peeled)	-	1.5	USA	15.0	159	123	USA	123	3	2a	40.50	410%

Note 1: Group maximum residue level proposed for pome fruit

Note 2: Group maximum residue level proposed for flowerhead brassicas

Note 3: Maximum residue level proposed for peppers includes both peppers, sweet and peppers, chili

Methoxyfenozide209 International estimate of short term intake (IESTI) for GENERAL POPULATION

Acute RfD= 0.900 mg/kg bw/day b(900 µg/kg bw/day) Maximum %ARfD: 100%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Country	Large portion diet		Unit weight				Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
					Body weight (kg)	Large portion, corrected, g/person	Unit weight, g	Country	% edible portion	Unit weight, edible portion, g				
FP 0226	Apple	-	1	USA	65.0	1348	138	USA	92%	127	3	2a	24.65	3%
VB 0400	Broccoli	-	1.6	USA	65.0	376	608	USA	78%	474	3	2b	27.79	3%
VB 0041	Cabbages, head	-	6.2	SAF	55.7	362	908	USA	79%	717	3	2b	120.90	10%
VS 0624	Celery (stalk)	-	7.8	FRA	62.3	225	40	USA	100%	40	3	2a	38.17	4%
FS 0013	Cherries	-	0.56	FRA	62.3	375	5	FRA	89%	4	1	1	3.37	0%
PE 0840	Chicken eggs	-	0.003	FRA	62.3	219	-	-	-	-	-	1	0.01	0%
SO 0691	Cotton seed	-	4.9	USA	65.0	3	-	-	-	-	-	3	-	-

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Country	Large portion diet		Unit weight				Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
					Body weight (kg)	Large portion, corrected, g/person	Unit weight, g	Country	% edible portion	Unit weight, edible portion, g				
MO 0096	Edible offal of cattle, goats, horses, pigs & sheep	-	0.017	FRA	62.3	277	-	-	-	-	-	1	0.08	0%
FB 0269	Grapes (fresh, wine, dried)	-	0.84	AUS	67.0	1004	125	FRA	94%	118	3	2a	15.54	2%
DF 0269	Grapes, dried (= currants, raisins and sultanas)	-	2.2	FRA	62.3	135	-	-	-	-	-	-	-	-
VL 0482	Lettuce, head	-	9.6	USA	65.0	213	539	USA	95%	512	3	2b	94.18	10%
VL 0483	Lettuce, leaf	-	18	NLD	63.0	152	10	USA	100%	10	1	1	43.38	5%
GC 0645	Maize (fresh, flour, oil)	-	0.02	FRA	62.3	260	-	-	-	-	-	3	-	-
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.046	AUS	67.0	104	-	-	-	-	-	1	0.07	0%
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0.0017	AUS	67.0	417	-	-	-	-	-	1	0.01	0%
ML 0106	Milks	0.0041	-	USA	65.0	2466	-	-	-	-	-	3	0.16	0%
VL 0485	Mustard greens	-	18	USA	65.0	228	-	-	-	-	-	-	-	-
FS 0245	Nectarine	-	1.4	USA	65.0	590	136	USA	92%	125	3	2a	18.10	2%
FS 0247	Peach	-	1.4	SAF	55.7	685	98	USA	87%	85	3	2a	21.51	2%
FP 0230	Pear	-	0.92	USA	65.0	693	166	USA	91%	151	3	2a	14.08	2%
VO 0444	Peppers, chili	-	0.94	USA	65.0	90	45	USA	96%	43	3	2a	2.56	0%
VO 0445	Peppers, sweet	-	0.94	FRA	62.3	207	119	USA	82%	98	3	2a	6.07	1%
FS 0014	Plums (fresh, prunes)	-	0.34	USA	65.0	413	66	USA	94%	62	3	2a	2.81	0%
PM 0110	Poultry meat: 10% as fat	-	0	AUS	67.0	43	-	-	-	-	-	1	0.00	0%
PM 0110	Poultry meat: 90% as muscle	-	0	AUS	67.0	388	-	-	-	-	-	1	0.00	0%
PO 0111	Poultry, edible offal of	-	0	USA	65.0	248	-	-	-	-	-	1	0.00	0%
DF 0014	Prunes	-	1.5	USA	65.0	303	6	FRA	83%	5	1	1	6.99	1%
VL 0502	Spinach (bunch)	-	43	NLD	63.0	820	340	USA	72%	245	3	2a	893.60	100%
VO 0447	Sweet corn (corn-on-	-	0.02	USA	65.0	367	200	JPN	100%	200	3	2a	0.24	0%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Country	Large portion diet Body weight (kg)	Large portion, corrected, g/person	Unit weight			Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded	
							Unit weight, g	Country	% edible portion					
	the-cob)													
VO 0448	Tomato (fresh, juice, paste, peeled)	-	1.8	USA	65.0	391	123	USA	100%	123	3	2a	17.63	2%
TN 0085	Tree nuts	-	0.074	JPN	52.6	107	-	-	-	-	-	-	-	-
-d	Wine only	0.13	-	AUS	67.0	1131	-	-	-	-	-	3	2.19	0%

METHOXYFENOZIDE (209) International Estimate of short term Intake (IESTI) for **CHILDREN UP TO 6 YEARS**

Acute RfD = 0.90 mg/kg bw/day (900 µg/kg bw/day)

Maximum %ARfD: 310%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Country	Large portion diet Body weight (kg)	Large portion, corrected, g/person	Unit weight			Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded	
							Unit weight, g	Country	% edible portion					
FP 0226	Apple	-	1	USA	15.0	679	138	USA	92%	127	3	2a	62.18	7%
VB 0400	Broccoli	-	1.6	USA	15.0	164	608	USA	78%	474	3	2b	52.56	6%
VB 0041	Cabbages, head	-	6.2	SAF	14.2	220	908	USA	79%	717	3	2b	288.30	30%
VS 0624	Celery (stalk)	-	7.8	FRA	17.8	111	40	USA	100%	40	3	2a	83.81	9%
FS 0013	Cherries	-	0.56	FRA	17.8	297	5	FRA	89%	4	1	1	9.34	1%
PE 0840	Chicken eggs	-	0.003	FRA	17.8	134	-	-	-	-	-	1	0.02	0%
SO 0691	Cotton seed	-	4.9	USA	15.0	1	-	-	-	-	-	3	-	-
MO 0096	Edible offal of cattle, goats, horses, pigs & sheep	-	0.017	FRA	17.8	203	-	-	-	-	-	1	0.19	0%
FB 0269	Grapes (fresh, wine, dried)	-	0.84	JPN	15.9	388	125	FRA	94%	118	3	2a	32.90	4%
DF 0269	Grapes, dried (= currants, raisins and sultanas)	-	2.2	USA	15.0	59	-	-	-	-	-	-	-	-
VL 0482	Lettuce, head	-	9.6	NLD	17.0	84	539	USA	95%	512	3	2b	141.70	20%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Country	Large portion diet Body weight (kg)	Large portion, corrected, g/person	Unit weight				Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
							Unit weight, g	Country	% edible portion	Unit weight, edible portion, g				
VL 0483	Lettuce, leaf	-	18	NLD	17.0	102	10	USA	100%	10	1	1	108.00	10%
GC 0645	Maize (fresh, flour, oil)	-	0.02	FRA	17.8	148	-	-	-	-	-	3	-	-
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.046	AUS	19.0	52	-	-	-	-	-	1	0.13	0%
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0.0017	AUS	19.0	208	-	-	-	-	-	1	0.02	0%
ML 0106	Milks	0.0041	-	USA	15.0	1286	-	-	-	-	-	3	0.35	0%
VL 0485	Mustard greens	-	18	USA	15.0	53	-	-	-	-	-	-	-	-
FS 0245	Nectarine	-	1.4	AUS	19.0	302	136	USA	92%	125	3	2a	40.70	5%
FS 0247	Peach	-	1.4	AUS	19.0	315	98	USA	87%	85	3	2a	35.81	4%
FP 0230	Pear	-	0.92	UNK	14.5	279	166	USA	91%	151	3	2a	36.87	4%
VO 0444	Peppers, chili	-	0.94	AUS	19.0	31	45	USA	96%	43	3	2b	4.53	1%
VO 0445	Peppers, sweet	-	0.94	AUS	19.0	60	119	USA	82%	98	3	2b	8.91	1%
FS 0014	Plums (fresh, prunes)	-	0.34	FRA	17.8	254	66	USA	94%	62	3	2a	7.23	1%
PM 0110	Poultry meat: 10% as fat	-	0	AUS	19.0	22	-	-	-	-	-	1	0.00	0%
PM 0110	Poultry meat: 90% as muscle	-	0	AUS	19.0	201	-	-	-	-	-	1	0.00	0%
PO 0111	Poultry, edible offal of	-	0	USA	15.0	37	-	-	-	-	-	1	0.00	0%
DF 0014	Prunes	-	1.5	AUS	19.0	170	6	FRA	83%	5	1	1	13.43	1%
VL 0502	Spinach (bunch)	-	43	SAF	14.2	420	340	USA	72%	245	3	2a	2755.39	310%
VO 0447	Sweet corn (corn-on-the-cob)	-	0.02	UNK	14.5	161	200	JPN	100%	200	3	2b	0.67	0%
VO 0448	Tomato (fresh, juice, paste, peeled)	-	1.8	USA	15.0	159	123	USA	100%	123	3	2a	48.60	5%
TN 0085	Tree nuts	-	0.074	AUS	19.0	28	-	-	-	-	-	-	-	-
-	Wine only	0.13	-	AUS	19.0	4	-	-	-	-	-	3	0.03	0%

OXAMYL (126) : International estimate of short term intake (IESTI) for GENERAL POPULATION

Acute RfD = 0.009 mg/kg bw

Maximum % ARfD: 510%

Codex Code	Commodity	HR or HR-P mg/kg	Large portion diet			Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
			Country	Body weight (kg)	Large portion, g/person							
FP 0226	Apple	1.2	USA	65.0	1348	138	USA	127	3	2a	29.58	330%
VC 0046	Melons, except watermelons (Cantaloupe 1/)	0.54	USA	65.0	606	552	USA	276	3	2a	9.62	110%
VC 0424	Cucumber	0.54	NLD	63.0	313	301	USA	286	3	2a	7.59	80%
FC 0203	Grapefruit	2	JPN	52.6	947	256	USA	125	3	2a	45.54	510%
FC 0204	Lemon	2	FRA	62.3	115	108	USA	72	3	2a	8.35	90%
FC 0206	Mandarin	2	JPN	52.6	409	168	USA	124	3	2a	24.99	280%
FC 0004	Oranges, sweet, sour (incl. Orange-like hybrids)	2	USA	65.0	564	131	USA	96	3	2a	23.24	260%
VO 0445	Peppers, sweet (incl. pim(i)ento)	4.3	FRA	62.3	207	119	USA	98	3	2a	27.79	310%
VO 0448	Tomato (fresh, juice, paste, peeled)	0.99	USA	65.0	391	123	USA	123	3	2a	9.70	110%

1/ Highest consumed commodity represents group when consumption is not available

OXAMYL (126) : International estimate of short term intake (IESTI) for CHILDREN UP TO 6 YEARS

Acute RfD = 0.009 mg/kg bw

Maximum % ARfD: 1050%

Codex Code	Commodity	HR or HR-P mg/kg	Large portion diet			Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
			Country	Body weight (kg)	Large portion, g/person							
FP 0226	Apple	1.2	USA	15.0	679	138	USA	127	3	2a	74.61	830%
VC 0046	Melons, except watermelons (Cantaloupe 1/)	0.54	USA	15.0	270	552	USA	276	3	2b	29.13	320%
VC 0424	Cucumber	0.54	NLD	17.0	162	301	USA	286	3	2b	15.44	170%
FC 0203	Grapefruit	2	FRA	17.8	381	256	USA	125	3	2a	71.05	790%
FC 0204	Lemon	2	JPN	15.9	88	108	USA	72	3	2a	29.32	330%
FC 0206	Mandarin	2	JPN	15.9	353	168	USA	124	3	2a	75.72	840%
FC 0004	Oranges, sweet, sour (incl. Orange-like hybrids)	2	UNK	14.5	495	131	USA	96	3	2a	94.66	1050%
VO 0445	Peppers, sweet (incl. pim(i)ento)	4.3	AUS	19.0	60	119	USA	98	3	2b	40.76	450%
VO 0448	Tomato (fresh, juice, paste, peeled)	0.99	USA	15.0	159	123	USA	123	3	2a	26.73	300%

1/ Highest consumed commodity represents group when consumption is not available

PARATHION (58) : International estimate of short term intake (IESTI) for GENERAL POPULATION

Acute RfD= 0.01 mg/kg bw/day (10 µg/kg bw/day) Maximum %acute RfD: 120%

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/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion g/kg bw/day	Large portion, g/person	Unit weight, g	Country % edible portion	Unit weight, edible portion, g	Unit weight, edible portion, g				
FP 0226	Apple	-	0.16	USA	65.0	20.74	1348	110	FRA	91%	100	3	2a	3.81	40%
GC 0640	Barley (fresh, flour, beer)	1.95	-	NLD	63.0	6.00	378	-	-	-	-	-	3	11.70	120%

PARATHION (58) : International estimate of short term intake (IESTI) for CHILDREN UP TO 6 YEARS

Acute RfD= 0.010 mg/kg bw/day (10 µg/kg bw/day) Maximum % acute RfD: 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/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion g/kg bw/day	Large portion, g/person	Unit weight, g	Country % edible portion	Unit weight, edible portion, g	Unit weight, edible portion, g				
FP 0226	Apple	-	0.16	USA	15.0	45.25	679	110	FRA	91%	100	3	2a	9.38	90%
GC 0640	Barley (fresh, flour, beer)	1.95	-	AUS	19.0	0.73	14	-	-	-	-	-	3	1.42	10%

PARATHION-METHYL (59) :International estimate of short term intake (IESTI) for GENERAL POPULATION

Acute RfD= 0.030 mg/kg bw/day (30 µg/kg bw/day) Maximum % acute RfD: 9 %

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/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion g/kg bw/day	Large portion, g/person	Unit weight, g	Country % edible portion	Unit weight, edible portion, g	Unit weight, edible portion, g				
FS 0245	Nectarine	0.095	0.22	USA	65.0	9.08	590	110	FRA	90%	99	3	2a	2.67	9 %

PARATHION-METHYL (59) : International estimate of short term intake (IESTI) for CHILDREN UP TO 6 YEARS

Acute RfD= 0.030 mg/kg bw/day (30 µg/kg bw/day) Maximum % acute RfD: 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/day	% acute RfD rounded	
				Country	Body weight (kg)	Large portion g/kg bw/day	Large portion, g/person	Unit weight, g	Country	% edible portion					Unit weight, edible portion, g
FS 0245	Nectarine	0.095	0.22	AUS	19.0	15.90	302	110	FRA	90%	99	3	2a	5.79	20 %

PIRIMIPHOS-METHYL (86) : International estimate of short term intake (IESTI) for GENERAL POPULATION

Acute RfD=Maximum % acute RfD:

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/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
GC 0640	Barley (beer only)	0.01	-	AUS	67.0	528	-	-	-	-	3	0.08	-
GC 0640	Barley (fresh, flour, beer)		4.5	NLD	63.0	378	-	-	-	-	1	27.00	-
GC 0645	Maize (fresh, flour, oil)		4.5	FRA	62.3	260	-	-	-	-	1	18.77	-
ML 0106	Milks	0.003	-	USA	65.0	2466	-	-	-	-	3	0.11	-
GC 0647	Oats		4.5	FRA	62.3	305	-	-	-	-	1	22.05	-
GC 0649	Rice		4.5	FRA	62.3	312	-	-	-	-	1	22.50	-
GC 0650	Rye		4.5	NLD	63.0	77	-	-	-	-	1	5.49	-
GC 0654	Wheat		4.5	USA	65.0	383	-	-	-	-	1	26.51	-
CM 0654	Wheat bran, unprocessed	5.1	-	USA	65.0	80	-	-	-	-	3	6.27	-
CF 1211	Wheat flour	0.39	-	USA	65.0	365	-	-	-	-	3	2.19	-
CF 1212	Wheat wholemeal	1.6	-	USA	65.0	155	-	-	-	-	3	3.82	-
CP 1211	White bread	0.22	-	SAF	55.7	479	-	-	-	-	3	1.89	-
CP 1212	Wholemeal bread	0.83	-	SAF	55.7	395	-	-	-	-	3	5.89	-

PIRIMIPHOS-METHYL (86) : International estimate of short term intake (IESTI) for CHILDREN UP TO 6 YEARS

Acute RfD= Maximum % acute RfD:

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/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
GC 0640	Barley (beer only)	0.01	-	AUS	19.0	12	-	-	-	-	3	0.01	-
GC 0640	Barley (fresh, flour, beer)		4.5	AUS	19.0	14	-	-	-	-	1	3.29	-
GC 0645	Maize (fresh, flour, oil)		4.5	FRA	17.8	148	-	-	-	-	1	37.49	-
ML 0106	Milks	0.003	-	USA	15.0	1286	-	-	-	-	3	0.26	-
GC 0647	Oats		4.5	USA	15.0	62	-	-	-	-	1	18.68	-
GC 0649	Rice		4.5	FRA	17.8	223	-	-	-	-	1	56.25	-
GC 0650	Rye		4.5	NLD	17.0	37	-	-	-	-	1	9.77	-
GC 0654	Wheat		4.5	USA	15.0	151	-	-	-	-	1	45.32	-
CM 0654	Wheat bran, unprocessed	5.1	-	USA	15.0	30	-	-	-	-	3	10.10	-
CF 1211	Wheat flour	0.39	-	AUS	19.0	194	-	-	-	-	3	3.99	
CF 1212	Wheat wholemeal	1.6	-	USA	15.0	74	-	-	-	-	3	7.86	
CP 1211	White bread	0.22	-	SAF	14.2	270	-	-	-	-	3	4.18	-
CP 1212	Wholemeal bread	0.83	-	SAF	14.2	240	-	-	-	-	3	14.03	-

PYRETHRINS (063) : International estimate of short term intake (IESTI) for GENERAL POPULATION

Acute RfD = 0.2 mg/kg bw Maximum % ARfD: 2%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person							
DF 0167	Dried fruits		0.11	FRA	62.3	138	-	-	-	-	1	0.24	0%
FC 0001	Citrus fruits (Grapefruit 1/)		0.04	JPN	52.6	947	256	USA	125	3	2a	0.91	0%
JF 0001	Citrus juice (Orange juice 1/)	0.0276		-	-	-	-	-	-	-	3	-	-
SO 0697	Peanut		0.23	FRA	62.3	161	-	-	-	-	1	0.60	0%
VD 0070	Pulses (Peas (dry) 1/)		0.05	FRA	62.3	445	-	-	-	-	1	0.36	0%
VO 0051	Peppers (Peppers, sweet (incl. pim(i)ento) 1/)		0.04	FRA	62.3	207	119	USA	98	3	2a	0.26	0%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person							
VR 0075	Root and tuber vegetables (Potato 1/)		0.04	NLD	63.0	687	122	USA	99	3	2a	0.56	0%
VO 0448	Tomato (fresh, juice, paste, peeled)		0.04	USA	65.0	391	123	USA	123	3	2a	0.39	0%
VC 0045	Fruiting vegetables, cucurbits (Watermelon 1/)		0.04	USA	65.0	1939	4518	USA	2078	3	2b	3.58	2%
GC 0080	Cereal grains (Wheat 1/)		0.19	USA	65.0	383	-	-	-	-	1	1.12	1%

1/ Highest consumed commodity represents group when consumption is not available

PYRETHRINS (063) :

International estimate of short term intake (IESTI) for

Acute RfD = 0.2 mg/kg bw

CHILDREN UP TO 6 YEARS

Maximum %ARfD: 5%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight, g	Country	Unit weight, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person							
DF 0167	Dried fruits		0.11	FRA	17.8	101	-	-	-	-	1	0.62	0%
FC 0001	Citrus fruits (Grapefruit 1/)		0.04	FRA	17.8	381	256	USA	125	3	2a	1.42	1%
JF 0001	Citrus juice (Orange juice 1/)	0.0276		-	-	-	-	-	-	-	3	-	-
SO 0697	Peanut		0.23	USA	15.0	78	-	-	-	-	1	1.19	1%
VD 0070	Pulses (Peas (dry) 1/)		0.05	FRA	17.8	107	-	-	-	-	1	0.30	0%
VO 0051	Peppers (Peppers, sweet (incl. pim(i)ento) 1/)		0.04	AUS	19.0	60	119	USA	98	3	2b	0.38	0%
VR 0075	Root and tuber vegetables (Potato 1/)		0.04	SAF	14.2	300	122	USA	99	3	2a	1.40	1%
VO 0448	Tomato (fresh, juice, paste, peeled)		0.04	USA	15.0	159	123	USA	123	3	2a	1.08	1%
VC 0045	Fruiting vegetables, cucurbits (Watermelon 1/)		0.04	AUS	19.0	1473	4518	USA	2078	3	2b	9.30	5%
GC 0080	Cereal grains (Wheat 1/)		0.19	USA	15.0	151	-	-	-	-	1	1.91	1%

1/ Highest consumed commodity represents group when consumption is not available

TEBUFENOZIDE : International estimate of short term intake (IESTI) for GENERAL POPULATION

Acute RfD= 0.900 mg/kg bw/day (900 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				Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, corrected, g/person	Unit weight, g	Country	Unit weight, edible portion, g	Variabi- lity factor			
TN 0660	Almonds	-	0.045	JPN	52.6	74	-	-	-	-	1	0.06	0%
FP 0226	Apple	-	1.1	USA	65.0	1348	138	USA	127	3	2a	27.11	3%
JF 0226	Apple juice	0.02	-	-	-	-	-	-	-	-	3	-	-
FI 0326	Avocado	-	0.5	FRA	62.3	260	300	FRA	180	3	2a	4.97	1%
FB 0020	Blueberries	-	1.7	AUS	67.0	158	-	-	-	-	1	4.01	0%
VB 0400	Broccoli	-	0.34	USA	65.0	376	150	JPN	150	3	2a	3.54	0%
VB 0041	Cabbages, head	-	4.6	SAF	55.7	362	908	USA	717	3	2b	89.70	10%
PE 0840 ¹	Chicken eggs	-	0.02	FRA	62.3	219	-	-	-	-	1	0.07	0%
FB 0265	Cranberry	-	0.28	USA	65.0	229	-	-	-	-	1	0.99	0%
MO 0105	Edible offal (mammalian)	-	0.02	FRA	62.3	277	-	-	-	-	1	0.09	0%
FC 0203	Grapefruit	-	0.18	JPN	52.6	947	340	UNK	160	3	2a	4.33	0%
FB 0269	Grapes (fresh, dried, excluding wine)	-	1.5	AUS	67.0	513	125	FRA	118	3	2a	16.75	2%
DF 0269	Grapes, dried (= currants, raisins and sultanas)	-	1.1	FRA	62.3	135	-	-	-	-	1	2.39	0%
VL 0480	Kale	-	8.1	NLD	63.0	337	-	-	-	-	1	43.34	5%
FI 0341	Kiwi fruit	-	0.22	NLD	63.0	355	75	FRA	65	3	2a	1.69	0%
FC 0204	Lemon	-	0.18	FRA	62.3	115	100	FRA	64	3	2a	0.70	0%
VL 0482	Lettuce, head	-	8.1	USA	65.0	213	539	USA	512	3	2b	79.46	9%
VL 0483	Lettuce, leaf	-	8.1	NLD	63.0	152	10	USA	10	1	1	19.52	2%
FC 0206	Mandarin	-	0.18	JPN	52.6	409	100	FRA	72	3	2a	1.89	0%
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.029	AUS	67.0	104	-	-	-	-	1	0.05	0%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight					IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, corrected, g/person	Unit weight, g	Country	Unit weight, edible portion, g	Variabi- lity factor	Case		
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0.006	AUS	67.0	417	-	-	-	-	1	0.04	0%
ML 0106	Milks	0.003	-	USA	65.0	2466	-	-	-	-	3	0.11	0%
HH 0738	Mints	-	8.6	AUS	67.0	8	-	-	-	-	1	1.00	0%
FS 0245	Nectarine	-	0.23	USA	65.0	590	110	FRA	99	3	2a	2.79	0%
FC 0004	Oranges, sweet, sour (incl. Orange-like hybrids)	-	0.18	USA	65.0	564	190	FRA	137	3	2a	2.32	0%
FS 0247	Peach	-	0.23	SAF	55.7	685	110	FRA	99	3	2a	3.65	0%
FP 0230	Pear	-	1.1	USA	65.0	693	166	USA	151	3	2a	16.84	2%
TN 0672	Pecan	-	0.01	AUS	67.0	23	-	-	-	-	1	0.00	0%
VO 0444	Peppers, chili	-	0.64	USA	65.0	90	45	USA	43	3	2a	1.74	0%
VO 0445	Peppers, sweet (incl. pim(i)ento)	-	0.64	FRA	62.3	207	172	UNK	160	3	2a	5.42	1%
PM 0110	Poultry meat: 10% as fat	-	0.0006	AUS	67.0	43	-	-	-	-	1	0.00	0%
PM 0110	Poultry meat: 90% as muscle	-	1E-09	AUS	67.0	388	-	-	-	-	1	0.00	0%
PO 0111	Poultry, edible offal of	-	0.02	USA	65.0	248	-	-	-	-	1	0.08	0%
OR 0495	Rape seed oil, edible	2.2	-	AUS	67.0	65	-	-	-	-	3	2.13	0%
FB 0272	Raspberries, red, black	-	0.86	FRA	62.3	324	-	-	-	-	1	4.47	0%
CM 0649	Rice, husked	-	0.07	JPN	52.6	319	-	-	-	-	1	0.42	0%
VL 0502	Spinach (bunch)	-	8.1	NLD	63.0	820	111	UNK	90	3	2a	128.50	10%
GS 0659	Sugar cane	-	0.62	SAF	55.7	89	-	-	-	-	1	0.99	0%
	Sugar, refined	0.003	-	-	-	-	-	-	-	-	3	-	-
VO 0448	Tomato (fresh, juice, paste, peeled)	-	0.53	USA	65.0	391	123	USA	123	3	2a	5.19	1%
JF 0448	Tomato juice	0.023	-	-	-	-	-	-	-	-	3	-	-
	Tomato paste	0.007	-	-	-	-	-	-	-	-	3	-	-
TN 0678	Walnuts	-	0.02	FRA	62.3	136	-	-	-	-	1	0.04	0%
	Wine only	0.081	-	AUS	67.0	1131	-	-	-	-	3	1.37	0%

¹Because of lack of information on large portion size of PE 0112 Eggs, the calculation was made for PE 0840 Chicken eggs.

TEBUFENOZIDE: International estimate of short term intake (IESTI) for CHILDREN UP TO 6 YEARS

Maximum %ARfD: 40%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight				Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, corrected, g/person	Unit weight, g	Country	Unit weight, edible portion, g	Variabi- lity factor			
TN 0660	Almonds	-	0.045	FRA	17.8	31	-	-	-	-	1	0.08	0%
FP 0226	Apple	-	1.1	USA	15.0	679	138	USA	127	3	2a	68.40	8%
JF 0226	Apple juice	0.02	-	-	-	-	-	-	-	-	3	-	-
FI 0326	Avocado	-	0.5	USA	15.0	131	300	FRA	180	3	2b	13.05	1%
FB 0020	Blueberries	-	1.7	FRA	17.8	138	-	-	-	-	1	13.21	1%
VB 0400	Broccoli	-	0.34	USA	15.0	164	150	JPN	150	3	2a	10.52	1%
VB 0041 ¹	Cabbages, head	-	4.6	SAF	14.2	220	908	USA	717	3	2b	213.90	20%
PE 0840	Chicken eggs	-	0.02	FRA	17.8	134	-	-	-	-	1	0.15	0%
FB 0265	Cranberry	-	0.28	USA	15.0	102	-	-	-	-	1	1.90	0%
MO 0105	Edible offal (mammalian)	-	0.02	FRA	17.8	203	-	-	-	-	1	0.23	0%
FC 0203	Grapefruit	-	0.18	FRA	17.8	381	340	UNK	160	3	2a	7.09	1%
FB 0269	Grapes (fresh, dried, excluding wine)	-	1.5	AUS	19.0	342	125	FRA	118	3	2a	45.55	5%
DF 0269	Grapes, dried (= currants, raisins and sultanas)	-	1.1	USA	15.0	59	-	-	-	-	1	4.35	0%
VL 0480	Kale	-	8.1	NLD	17.0	149	-	-	-	-	1	70.79	8%
FI 0341	Kiwi fruit	-	0.22	JPN	15.9	162	75	FRA	65	3	2a	4.03	0%
FC 0204	Lemon	-	0.18	JPN	15.9	88	100	FRA	64	3	2a	2.45	0%
VL 0482	Lettuce, head	-	8.1	NLD	17.0	84	539	USA	512	3	2b	119.56	10%
VL 0483	Lettuce, leaf	-	8.1	NLD	17.0	102	10	USA	10	1	1	48.60	5%
FC 0206	Mandarin	-	0.18	JPN	15.9	353	100	FRA	72	3	2a	5.63	1%
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.029	AUS	19.0	52	-	-	-	-	1	0.08	0%
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0.006	AUS	19.0	208	-	-	-	-	1	0.07	0%
ML 0106	Milks	0.003	-	USA	15.0	1286	-	-	-	-	3	0.26	0%
HH 0738	Mints	-	8.6	AUS	19.0	34	-	-	-	-	1	15.28	2%
FS 0245	Nectarine	-	0.23	AUS	19.0	302	110	FRA	99	3	2a	6.05	1%

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion diet			Unit weight					IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, corrected, g/person	Unit weight, g	Country	Unit weight, edible portion, g	Variabi- lity factor	Case		
FC 0004	Oranges, sweet, sour (incl. Orange-like hybrids)	-	0.18	UNK	14.5	495	190	FRA	137	3	2a	9.54	1%
FS 0247	Peach	-	0.23	AUS	19.0	315	110	FRA	99	3	2a	6.22	1%
FP 0230	Pear	-	1.1	UNK	14.5	279	166	USA	151	3	2a	44.08	5%
TN 0672	Pecan	-	0.01	AUS	19.0	22	-	-	-	-	1	0.01	0%
VO 0444	Peppers, chili	-	0.64	AUS	19.0	31	45	USA	43	3	2b	3.08	0%
VO 0445	Peppers, sweet (incl. pim(i)ento)	-	0.64	AUS	19.0	60	172	UNK	160	3	2b	6.07	1%
PM 0110	Poultry meat: 10% as fat	-	0.0006	AUS	19.0	22	-	-	-	-	1	0.00	0%
PM 0110	Poultry meat: 90% as muscle	-	1E-09	AUS	19.0	201	-	-	-	-	1	0.00	0%
PO 0111	Poultry, edible offal of	-	0.02	USA	15.0	37	-	-	-	-	1	0.05	0%
OR 0495	Rape seed oil, edible	2.2	-	AUS	19.0	18	-	-	-	-	3	2.13	0%
FB 0272	Raspberries, red, black	-	0.86	FRA	17.8	76	-	-	-	-	1	3.68	0%
CM 0649	Rice, husked	-	0.07	FRA	17.8	223	-	-	-	-	1	0.88	0%
VL 0502	Spinach (bunch)	-	8.1	SAF	14.2	420	111	UNK	90	3	2a	342.33	40%
GS 0659	Sugar cane	-	0.62	SAF	14.2	60	-	-	-	-	1	2.60	0%
	Sugar, refined	0.003	-	-	-	-	-	-	-	-	3	-	-
VO 0448	Tomato (fresh, juice, paste, peeled)	-	0.53	USA	15.0	159	123	USA	123	3	2a	14.31	2%
FJ 0448	Tomato juice	0.023	-	-	-	-	-	-	-	-	3	-	-
	Tomato paste	0.007	-	-	-	-	-	-	-	-	3	-	-
TN 0678	Walnuts	-	0.02	USA	15.0	6	-	-	-	-	1	0.01	0%
	Wine only	0.081	-	AUS	19.0	4	-	-	-	-	3	0.02	0%

0 Because of lack of information on large portion size of PE 0112 Eggs, the calculation was made for PE 0840 Chicken eggs

TOLYLFLUANID (162) : International estimate of short term intake (IESTI) for GENERAL POPULATION

Acute RfD= 0.5 mg/kg bw/day (500 µg/kg bw/day) Maximum % acute RfD: 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/day	% acute RfD rounded
				Country	Body weight, kg	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
VL 0482	Lettuce, head	3.75	12	USA	65.0	213	754	UNK	558	3	2b	117.72	20%

TOLYLFLUANID (162) : International estimate of short term intake (IESTI) for CHILDREN UP TO 6 YEARS

Acute RfD= 0.500 mg/kg bw/day (500 µg/kg bw/day) Maximum % acute RfD: 40%

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/day	% acute RfD rounded
				Country	Body weight (kg)	Large portion, g/person	Unit weight, g	Country	Unit weight, edible portion, g				
VL 0482	Lettuce, head	3.75	12	NLD	17.0	84	754	UNK	558	3	2b	177.12	40%

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 WHO EXPERT GROUPS ON PESTICIDE RESIDUES**

1. Principles governing consumer safety in relation to pesticide residues. Report of a meeting of a WHO Expert Committee on Pesticide Residues held jointly with the FAO Panel of Experts on the Use of Pesticides in Agriculture. FAO Plant Production and Protection Division Report, No. PL/1961/11; WHO Technical Report Series, No. 240, 1962.
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.
7. Evaluation of some pesticide residues in food. FAO/PL:CP/15; WHO/Food Add./67.32, 1967.
8. Pesticide residues. Report of the 1967 Joint Meeting of the FAO Working Party and the WHO Expert Committee. FAO Meeting Report, No. PL:1967/M/11; WHO Technical Report Series, No. 391, 1968.
9. 1967 Evaluations of some pesticide residues in food. FAO/PL:1967/M/11/1; WHO/Food Add./68.30, 1968.
10. Pesticide residues in food. Report of the 1968 Joint Meeting of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Committee on Pesticide Residues. FAO Agricultural Studies, No. 78; WHO Technical Report Series, No. 417, 1968.
11. 1968 Evaluations of some pesticide residues in food. FAO/PL:1968/M/9/1; WHO/Food Add./69.35, 1969.
12. Pesticide residues in food. Report of the 1969 Joint Meeting of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Group on Pesticide Residues. FAO Agricultural Studies, No. 84; WHO Technical Report Series, No. 458, 1970.

13. 1969 Evaluations of some pesticide residues in food. FAO/PL:1969/M/17/1; WHO/Food Add./70.38, 1970.
14. Pesticide residues in food. Report of the 1970 Joint Meeting of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Committee on Pesticide Residues. FAO Agricultural Studies, No. 87; WHO Technical Report Series, No. 4574, 1971.
15. 1970 Evaluations of some pesticide residues in food. AGP:1970/M/12/1; WHO/Food Add./71.42, 1971.
16. Pesticide residues in food. Report of the 1971 Joint Meeting of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Committee on Pesticide Residues. FAO Agricultural Studies, No. 88; WHO Technical Report Series, No. 502, 1972.
17. 1971 Evaluations of some pesticide residues in food. AGP:1971/M/9/1; WHO Pesticide Residue Series, No. 1, 1972.
18. Pesticide residues in food. Report of the 1972 Joint Meeting of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Committee on Pesticide Residues. FAO Agricultural Studies, No. 90; WHO Technical Report Series, No. 525, 1973.
19. 1972 Evaluations of some pesticide residues in food. AGP:1972/M/9/1; WHO Pesticide Residue Series, No. 2, 1973.
20. Pesticide residues in food. Report of the 1973 Joint Meeting of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Committee on Pesticide Residues. FAO Agricultural Studies, No. 92; WHO Technical Report Series, No. 545, 1974.
21. 1973 Evaluations of some pesticide residues in food. FAO/AGP/1973/M/9/1; WHO Pesticide Residue Series, No. 3, 1974.
22. Pesticide residues in food. Report of the 1974 Joint Meeting of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Committee on Pesticide Residues. FAO Agricultural Studies, No. 97; WHO Technical Report Series, No. 574, 1975.
23. 1974 Evaluations of some pesticide residues in food. FAO/AGP/1974/M/11; WHO Pesticide Residue Series, No. 4, 1975.
24. Pesticide residues in food. Report of the 1975 Joint Meeting of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Committee on Pesticide Residues. FAO Plant Production and Protection Series, No. 1; WHO Technical Report Series, No. 592, 1976.
25. 1975 Evaluations of some pesticide residues in food. AGP:1975/M/13; WHO Pesticide Residue Series, No. 5, 1976.
26. Pesticide residues in food. Report of the 1976 Joint Meeting of the FAO Panel of Experts on Pesticide Residues and the Environment and the WHO Expert Group on Pesticide Residues. FAO Food and Nutrition Series, No. 9; FAO Plant Production and Protection Series, No. 8; WHO Technical Report Series, No. 612, 1977.
27. 1976 Evaluations of some pesticide residues in food. AGP:1976/M/14, 1977.

28. Pesticide residues in food—1977. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues and Environment and the WHO Expert Group on Pesticide Residues. FAO Plant Production and Protection Paper 10 Rev, 1978.
29. Pesticide residues in food: 1977 evaluations. FAO Plant Production and Protection Paper 10 Suppl., 1978.
30. Pesticide residues in food—1978. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues and Environment and the WHO Expert Group on Pesticide Residues. FAO Plant Production and Protection Paper 15, 1979.
31. Pesticide residues in food: 1978 evaluations. FAO Plant Production and Protection Paper 15 Suppl., 1979.
32. Pesticide residues in food—1979. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues. FAO Plant Production and Protection Paper 20, 1980.
33. Pesticide residues in food: 1979 evaluations. FAO Plant Production and Protection Paper 20 Suppl., 1980
34. Pesticide residues in food—1980. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues. FAO Plant Production and Protection Paper 26, 1981.
35. Pesticide residues in food: 1980 evaluations. FAO Plant Production and Protection Paper 26 Suppl., 1981.
36. Pesticide residues in food—1981. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues. FAO Plant Production and Protection Paper 37, 1982.
37. Pesticide residues in food: 1981 evaluations. FAO Plant Production and Protection Paper 42, 1982.
38. Pesticide residues in food—1982. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues. FAO Plant Production and Protection Paper 46, 1982.
39. Pesticide residues in food: 1982 evaluations. FAO Plant Production and Protection Paper 49, 1983.
40. Pesticide residues in food—1983. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues. FAO Plant Production and Protection Paper 56, 1985.
41. Pesticide residues in food: 1983 evaluations. FAO Plant Production and Protection Paper 61, 1985.
42. Pesticide residues in food—1984. Report of the Joint Meeting on Pesticide Residues. FAO Plant Production and Protection Paper 62, 1985.

43. Pesticide residues in food—1984 evaluations. FAO Plant Production and Protection Paper 67, 1985.
44. Pesticide residues in food—1985. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and a WHO Expert Group on Pesticide Residues. FAO Plant Production and Protection Paper 68, 1986.
45. Pesticide residues in food—1985 evaluations. Part I. Residues. FAO Plant Production and Protection Paper 72/1, 1986.
46. Pesticide residues in food—1985 evaluations. Part II. Toxicology. FAO Plant Production and Protection Paper 72/2, 1986.
47. Pesticide residues in food—1986. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and a WHO Expert Group on Pesticide Residues. FAO Plant Production and Protection Paper 77, 1986.
48. Pesticide residues in food—1986 evaluations. Part I. Residues. FAO Plant Production and Protection Paper 78, 1986.
49. Pesticide residues in food—1986 evaluations. Part II. Toxicology. FAO Plant Production and Protection Paper 78/2, 1987.
50. Pesticide residues in food—1987. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and a WHO Expert Group on Pesticide Residues. FAO Plant Production and Protection Paper 84, 1987.
51. Pesticide residues in food—1987 evaluations. Part I. Residues. FAO Plant Production and Protection Paper 86/1, 1988.
52. Pesticide residues in food—1987 evaluations. Part II. Toxicology. FAO Plant Production and Protection Paper 86/2, 1988.
53. Pesticide residues in food—1988. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and a WHO Expert Group on Pesticide Residues. FAO Plant Production and Protection Paper 92, 1988.
54. Pesticide residues in food—1988 evaluations. Part I. Residues. FAO Plant Production and Protection Paper 93/1, 1988.
55. Pesticide residues in food—1988 evaluations. Part II. Toxicology. FAO Plant Production and Protection Paper 93/2, 1989.
56. Pesticide residues in food—1989. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and a WHO Expert Group on Pesticide Residues. FAO Plant Production and Protection Paper 99, 1989.
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61. Pesticide residues in food—1990 evaluations. Part II. Toxicology. World Health Organization, WHO/PCS/91.47, Geneva, 1991.
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64. Pesticide residues in food—1991 evaluations. Part II. Toxicology. World Health Organization, WHO/PCS/92.52, Geneva, 1992.
65. Pesticide residues in food—1992. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and a WHO Expert Group on Pesticide Residues. FAO Plant Production and Protection Paper 116, Rome, 1993.
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67. Pesticide residues in food—1992 evaluations. Part II. Toxicology. World Health Organization, WHO/PCS/93.34, Geneva, 1993.
68. Pesticide residues in food—1993. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and a WHO Expert Group on Pesticide Residues. FAO Plant Production and Protection Paper 122, Rome, 1994.
69. Pesticide residues in food—1993 evaluations. Part I. Residues. FAO Plant Production and Protection Paper 124, Rome, 1994.
70. Pesticide residues in food—1993 evaluations. Part II. Toxicology. World Health Organization, WHO/PCS/94.4, Geneva, 1994.
71. Pesticide residues in food—1994. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and a WHO Expert Group on Pesticide Residues. FAO Plant Production and Protection Paper 127, Rome, 1995.
72. Pesticide residues in food—1994 evaluations. Part I. Residues. FAO Plant Production and Protection Paper 131/1 and 131/2 (2 volumes), Rome, 1995.
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ANNEX 6

CORRECTIONS TO SECTION 4 AND ANNEX 1 OF THE REPORT OF THE 2002 MEETING

Replacement matter is shown deleted and new matter in bold. Only significant errors of fact are listed

It should be noted that the Joint Meeting cannot withdraw Codex MRLs or draft MRLs; it can only recommend their withdrawal. The numerous instances of phrases such as ‘the Meeting agreed to withdraw the current MRL’ should therefore be interpreted as meaning ‘the Meeting agreed to recommend withdrawal of the current MRL’, but this change has not been included in the following list.

The corrections to the ‘Residue and Analytical aspects’ parts of the Report also apply to the Appraisals of the compounds in the 2002 Residue Evaluations. However in the Evaluations the lists of recommendations for MRLs and estimates of STMRs and HRs at the ends of the Appraisals and in Annex I have been corrected.

Section 4

4.3 Carbaryl

p. 42, para 1, last sentence

The radioactivity in the cellulose fraction was the largest portion in the root (0.694 ~~mg/g~~ µg/g ¹⁴C-carbaryl eq), and in tops accounted for 3.27 µg/g ¹⁴C-carbaryl eq.

p. 44, Water and water/sediment, para 1, last sentence

1-naphthol was the only major product. A half-life of 21 days for a 12-hour light/12-hour darkness period was calculated using the degradation rate constants under irradiated and non-irradiated conditions.

p. 44, para 3, line 3

Total radioactivity in methylene chloride ~~water~~ extracts of the water ranged from 81.4 % at day 0 declining to 5.4% at day 14, after ~~what maintained~~ which it remained from 2.9 to 5.4 % up to 26 days.

p. 46, first line

...post column hydrolysis derivatization system and ~~fluorescent~~ fluorescence detector.

p. 46, last para, line 4

...wet pomace, purée, paste and juice...

p. 51 Pepper

Pepper. Five trials were conducted in USA ~~in pepper at~~ on bell peppers at the maximum GAP rate for pepper and tomato...

The Meeting agreed to ~~confirm~~ recommend replacement of the current temporary CXL of 5 mg/kg for peppers with an MRL of 5 mg/kg ~~and recommends for sweet peppers and estimated~~ an STMR of 1.8 mg/kg and an HR of 3.8 mg/kg for carbaryl in ~~pepper~~ sweet peppers.

p. 52 Garden beets, para 2

The Meeting recommends a maximum residue level of 0.1 mg/kg, an STMR of 0.025 mg/kg and an HR of 0.06 mg/kg for carbaryl in ~~garden beets~~ beetroot.

p. 55 Maize fodder and forage, para 2, line 5

...the ~~medium~~median and the highest residues of carbaryl in maize forage, on a dried ~~base, is 20 mg/kg [(7.7+10)/2 * 0.44]~~ basis, are 20 mg/kg [(7.7+10)/2] ÷ 0.44 and 370 mg/kg (163/0.44) respectively.

p. 57, fate of residues in processing, para 1, lines 5-7

In molasses, the residues concentrated in grapefruit and lemon (PF of ~~3.2~~ 1.4 and 1.2, respectively), but not in orange (0.34 and 0.08, average 0.21). Residues were 10-30% higher in peel...and reduced in juice (average PF of ~~0.03~~ 0.024 for citrus,...

p. 58, para 1, line 3

...but concentrated in wet and dry pomace (PF of 1.4 and ~~2.0~~, 2.5 respectively, n=2)...

p. 58, para 7, line 2

...in fries with a PF of ~~0.04~~ 0.4, and in chips and flakes with a PF of 0.03.

p. 58, last para, line 4

...they were reduced by a factor of ~~<0.05~~ 0.5.

p. 60, paras 1 and 2

Based on a processing factor of ~~0.03~~ 0.024 for citrus juice, ... the Meeting agreed to recommend a maximum residue level of 0.5 mg/kg and an STMR-P of ~~0.13~~ 0.10 mg/kg for carbaryl in citrus juice,...

Based on a ~~processing factor of 2 for grape pomace, dry, factors~~ of 1.2 for raisins and ~~of~~ 0.65 for grape juice, ~~the estimations for grape and the estimates for grapes~~ (maximum residue level of 40 mg/kg, STMR of 4.9 mg/kg and an HR of 33 mg/kg), the Meeting recommends ~~a maximum residue level of 80 mg/kg and an STMR-P of 9.8 mg/kg for carbaryl in grape pomace, dry; a maximum residue level an MRL of 50 mg/kg, an STMR-P of 5.9 mg/kg and an HR of 39.6 mg/kg for carbaryl in dried grapes, and an MRL of 30 mg/kg, an STMR-P~~ raisins; ~~and a maximum residue level of 30 mg/kg and an STMR-P of 3.2~~ of 3.2 mg/kg and an HR of 21.45 mg/kg for carbaryl in grape juice.

p. 60, last para, line 2

...the results from two studies in meal and flour varied significantly (~~0.05~~ about 0.5 and 1.5).

p. 61, para 2

Based on processing factors of 1, 0.09 and 0.49 from wheat to bran, flour and germ and the estimations for wheat (maximum residue level of 2 mg/kg, and STMR of ~~0.26~~ 0.245 mg/kg), the Meeting ~~recommends~~ estimates a maximum residue level of 2 mg/kg and an STMR-P of ~~0.26~~ 0.245 mg/kg for carbaryl in wheat bran, ~~a maximum residue level of 0.2 mg/kg, and an STMR-P of 0.2 mg/kg, and an STMR-P of 0.2 mg/kg for carbaryl in wheat flour; a maximum residue level of 0.02 mg/kg for carbaryl in wheat flour,~~ and a maximum residue level of 1 mg/kg and an STMR-P of ~~0.13~~ 0.12 mg/kg for carbaryl in wheat germ.

p. 61, Table

Maximum farm animal dietary burden estimation

						% of diet			Residue contribution, mg/kg		
Commodity	Group	Residues mg/kg	Basis	% dry matter	Residues, in dry basis, mg/kg	Beef	Dairy	Poultry	Beef	Dairy	Poultry
Almond hulls	AM	50	MRL	90	45 55.5	10	10	-	4.5 5.6	4.5 5.6	-
Sweet corn cannery waste		2.22	STPM-P	30	7.4	35	20	-	2.59	1.48	-
		1.48	STMR-P		4.93				1.73	0.99	
Maize forage	AF	400	MRL	100	400	40	50	-	160	250 200	-

						% of diet			Residue contribution, mg/kg		
Commodity	Group	Residues mg/kg	Basis	% dry matter	Residues, in dry basis, mg/kg	Beef	Dairy	Poultry	Beef	Dairy	Poultry
Sorghum forage	AF	50	MRL	100	50	40	50	-	10.20	25	-
Maize	GC	0.02	MRL	88	0.023	80	40	40	0.018	0.009	0.018
Wheat grain	GC	2	MRL	89	2.24	50	40	80	1.12	0.90	1.8
TOTAL						100	100	100	208.6	279.6	34.3
									205.3	231.3	34.1

p. 62, Table

STMR farm animal dietary burden estimation

						% of diet			Residue contribution, mg/kg		
Commodity	Group	Residues mg/kg	Basis	% dry matter	Residues, in dry basis, mg/kg	Beef	Dairy	Poultry	Beef	Dairy	Poultry
Rice hulls		27.7 <u>25.7</u>	STMR-P	90	30.8 <u>28.5</u>	10	10	15	3.1 <u>2.85</u>	3.1 <u>2.85</u>	
Sweet corn cannery waste		2.22 <u>1.48</u>	STPM-P	30	7.4 <u>4.93</u>	35	20	-	2.59 <u>1.73</u>	1.48 <u>0.99</u>	
Rice	GC	8.4	STMR	88	9.3 <u>9.5</u>	<u>10</u>	<u>10</u>	<u>60</u>	0.93 <u>0.95</u>	0.93 <u>0.95</u>	6.6 <u>5.7</u>
Maize	GC	0.02	STMR	88	0.23 <u>0.023</u>	80	40	40	0.18 <u>0.018</u>	0.09 <u>0.009</u>	0.09 <u>0.009</u>
Wheat grain	GC	0.26 <u>0.245</u>	STMR	89	0.29 <u>0.275</u>	50	40	80	0.15 <u>0.14</u>	0.12 <u>0.11</u>	
TOTAL						100	100	100	17.3 <u>17.2</u>	17.3 <u>18.4</u>	6.7 <u>5.7</u>

p. 63 Cattle, para 1

As the maximum dietary burden of beef and dairy cattle estimated by the Meeting were ~~208.6 and 279.6~~ 205.3 and 231.3 mg/kg feed, respectively, the highest value (~~279.6~~ 231.3 mg/kg feed) will be used....For the STMR estimation, the residue levels at 17.3 18.4 mg/kg feed (dietary burden for ~~both beef and~~ dairy cattle), will be derived by applying...

p. 63, Table

Dose (ppm)	Carbaryl concentration (mg/kg)								
	Milk	Liver		Kidney		Muscle		Fat	
(Interpolated)	(mean)	Highest	Mean	Highest	Mean	Highest	Mean	Highest	Mean
MRL									
(279.6)		(0.907)		(1.90)		(<0.042)		(0.062)	
<u>(231.3)</u>	(0.034)	<u>(0.835)</u>		<u>(162)</u>		<u>(<0.035)</u>		<u>(0.081)</u>	
[114/342]	[0.02/0.04]	[0.66/1.0]		[0.85/2.3]		[<0.02/0.05]		[0.04/0.12]	
STMR									
(17.3)			(0.085)		(0.119)				
<u>(18.4)</u>	(0.003)		<u>†</u>		<u>(0.111)</u>		<u>(<0.003)</u>		<u>(0.003)</u>

Dose (ppm) (Interpolated) [actual]	Carbaryl concentration (mg/kg)								
	Milk (mean)	Liver		Kidney		Muscle		Fat	
		Highest	Mean	Highest	Mean	Highest	Mean	Highest	Mean
[114]	[0.02]		<u>(0.079)</u>		[0.69]		[<0.02]		[0.02]
]						
			[0.49]						

[Recommendations based on the original figures and already published have not been corrected]

p. 64, Poultry, line 1

For poultry, the maximum and the STMR estimated dietary burden were ~~34.4 and 6.4~~ 34.1 and 5.7 mg/kg feed, respectively.

4.5 Carbofuran

p. 68, para 3

The Meeting ~~agreed to recommend estimated~~ a maximum residue level of 0.3 mg/kg, an STMR of 0.10 mg/kg and an HR of 0.17 mg/kg for carbofuran in rice grain. [No recommendation was made]

p. 69, Fate of residues in processing, para 1, line 3

... Total carbofuran residues in dried grain were ~~<0.05 (LOD), 0.18 and <0.05~~ <0.02 (LOD), 0.17 and <0.02 mg/kg. Residues in hulled grain were (0.02), (0.02) and <0.05 mg/kg. A processing factor of about 0.25 from the second trial can be derived. No detailed information on the milling process was provided.

The calculated processing factor from rice to husked rice (0.25) was applied to the recommendations estimates for rice (maximum residue level of 0.3 mg/kg, an STMR of 0.10 mg/kg and an HR of 0.17 mg/kg). The Meeting recommends a maximum residue level of 0.1 mg/kg, an STMR-P of 0.025 mg/kg and an HR-P of 0.042 mg/kg for carbofuran in rice, husked.

4.8 Deltamethrin

p. 90, para 2, line 3

... The Meeting estimated a maximum residue level, an STMR value and an HR value for deltamethrin in hazelnuts and pulses walnuts of 0.02*, 0.02 and 0.02 mg/kg, respectively.

4.9 Diflubenzuron

p. 113, para 8

The Meeting estimated a highest maximum residue level of 5 mg/kg (fresh weight) and an STMR of 1.65 mg/kg in fresh grass.

p. 119, para 2, last sentence

The Meeting estimated STMRs for milks of 0.02 mg/kg, and for meat (fat) and edible offal of 0.1 mg/kg.

para 3, last sentence

The Meeting estimated STMRs for poultry meat (fat) and eggs of 0.05 mg/kg.

4.10 Esfenvalerate

p. 132, 1st Table

Commodity	group	residue mg/kg	basis	% dry matter	residue, on dry wt mg/kg	Choose diets, %			Residue contribution, mg/kg		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
						Maximum dietary burden			<u>0.61</u>	1.6 <u>1.42</u>	<u>0.045</u>

p. 132, 2nd Table and text below

Commodity	group	residue mg/kg	basis	% dry matter	residue, on dry wt mg/kg	Choose diets, %			Residue contribution, mg/kg		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
Cotton seed	SO	0.01	MRL STMR	88	0.011	25			0.003		

The esfenvalerate dietary burdens...are: beef cattle 0.61 and 0.14 mg/kg, dairy cattle ~~1.6~~ 1.4 and 0.32 mg/kg and poultry 0.045 and 0.009 mg/kg.

4.13 Flutolanil

p. 146, Table

Commodity	group	residue mg/kg	basis	% dry matter	residue, on dry wt mg/kg	Choose diets, %			Residue contribution, mg/kg		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
Rice grain <u>Brown rice</u>	GC CM	2	MRL	88	2.3	40	40	60	0.91	0.91	1.36

p. 147, Table

Commodity	group	residue mg/kg	basis	% dry matter	residue, on dry wt mg/kg	Choose diets, %			Residue contribution, mg/kg		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
Rice grain <u>Brown rice</u>	GC CM	0.39	STMR	88	0.44	40	40	60	0.18	0.18	0.27

4.15 Imidacloprid

p. 150, Metabolic products

Code	Chemical name	Short name
M04	1-(6-chloro-3-pyridylmethyl)-5-hydroxy- <i>N</i> -nitroimidazolidin-2-ylideneamine 5-hydroxy glucuronide	5-hydroxy glucuronide
M05	1-(6-chloro-3-pyridylmethyl)-4-hydroxy- <i>N</i> -nitroimidazolidin-2-ylideneamine 4-hydroxy glucuronide	4-hydroxy glucuronide

p. 174, penultimate para, Citrus fruits, line 3

...Based on the STMR value of ~~0.05~~ 0.26 mg/kg for unprocessed whole citrus fruits, the STMR-Ps were ~~0.03~~ 0.16 mg/kg for marmalade and ~~0.014~~ 0.07 mg/kg for citrus juice. A maximum residue level of 10 mg/kg and an STMR of ~~0.374~~ 1.94 mg/kg is estimated for citrus dried pulp.

pp. 176 and 177, Tables

Estimated maximum dietary burden of farm animals

Commodity	Codex Commodity Group	Residue mg/kg	Basis	% Dry matter	Residue dry wt (mg/kg)	Choose diets, %			Residue contribution (mg/kg)		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
Citrus pulp, dried	AB	0.374 1.94	STMR P	91	0.44 2.13	20	20		0.082 0.427	0.082 0.427	
Wheat milled by-	CF	0.175	STMR-P	88	0.199	<u>35</u>	<u>10</u>	50	0.07	0.0199	0.0995

Commodity	Codex Commodity Group	Residue mg/kg	Basis	% Dry matter	Residue dry wt (mg/kg)	Choose diets, %			Residue contribution (mg/kg)		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
products											
TOTAL						100	100	100	2.402 2.75	3.6019 3.95	0.128

Estimated STMR dietary burden of farm animals

Commodity	Codex Commodity Group	Residue mg/kg	Basis	% Dry matter	Residue dry wt (mg/kg)	Choose diets, %			Residue contribution (mg/kg)		
						Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
Citrus pulp, dried	AB	0.374 1.94	STMR-P	91	0.41 2.13	20	20		0.082 0.427	0.082 0.427	
TOTAL						100	100	100	0.592 0.937	0.4739 0.819	0.128

p. 178, para 1

The dietary burdens of imidacloprid for estimating MRLs, STMR and HR values for animal commodities ...are: ~~2.4 and 0.59~~ **2.75 and 0.94** mg/kg for beef cattle, ~~3.6 and 0.47~~ **3.95 and 0.82** mg/kg for dairy cattle and 0.13 mg/kg each for poultry.

p. 179, paras 2-7

As the maximum dietary burdens of beef and dairy cattle (~~2.4 and 3.6~~ **2.75 and 3.95** ppm) were lower than the lowest feeding level of 5 ppm, the highest residues in tissues and milk were therefore calculated by applying the transfer factors to the maximum dietary burdens (transfer factor • dietary burden in mg/kg feed).

As the maximum dietary burden of dairy cows exceeds that for beef cattle, the former (~~3.6~~ **3.95** mg/kg) was used to estimate the maximum residue level in muscle, liver and kidney.

As the STMR dietary burdens of beef and dairy cattle (~~0.59 and 0.47~~ **0.94 and 0.82** ppm) were lower than the lowest feeding level of 5 ppm, the resulting STMRs in tissues and milk were calculated by applying the transfer factors to the STMR dietary burdens.

Dietary burden (ppm) Feeding level [ppm]	Imidacloprid total residue, mg/kg								
	Milk mean	Muscle highest	mean	Liver highest	mean	Kidney highest	mean	Fat highest	mean
MRL dairy/beef cattle (3.6) (3.95) [5]	(0.01) <0.02	0.007 (0.008)		(0.036) (0.04)		(0.022) (0.024)		(0.004) (0.005)	
STMR beef cattle (0.59) (0.94) [5]			(0.0012) (0.002) <0.02		(0.006) (0.009) 0.05		(0.0035) (0.0056) 0.03		(0.0007) (0.001) <0.02
STMR dairy cattle (0.47) (0.82) [5]	(0.0014) (0.0024) <0.02								

The maximum concentrations of residues expected in tissues are ~~0.007~~ **0.008** mg/kg in muscle, ~~0.036~~ **0.04** mg/kg in liver, ~~0.022~~ **0.024** mg/kg in kidney, ~~0.004~~ **0.005** mg/kg in fat and 0.01 mg/kg in milk. The mean extrapolated concentrations are ~~0.0012~~ **0.002** mg/kg in muscle, ~~0.006~~ **0.009** mg/kg in liver, ~~0.0035~~ **0.0056** mg/kg in kidney, ~~0.0007~~ **0.001** mg/kg in fat and ~~0.0014~~ **0.0024** mg/kg in milk.

The Meeting estimated maximum residue levels of 0.02* mg/kg for meat (mammalian) and milks. For edible offal (mammalian), the estimated maximum residue level is 0.05 mg/kg. The Meeting recommended that the HR values should be ~~0.007~~ 0.008 mg/kg in meat (mammalian), ~~0.036~~ 0.04 mg/kg in edible offal (mammalian) and ~~0.004~~ 0.005 mg/kg in fat (mammalian). The estimated STMR values are ~~0.001~~ 0.002 mg/kg for meat (mammalian), ~~0.006~~ 0.009 mg/kg for edible offal (mammalian), 0 for fat (mammalian) and ~~0.0014~~ 0.0024 mg/kg for milks.

Note. The changes to the STMR and HR values have no effect on the estimates of long- or short-term dietary intake.

4.22 Piperonyl butoxide

p. 224, para 7, line 3

...The median (29.5 mg/kg) and the maximum (153 mg/kg) values were corrected for the moisture content of pea hay (12%, *FAO Manual*, p. 125), and became ~~19.9~~ 33.5 and 174 mg/kg, respectively, on a dried basis. The Meeting estimated a maximum residue level of 200 mg/kg and an STMR of ~~19.9 mg/kg~~ 33.5 mg/kg for piperonyl butoxide in bean hay and pea hay or fodder.

p. 225, para 3

The Meeting estimated a maximum residue level of 0.2 mg/kg, and an STMR value of 0.05 ~~and a highest residue of 0.17~~ mg/kg for piperonyl butoxide in pulses after post-harvest use.

p. 226, para 2

As insufficient data from trials performed according to GAP were submitted, the Meeting agreed not to recommend a maximum residue level for piperonyl butoxide in cacao beans ~~or wheat flour~~ after post-harvest treatment.

p. 230, para 3, line 6

...a maximum residue level of 30 mg/kg and an STMR-P value of 10.8 mg/kg for wheat ~~whole meal and a maximum residue level of 100 mg/kg and an STMR-P value of 30.8 mg/kg for piperonyl butoxide in wheat germ.~~ wholemeal.

para 4, line 4

...The concentrations of residues in germ ~~and oil~~ decreased, and that in oil increased, with average processing factors of < 0.3 and < 2.7, respectively ($n = 6$).

p. 231, Tables

Estimate of maximum dietary burden of farm animals

Commodity	Group	Residues (mg/kg)	Basis	Dry matter (%)	Residues, weight (mg/kg)	% of diet			Residue contribution (mg/kg)		
						dry Beef cattle	Dairy cows	Poultry	Beef cattle	Dairy cows	Poultry
Citrus, dried pulp	AB	5.7	STMR-P	91	6.2 <u>6.3</u>	20	10	–	1.2 <u>1.3</u>	0.6	–
Potato peel, wet	AB	0.15	STMR-P	20	0.27 <u>0.75</u>			=			=
Sorghum	GC	30	MRL	86	34.2 <u>34.9</u>	5		20	1.7		27.4 <u>7.0</u>
Wheat	GC	30	MRL	89	33.3 <u>33.7</u>						
Rice	GC	30	MRL	88	33.6 <u>34.1</u>						
Maize	GC	30	MRL	88	33.6 <u>34.1</u>						

Commodity	Group	Residues (mg/kg)	Basis	Dry matter (%)	Residues, dry weight (mg/kg)	% of diet			Residue contribution (mg/kg)		
						Beef cattle	Dairy cows	Poultry	Beef cattle	Dairy cows	Poultry
					Total	100	100	100	144.9	236.6	99.3
									147.9		78.9

Estimated STMR value for dietary burden of farm animals

Commodity	Group	Residues (mg/kg)	Basis	Dry matter (%)	Residues, dry weight (mg/kg)	% of diet			Residue contribution (mg/kg)		
						Beef cattle	Dairy cows	Poultry	Beef cattle	Dairy cows	Poultry
Citrus, dried pulp	AB	5.7	STMR-P	91	6.2 <u>6.3</u>	20	10	-	1.2 <u>1.3</u>	0.6	=
Potato peel, wet	AB	0.15	STMR-P	20	0.27 <u>0.75</u>			=			=
Sorghum	GC	11	STMR	86	12.5 <u>12.8</u>	5		20	0.6		2.5
Wheat	GC	11	STMR	89	12.2 <u>12.4</u>						
Wheat bran	GC	29.7	STMR	89	31.1 <u>33.4</u>	50	40	80	15.6 <u>16.7</u>	12.4 <u>13.4</u>	24.9 <u>26.7</u>
Rice	GC	11	STMR	88	12.3 <u>12.5</u>						
Maize	GC	11	STMR	88	12.3 <u>12.5</u>						
				Total		100	100	100	44.4 <u>45.6</u>	67 <u>68</u>	27.4 <u>29.3</u>

p. 232 Residues in animal products

Cattle, para 1

The maximum calculated dietary burden of piperonyl butoxide for cattle was ~~144.9~~ 147.9 mg/kg feed for beef cattle and 236.6 mg/kg for dairy cows.... The mean intake calculated for dairy cattle (67 mg/kg feed) was higher than that for beef cattle (~~44.4~~ 45.6 mg/kg) and was used to estimate the STMR value for milk and cattle tissues.

p. 233

Poultry

The calculated maximum and mean intakes of piperonyl butoxide for poultry, ~~99.3 and 27.4~~ 78.9 and 29.3 mg/kg feed respectively, were used in the estimations for tissues and egg. For the estimation of the maximum residue level in tissues, the values at the calculated dietary burden (~~99.3~~ 78.9 mg/kg feed) were estimated by interpolation from the highest residue values at 61.2 and 199 ppm in feed. For the STMR estimation, the values at the ~~27.4~~ 29.3 mg/kg feed dietary burden were estimated by interpolation of the mean residue data at 20.4 and 61.2 ppm....

p. 234, Table

Residues in poultry products from poultry treated orally

Dose (ppm)	Piperonyl butoxide (mg/kg)							
	Eggs		Liver		Muscle		Fat	
Actual	Highest	Mean	Highest	Mean	Highest	Mean	Highest	Mean
<u>MRL</u>								
99.3	0.88		<0.08		0.38		5.6	
78.9/	0.549/		<0.063/		0.218/		3.15/	
61.2	0.35		< 0.05		0.12		1.7	
199	1.9		0.15		0.88		13	
<u>STMR</u>								
27.4		0.056						
29.3/		0.063/		<0.01/		<0.058/		0.52/
20.4		0.03		–		< 0.05		0.30
61.2		0.18		< 0.05		0.09		1.3

4.23 Phosmet

p. 238, para 2

The phosmet processing factors for oranges to juice and dried pulp were ~~<0.05 and <0.05 respectively. These factors both <0.05. This factor~~ applied to the STMR (0.64 mg/kg) ~~and MRL (3 mg/kg)~~ for citrus whole fruit provided the STMR-P for orange juice (~~0.03 mg/kg~~) ~~and STMR-P for dried processed citrus pulp~~ (0.03 mg/kg).

4.24 Propargite

p. 245, 1st line

...Ten trials support this GAP: ~~0.38~~, 0.39, 0.59, 0.63, 0.65, ~~0.71~~, 0.74, 0.81, 0.97, 1.1, 1.2, 3.0 mg/kg.

Peach, para 2

The Meeting agreed that the residue data for peach, nectarine, and plum were from the same population and could be combined. The GAPs are similar, 1.5 – 3.2 kg ai/ha, PHI 14 or 21 days. The 25 values in ranked order are: ~~0.38~~, 0.39, 0.57, 0.59, 0.63, 0.65, ~~0.71~~, 0.73, 0.74, 0.80, 0.81, 0.82, 0.86, 0.87, 0.89, 0.94, 0.97, 0.99, 1.0, 1.1, 1.2 (~~2~~), (3), 1.3, 1.4, 1.9, 3.0 mg/kg. The Meeting estimated a maximum residue level of 4 mg/kg for stone fruit (excluding cherry)...The Meeting estimated an STMR of ~~0.87~~ 0.89 mg/kg for stone fruit (excluding cherry) with stone.

252, penultimate para, line 4

~~...This confirms...These replace~~ the previous recommendations for maximum residue levels ~~of 0.1 F and 0.1 (fat)~~. The Meeting also estimated a maximum residue level for offal of mammals at 0.1 (*) mg/kg.

p. 253, main para, line 6

...The Meeting ~~confirmed the existing estimated~~ maximum residue levels for poultry meat (0.1 mg/kg * (fat)) and eggs (0.1 mg/kg *) ~~to replace 0.1 mg/kg (fat) and 0.1 mg/kg~~, and estimated a maximum residue level of 0.1 mg/kg * for poultry offal.

4.25 Tolyfluanid

p. 267, para 1

These two sets of results seem to belong to similar populations. The combined concentrations from 25 trials in ranked order were: 0.03(2), 0.05, 0.08, 0.12, 0.14, 0.20, 0.23, 0.32, 0.35, 0.41, 0.43, 0.47, 0.55, 0.73, 0.75, 0.77(2), 0.90, 1.1, 1.4, ~~1.5~~, 1.7, 1.9, 2.6 and 2.65 mg/kg for tolyfluanid;...

Annex 1

Pesticide	ADI, mg/kg bw	CCN	Commodity	Recommended MRL, mg/kg		STMR or STMR-P, mg/kg	HR or HR-P, mg/kg
				New	Previous		
Carbaryl ** (008)			Citrus fruit, edible portion			0.487	1.6 1.16
		JF 0001	Citrus fruit juice	0.5		0.13 0.10	
		MF 0100	Fat from mammals other than marine mammals Mammalian fats (except milk fats)			0.003	0.062
		JF 0269	Grape juice	30		3.2	21.45
[Delete row]		AB 0269	Grape pomace, dry	80		9.8	
		ML 0106	Milks	0.05	0.1 (*) T	0.03 0.003	
		AO5 1900	Nuts (whole in shell)	W	10 T		
		VO 0445	Peppers, Sweet	5	5 T for Peppers		
		FS 0012	Stone fruits, except Cherries ¹	10		2.05	7.8
		VR 508	Sweet potato	0.02 (*)		0.02	0.02
		CM 0654	Wheat bran, unprocessed	2	20	0.17 0.245	
Carbofuran (096)	0-0.002	VO 0447	Sweet corn (corn-on-the-cob)	0.1	W	0.03 0.04	0.1 0.08
Deltamethrin**(135)	0-0.01	MM 0095	Meat (from mammals other than marine mammals)	0.5 (fat)	0.5 (fat)	0.155 (fat)	0.186 (fat)
		FT 0305	Olives	1	0.1	0.21 (pulp)	0.31 (pulp)
		PM 0110	Poultry meat	0.1 (fat)	0.01 (*)	0.038 (fat)	0.09 (fat)
			<p><u>Residue</u> (For compliance with MRLs and estimations of dietary intake): sum of deltamethrin, α-R-deltamethrin ([1R-[1α(R*),3α]]-α-cyano-3-phenoxybenzyl 3-(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylate) and trans-deltamethrin ([1R-[1α(S*),3β]]-α-cyano-3-phenoxybenzyl 3-(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylate)</p> <p>The residue is fat-soluble</p> <p>¹ The information provided to the JMPR precludes an estimate that the dietary intake would be below the acute reference dose.</p> <p>Acute RfD: 0.05 mg/kg bw</p>				
Diflubenzuron ** (130)	0-0.02	JF 0226	Apple juice	-	-	0.072	0.072
		AS 0649	Rice straw and fodder, dry	0.7		0.04 0.02	
Esfenvalerate*(204)	0-0.02				Fenvalerate (CXL)		
		GC 0654	Wheat	0.05		0.01	0.03
		AS 0654	Wheat straw and fodder, dry	2	2 (cereal grains)	0.47	
Imidacloprid (206)	0-0.06	JF 0001	Citrus juice			0.014 0.07	
		AB 0001	Citrus pulp, dry	10		0.374 1.94	
			Citrus marmalade (orange)			0.03 0.16	
		MO 0105	Edible offal (Mammalian)	0.05		0.006 0.009	0.036

Pesticide	ADI, mg/kg bw	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)	0.02*		0.001 0.002 (muscle) 0 (fat)	0.007 0.008 (muscle) 0.004 0.005 (fat)
		ML0106	Milks	0.02*		0.0014 0.0024	
		VO 0051	Peppers ^a [Delete superscript]	1		0.15	0.48
		^a Expressed on dry weight basis Residue (For compliance with MRLs and for estimation of dietary intake): Sum of imidacloprid and its metabolites transformation products containing the 6-chloropyridinyl moiety, expressed as imidacloprid. Acute RfD: 0.4 mg/kg bw					
Oxamyl** (126)	0-0.009	ML 0106	Milks	0.02 (*)		0	0
		AL 0697	Peanut fodder	0.2 (dry wt)	2	0.041 (dry wt)	
		OC 0697	Peanut oil, crude			0.0034	
		OR 0697	Peanut oil, refined			0.0034	
Phosmet (103)	0-0.01	AB 0001	Citrus pulp, dry			0.03	
		FP 0230 FP 0009	Pome fruits ¹			3.3	7.3
Piperonyl butoxide (062)	0-0.2	MM 0812	Cattle meat	5- 0 ^a (fat)		2.6 (fat) ^{a,b}	
		MM 0095	Meat fat (from mammals others than marine mammals), except cattle	2 (fat)		0.14 (fat)	
		PM 0110	Poultry meat	7 (fat) ^a		2.0 (fat) ^{a,b}	
		GC 0654	Wheat	30 Po W ^d	10 Po	11	
		Residue (For compliance with MRLs and for estimation of dietary intake) for plant and animal commodities: piperonyl butoxide The residue is fat soluble ^a The MRL accommodates external animal treatment ^b Not STMR value but median residue concentrations in animals in a treated group ^c The MRL for cattle kidney (MO 1280) is higher than for other species of kidneys because of direct treatment of cattle. The Codex commodity MO 0098 includes cattle in its standard wording, but cattle kidney has to be excluded in this case because of the higher cattle kidney MRL ^d Now included in Cereal grains Acute RfD: Unnecessary					
Propargite **(113)	0-0.01	AM 0738 AM 0660	Almond hulls	50	-	15	
		SO 0691	Cottonseed	0.1	0.1*	0.02	
		GC 0645	Maize	0.1	0.1 0.1*	0.05	
		MO0105	Offal of mammals Edible offal (Mammalian)	0.1 *	-	0.004	
		FB1236	Wine from grapes	0.2	-	0.01	
Tolylfluanid** (162)	0-0.08		Grape wine			0.75	

