PESTICIDE RESIDUES IN FOOD

REPORT OF THE 2009 JOINT FAO/WHO MEETING OF EXPERTS

1. INTRODUCTION

A Joint FAO/WHO Meeting on Pesticide Residues (JMPR) was held at the headquarters of the World Health Organization (WHO), Geneva, Switzerland, from 16 to 25 September 2009. The Meeting brought together the Food and Agriculture Organization (FAO) Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group.

The meeting was opened by Dr Bruce Aylward, Director, WHO, on behalf of the Directors-General of WHO and FAO.

Dr Aylward acknowledged the impressive and successful work performed by this programme for over 45 years, and the important role played by the Meeting in the establishment of international food safety standards, thereby contributing to the improvement of public health. The provision of independent scientific advice as a basis for public-health decision-making lies at the core of work carried out by WHO and the experts participating in the Meeting are thus contributing directly to the goals of the organization. The process of furnishing independent scientific advice and a rapid coordinated response to incidents involving food safety is of increasing importance in the current global environment. The new International Health Regulations (IHR) will play an important role in facilitating this process. Previously concerning only some communicable diseases, the IHR have been expanded to include events of non-communicable origin. Reorganization has taken place at WHO to reflect this change and the formation of the new cluster on Health Security and the Environment (HSE) will allow closer collaboration in this area. In closing, Dr Aylward noted the challenging tasks to be accomplished by the present Meeting and gratefully acknowledged the invaluable contribution made by the participating experts, including the tremendous efforts put into preparation of the Meeting.

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

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

The Meeting evaluated 25 pesticides, including three new compounds and eight compounds that were re-evaluated within the Code Committee on Pesticide Residues (CCPR) periodic review programme for toxicity or residues, or both. The Meeting established ADIs and ARfDs, estimated MRLs and recommended them for use by the Codex Committee on Pesticide Residues (CCPR), and estimated STMR and highest residue (HR) levels as a basis for estimating dietary intakes.

The Meeting also estimated the dietary intakes (both short-term and long-term) of the pesticides reviewed and, on this basis, performed a dietary risk assessment in relation to their ADIs or

ARfDs. Cases in which ADIs or ARfDs may be exceeded were clearly indicated in order to facilitate the decision-making process by the CCPR. The rationale for methodologies for long-term and short-term dietary risk assessment are described in detail in the reports of the 1997 JMPR (Annex 5, reference 80, section 2.3) and 1999 JMPR (Annex 5, reference 86, section 2.2). Additional considerations are described in the report of the 2000 JMPR (Annex 5, reference 89, sections 2.1–2.3).

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

1.1 DECLARATION OF INTERESTS

The Secretariat informed the Committee that all experts participating in the 2009 JMPR had completed declaration-of-interest forms, and that no conflicts had been identified. Professor Alan Boobis and Dr Douglas McGregor had undertaken minor consultancies, but these were not related to compounds on the agenda. Experts were then asked to inform the meeting of any new potential interests that had arisen since submitting the forms and no interests were declared.

2. GENERAL CONSIDERATIONS

2.1 TRANSPARENCY IN THE MAXIMUM RESIDUE LEVEL ESTIMATION PROCESS: FURTHER CONSIDERATIONS

The Forty-first Session of the CCPR discussed transparency in the process by which maximum residue levels are estimated by the JMPR, as a response to General consideration 2.7 in the JMPR 2008 report. The Meeting in 2008 had, in addition to its usual procedure, used the North American Free Trade Agreement (NAFTA) MRL calculator to estimate maximum residue levels and had produced a summary table in which it was explained when JMPR estimates differed from estimates derived by the NAFTA calculator.

The CCPR recommended that "for the 2009 JMPR meeting the OECD statistical calculation method would be used, if available, and if not available the NAFTA calculator method would continue to be used and reported and, to the extent possible, brief explanations of derivation of the maximum residue levels would be provided when the calculator was not used".[1] The present Meeting decided that, instead of producing a summary table for these cases, it would provide additional explanation on how the value was derived for each pesticide × commodity maximum residue level recommendation.

The present Meeting noted that a MRL is the maximum residue anticipated in a commodity produced in accordance with good agricultural practice (GAP). The process of estimating a value for use as a MRL involves selection of residue trials conducted according to a critical GAP. It is generally the highest observed residue value that has the greatest influence on the estimated MRL. Small datasets (those with less than 15 data points), represent a particular challenge when undertaking an estimation. The JMPR has previously noted that 95th or 99th percentiles estimated on the basis of statistical methods are increasingly inaccurate for datasets of less than 15 points and such estimates should not be automatically used. The Meeting agreed that the estimates provided using statistical methods are generally acceptable for larger datasets. Data available to the JMPR generally have additional limitations that can compromise the use of statistical approaches, including whether the trials represent a random sample. Some of these limitations have been elaborated in previous reports of the JMPR, principally in 2008.

The JMPR employs expert judgement informed by the available tools, such as statistical approaches to estimate maximum residue levels. Additional factors are taken into account by the JMPR as part of the application of expert judgement, as discussed below.

Experience leads to an understanding of the uncertainties in the parameters involved in the estimation of maximum residue levels. From the information considered, the most appropriate value must be identified in a decision that makes the best use of all the available evidence. The initial deposit of a pesticide on a crop is the best indicator of the proper application of a pesticide when the edible part of the crop is present and well-developed at the time of application. For example, the analysis of available data on pesticides has enabled estimates to be made for the upper limits and ranges of initial deposits for many crops.[2] Various factors beyond those used in statistical calculation, such as the examples listed below, may be taken into account in the estimation of maximum residue levels.

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[1] Codex Alimentarius Commission (2009) Report of the Forty-first Session of the Codex Committee on Pesticide Residues, Beijing, China, 20–25 April 2009 (ALINORM 09/32/24), paras 30–45.

[2] Bates JAR (1990) The prediction of pesticide residues in crops by the optimum use of existing data. Pure & Applied Chemistry 62: 337–350.

Table 1 Factors to be taken into account when estimating maximum residue levels

Issue or factor	Action or comment
Accumulated data on the distribution of residues from supervised trials for residues of pesticides on a crop provide a reliable basis for the likely spread of residues within a dataset. Such data complement the limited information that can be obtained from the small datasets usually available.	The Meeting regularly considers the typical distribution of residues between trials, including initial deposits, and where limited trial data are available for a particular pesticide crop combination, adjusts the estimated maximum residue level appropriately.
Some latitude is allowed regarding how closely trials comply with GAP in selecting the dataset for maximum residue estimation (typically, a change in parameters leading to a ±25% change in residues), if the majority of trials have been conducted at the lower or higher ends of the range used to select data, this should be taken into account when recommending a maximum residue level	The Meeting makes an allowance to account for how close the majority of selected residue trials match the critical GAP.
Residues resulting from rates of application that are higher or lower than GAP, as well as studies of metabolism are taken into account in the context of the use to predict a pattern of likely residue concentrations, but are not used directly in the set of numbers that support a maximum residue level estimation or in the risk assessment.	These values may provide information on situations where no residues are expected or provide information as to whether residues scale with application rate.
Noting the effect of crop-growth stage where this aspect is particularly important. Examples of this are the herbicides haloxyfop and glyphosate, for which data selection concentrated on the growth stages that might occur before PHI rather than the time before harvest itself.	This example underlines the importance of expert judgement in selecting the suitable residue data for estimation of residue levels.
Should greater weight be given to different data within a dataset to account for differences between commercial practice and available trial conditions, e.g., varieties or cultivars grown, crops grown under protected cover versus field grown crops?	The JMPR may take into account the varieties and cultivars used in the available residue dataset. Allowances may need to be made in maximum residue level estimates, depending on the range of varieties used in the trials. For example, if no trials have been provided on small tomato varieties, a higher maximum residue level might be recommended.
Whether or not the trial data are representative of differences in cultural practices, e.g., orchard and vine crop-production techniques, planting density, hedging versus spindle versus vase in tree architecture.	The JMPR may make an allowance for unavoidable bias associated with differences in the cultural practices observed in the residue trials available.
Whether or not the trial data are representative of differences in application equipment	The JMPR may make allowance for unavoidable bias associated with differences in the application equipment used in the residue trials available
Data from trials on one crop are sometimes extrapolated to other members of a crop group or used to recommend a maximum residue level for the entire group.	The JMPR may need to make allowances for differences in crops when making recommendations based on extrapolation or for crop group MRLs
For post-harvest use of grain protectants, the application rates of the active ingredient provide a precise estimate of expected residue levels at the time of application. Additionally, the Meeting generally gives more weight to commercial-size trials than to laboratory-scale trials	The JMPR may recommend maximum residue levels at the application rate as residues higher than the amount added are not expected

Issue or factor	Action or comment
Foliar application of a non-systemic pesticide to certain crops (root and tuber, cotton, tree nuts) may result in occasional residues on the harvested commodity owing to the commodity sometimes being exposed to direct spray (e.g., open cotton bolls).	The Meeting may recognize this in estimating maximum residues.
Commercial shelling of nuts may give rise to low levels of residues in nutmeat that need to be taken into account	The Meeting may recognize this when estimating maximum residues for tree nuts.

GAP, good agricultureal practice; PHI, pre-harvest interval.

It is possible that innovation will lead to new methods (such as predictive models for residues on crops and derived commodities) that might allow improved estimation of maximum residue levels.

Conclusion

The above examples of how the JMPR uses expert judgement indicate that evaluation of residue data is a complex task that requires the consideration of factors and parameters additional to the numerical residue values. Consequently, MRL estimates cannot be based solely on automatic calculation using any currently available "statistical" methods.

2.2 THE OECD GUIDANCE DOCUMENT ON LIVESTOCK FEEDING

The Meeting was informed that the Organisation for Economic Co-operation and Development (OECD) Guidance Document on Livestock Feeding is being written and will go through the OECD approval process in 2010. Meanwhile, many essential items on livestock feeding have been included in the OECD Overview Guidance[3]. Included in the Overview is an updated version of the OECD Table on feedstuffs derived from field crops. The original version was previously adopted by the JMPR in 2007.[4] The table presents information on the consumption of various feed commodities by livestock in various regions of the world. The original version has been expanded by OECD to include several additional commodities and notably to include information on consumption by livestock in Japan.

The OECD Overview Guidance is currently intended to calculate the dietary burdens for livestock within OECD countries for the purpose of selecting appropriate doses for livestock feeding studies. However, the feedtables may also be used to construct livestock dietary burdens for the purpose of interpreting the results of feeding studies. The consumption information is combined with estimates of residues on the feed items (STMR or MRL values, as appropriate) to arrive at estimates of the total dietary burden of beef cattle, dairy cattle, sheep, pigs, and poultry for the pesticide under consideration. These values are then compared to the results of feeding studies to arrive at estimates of the levels of pesticides in milk, eggs, meat, fat, and edible offal. Results for cattle and poultry will be extrapolated to all relevant livestock.

The new method for calculating livestock dietary burden used by the NAFTA countries was noted. Commodities are classified by nutrition type (roughage, carbohydrate, protein) and maximum percentages of the total diet are set for each category for the various livestock. For example, the beef cattle diet is set at 15% roughage, 80% carbohydrate concentrate, and 5% protein concentrate. The aim of taking into account the animals' nutritional requirements is to arrive at a more realistic, less

[3] OECD Environment, Health and Safety Publications. Guidance Document on overview of residue chemistry studies. Series on Testing and Assessment No. 64 and Series on Pesticides No. 32. Revised February 2009, Environment Directorate, Paris.

[4] Food and Agriculture Organization (2007) General consideration 2.10: OECD livestock feed tables. In: Pesticide residues in food – 2007, FAO Plant Production and Protection Paper 191.

extreme diet. This reflects the situation in Canada and the United States of America (USA), but may not be applicable to other regions. OECD guidance continues to recommend the calculation of livestock dietary burden for regions other than Canada and the USA in a manner similar to that used by JMPR.

The Meeting considered that the NAFTA procedure was not applicable at the international level. This procedure relies upon intensive feeding, such as exists in very controlled situations in feed lots, and does not represent the situation in other parts of the world. The JMPR procedure maximizes livestock dietary-intake burdens of the pesticide by taking into account the feed items from different Codex classes (forage, grain, byproducts, etc.) and emphasizes the use of diverse feed items with maximum pesticide residues. This calculation is performed for every region for which there is information on livestock burden is available, the intention being to arrive at estimates that are inclusive of livestock burdens worldwide.

The JMPR procedure, as detailed in the FAO Manual[5], will be continued. The present Meeting agreed to use the latest available version of the OECD feed table and to include it in the FAO Manual, Second Edition. The revised table will be used by the Meeting in 2010. The Meeting also decided that some modification to the OECD feed table would be needed for the version placed in the FAO Manual. The OECD had grouped feed items into four broad categories: forages; roots and tubers; cereal grains/crop seeds; byproducts of processing. The category "forages" as used by OECD includes virtually all plant commodities other than grains and roots and tubers (forage, fodder, silage, hay, straw, leaves and tops, and grasses), and thus encompasses a much wider selection of commodities than the narrower Codex definition.

The feed table will be modified to indicate the Codex crop group of each commodity (see Figure 1). This is important because in performing the calculation of livestock dietary burden, the total burden for the group is considered as well as the burden from each individual commodity. For example, if residues occurred in clover, alfalfa fodder, and bean fodder (the group of legume animal feeds), they should be considered in sequence, beginning with the calculated highest residue in the dry-weight feed. The detailed procedure is described in the FAO Manual.

In 2005, the JMPR expressed the opinion that fresh forages for animals were not an item of international trade requiring Codex MRLs and decided not to recommend further forage MRLs (Annex 5, reference *104*).[6] The Meeting stated that data on forage residues would continue to be evaluated and used in the estimation of farm-animal dietary burden. There may be situations in which fresh forages should be evaluated as being consumed only locally. i.e., being added to livestock dietary burden only in regions where relevant GAP produces residues in the fresh forage.

5 Food and Agriculture Organization. 2002. Submission and evaluation of pesticide residues data for the estimation of maximum residue levels in food and feed.

6 Food and Agriculture Organization (2005) General consideration 2.1: JMPR recommendations for animal forage. In: Pesticide residues in food – 2005. FAO Plant Production and Protection Paper, 183:32.

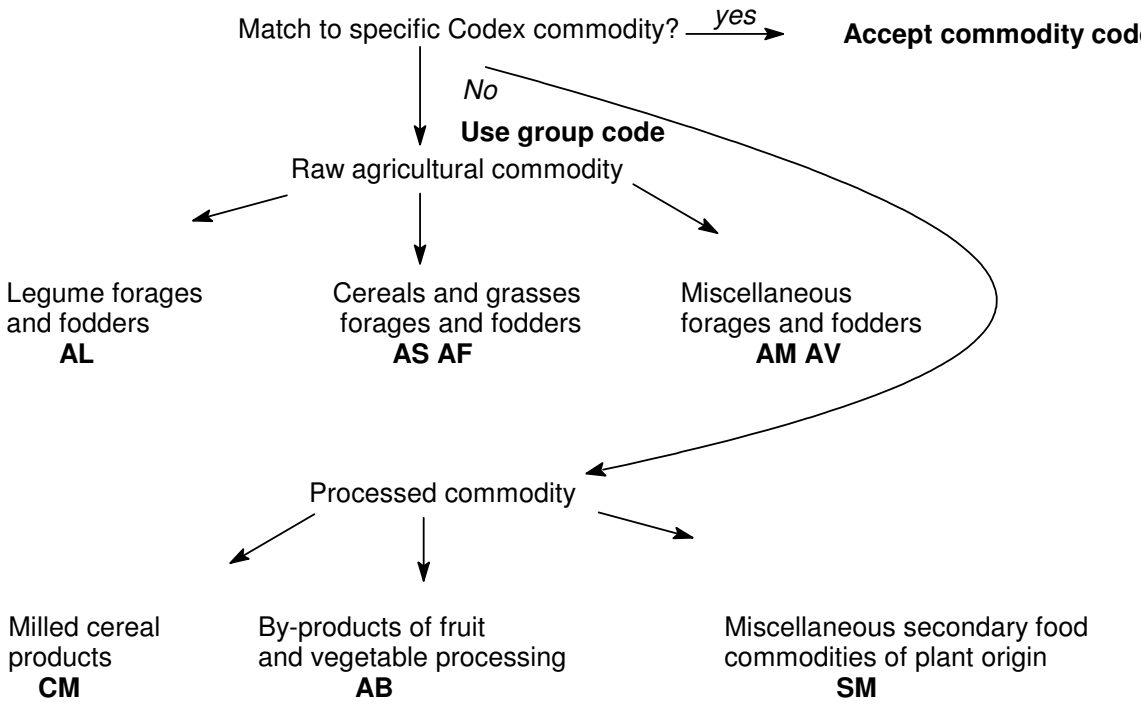

Figure 1 Determination of Codex commodity codes for the OECD category "forages"

2.3 GUIDANCE FOR DATA SUBMISSION FOR ESTIMATION OF RESIDUE LEVELS IN/ON SPICES

In response to the request of the CCPR at its Thirty-fourth Session, the 2002 JMPR considered the options for estimating maximum residue levels for spices based on monitoring data (Annex 5, reference 95, section 2.7) and provided guidance on the format for reporting such data. As the CCPR at its Thirty-fifth Session had decided to elaborate MRLs based on monitoring data (Annex 5, reference *95*, section 2.7), the 2003 JMPR gave further consideration to possible options for estimating maximum residue levels where sufficient monitoring data were not available and prepared guidelines for conducting selective surveys to generate pesticide residue data reflecting the field and post-harvest application of pesticides (Annex 5, reference *95*, section 2.5).

The 2004 JMPR considered the nature of monitoring results and defined the basic principles for the evaluation of monitoring data to estimate maximum residue levels (Annex 5, reference *95*, section 2.6). The Meeting at that time recommended maximum residue levels that encompass at least 95% of the residues with 95% probability (in 95% of cases). To satisfy this requirement, a minimum of 59 residue datapoints for each spice commodity × pesticide residue combination is required.

The Meeting at that time further recommended that monitoring results should not be used for estimating maximum residue levels that reflect post-harvest use, which results in much higher residue values than foliar application or exposure to spray drift.

The present Meeting noted that the guidance given by the JMPR in previous reports might have been misinterpreted and, as a consequence, the residue data submitted were insufficient for evaluation.

In order to assist collection and submission of the appropriate information, the Meeting re-emphasized that:

- The minimum number of datapoints required for each pesticide × spice commodity combination is 59;
- Where residue data are available for several spice commodities belonging to one group of spices, the JMPR will evaluate the residue data and if the residue distributions can be considered similar, then the JMPR may recommend a MRL for the commodity group;
- The JMPR cannot make any recommendations for pesticide classes such as organophosphates, carbamates, pyrethroids. If it is claimed, for instance, that no organophosphorous compounds were detected in 20 samples of a spice commodity, then it must be specified which compounds have been looked for and what were the respective LOQ and recovery values. The method performance parameters indicated must be supported with appropriate data on method validation.

In addition, the supporting information should be provided as specified in the JMPR reports on actual agricultural, storage and processing practice, the need for post-harvest protection, etc.

Comprehensive information on data requirements is also available in the second edition of the FAO Manual (section 3.6).

2.4 UPDATE OF THE FAO MANUAL ON THE SUBMISSION AND EVALUATION OF DATA ON PESTICIDE RESIDUES FOR THE ESTIMATION OF MAXIMUM RESIDUE LEVELS IN FOOD AND FEED

The first version of this manual, published in 1997, presented the principles applied by the JMPR. As the evaluation process is continually evolving, the first version of the manual was revised in 2002 and published as the first official edition. It incorporated additional information from the JMPR reports of 1997–2001. The last eight years have seen many changes in residue evaluations. The JMPR has elaborated some new principles, as well as revised many existing principles used for the evaluation of pesticide residues, which have been reproduced in the reports of its meetings.

The OECD Working Group on Pesticide has also elaborated several guidelines and guidance documents that are directly related to the design of supporting studies used in the evaluation of pesticide residues. The activities of the JMPR FAO Panel and the OECD Working Group were complementary, as several experts contributed to both activities. The OECD Working Group considered the principles applied by the JMPR, and the JMPR incorporated a number of the OECD guidelines in its evaluations. The 2006 JMPR (Annex 5, reference *107*, section 2.1) decided that the OECD guidelines and guidance documents would be used in the preparation of future versions of the FAO Manual with the aims of maximum harmonization and future opportunities for work share.

The present second edition of the FAO Manual describes the basic principles currently applied by the FAO Panel in the evaluation of pesticide residues for recommending maximum residue levels. Some elements of the OECD documents have been incorporated in the manual without specific attribution. These guidelines and guidance documents have been cited in the references. In cases where more detailed information relating to a specific subject was considered to be particularly useful for the reader, the reference to the relevant guideline is given.

In addition to general updating of the text, the second edition contains new information on:

- Metabolism studies;
- Requirements regarding on environmental fate;
- Performance characteristics of analytical methods;
- Planning and implementing supervised residue trials;

- Use of residue monitoring data for estimation of maximum residue levels for spices;
- Statistical evaluation of residue data;
- Calculation of burden in animals, based on expanded feed consumption tables;
- Estimation of dietary intake of residues.

In order to improve the ease with which the subject of interest can be located in the manual, the sections are numbered. The chapter number is indicated in bold type, and the appendices are referenced with Roman numbers.

The second edition of the manual will be published by FAO and will be placed on the FAO website.

3. RESPONSES TO SPECIFIC CONCERNS RAISED BY THE CODEX COMMITTEE ON PESTICIDE RESIDUES (CCPR)

The Meeting noted that the information supplied on some of the concern forms submitted by CCPR Members was insufficient to allow the JMPR to clearly identify the critical issues underlying the indicated concerns. Consequently, the Meeting had great difficulty in determining the issues involved, raising the possibility that the response provided by the Meeting might not actually address the true concern. The Meeting requested that any future concerns submitted to JMPR should be accompanied by comprehensive and transparent supporting information. If such information is not provided, the Meeting might be forced to conclude that it is not able to provide a meaningful response.

3.1 BOSCALID (221)

Background

Boscalid is a systemic fungicide that was first evaluated by JMPR in 2006 for residues and toxicology as a new active substance. The Meeting established an ADI for boscalid of 0–0.04 mg/kg bw and considered that an ARfD was unnecessary. Owing to the incomplete data submission for residues in follow-up crops, the Meeting decided that a risk assessment of residues in rotational crops could not be finalised at that time. The 2008 JMPR reviewed residue data for additional uses involving banana and kiwifruit.

In response to the request of the CCPR at its Forty-first Session,[7] the present Meeting reconsidered all the available data for a finalization of the dietary risk assessment for boscalid. New data were submitted regarding the metabolism and degradation of boscalid in soil, uptake in follow-up crops and livestock feeding to the 2009 JMPR. Further studies, GAP information and supervised residue trials referred to in the present report are described in the evaluation of boscalid as a new active substance by the 2006 JMPR.

Overview on the evaluation procedure for boscalid in rotational crops as applied by JMPR

The Meeting followed the general procedure outlined under point 2.9 in the JMPR report of 2008. In the first step, field-decline studies were used to estimate the half-life of boscalid in soil under the assumption of first-order kinetics. The Meeting identified DT_{50} values of 208, 365 and 746 days as values representing the total range of possible half-lives of boscalid in soil.

After the estimation of half-lives, the highest plateau-level concentrations of boscalid in soil after annual application according to GAPs reported in 2006 were estimated. The calculation indicated that all uses reported globally, except those involving 4.5 kg ai/ha per year, resulted in boscalid plateau-level residues in soil equivalent to an application rate of 2.1 kg ai/ha or less.

In the next step, field rotational-crop studies on various commodities conducted at rates of 2.1 kg ai/ha per year were reviewed to estimate mean, median and highest residues expected following uptake of boscalid via plant roots. These additional residues were compared to boscalid levels found in the corresponding commodities after direct treatment according to GAPs described in the 2006 JMPR report. In case of a significant contribution of residues, arising after crop rotation, to residues following direct treatment, both pathways were taken into account simultaneously for an overall estimation of maximum residue levels as well as for STMR and highest residue values.

[7] Codex Alimentarius Commission (2009) Report of the Forty-first Session of the Codex Committee on Pesticide Residues, Beijing, China, 20–25 April 2009 (ALINORM 09/32/24), para 124.

Whenever appropriate, the Meeting decided to extrapolate its recommendations to whole commodity groups to include as many minor crops as possible that are likely to be exposed to boscalid via crop rotation as well as direct application.

Example 1: Root and tuber vegetables

Based on the use of boscalid on carrots, boscalid residues in the roots following direct treatment were: < 0.05, 0.06, 0.12, 0.17, 0.18, 0.19, 0.28, 0.34 mg/kg.

For carrot roots, residues were found with mean, median and highest residues of 0.13 mg/kg, 0.065 mg/kg and 0.37 mg/kg, respectively. The Meeting concluded that root and tuber vegetables may be influenced significantly by an additional uptake of boscalid via the roots. The Meeting decided to add the mean residue of 0.13 mg/kg found in field studies on carrots roots to the median residue of 0.175 mg/kg obtained from supervised field trials on carrot roots for an overall STMR for boscalid in carrot roots of 0.305 mg/kg. In addition, the Meeting recommended a maximum residue level of 2 mg/kg for the group of root and tuber vegetables, based on the use of boscalid on carrot roots.

Example 2: Oilseeds

Based on the use of boscalid on sunflowers, boscalid residues in the seeds following direct treatment were: < 0.05, 0.08, 0.09, 0.13, 0.16, 0.16, 0.23, 0.45 mg/kg.

In field studies on succeeding crops, the mean, median and highest residues in alfalfa, soya bean and cotton seeds were 0.05 mg/kg, 0.05 mg/kg and 0.06 mg/kg, respectively, with most of the values below the LOQ of 0.05 mg/kg. The Meeting concluded that residues in oilseeds caused by an additional uptake of boscalid via the roots are insignificant in comparison to residue levels following direct treatment. The Meeting estimated a maximum residue level and an STMR value for boscalid in oilseeds of 1 mg/kg and 0.145 mg/kg, respectively, based on sunflower seeds.

Owing to the large number of commodities that are subject to crop rotation and new studies submitted to JMPR 2009, a detailed report, a long-term dietary risk assessment and a recommendation table are presented in Annex 1 of the present report.

3.2 CARBOFURAN (096)

Background

At the Forty-first Session of the CCPR,[8] the Delegation of the European Community (EC) raised concerns regarding the ADI and ARfD for carbofuran that had been established by the JMPR in 2008, both these values being higher than those established by the EC.

Evaluation of carbofuran by the JMPR

In 2008, the Meeting established an ARfD of 0.001 mg/kg bw based on the "overall NOAEL" identified by the 2004 JMPR (Annex 5, reference *101*, p. 9) of 0.03 mg/kg bw per day identified on the basis of inhibition of brain acetylcholinesterase activity in rat pups aged 11 days. This NOAEL was supported by the BMD_{10} (benchmark dose at the 10% effect level) of 0.04 mg/kg bw and the $BMDL_{10}$ (lower 95% confidence limit for the BMD_{10}) of 0.03 mg/kg bw extrapolated by the United States EPA[9] from data on the inhibition of brain acetylcholinesterase activity in pups aged 11 days

[8] Codex Alimentarius Commission (2009) Report of the Forty-first Session of the Codex Committee on Pesticide Residues, Beijing, China, 20–25 April 2009 (ALINORM 09/32/24), para 85.

[9] US EPA (2008a) Carbofuran: HED revised risk assessment for the Notice of Intent to Cancel (NOIC). Memorandum from Drew D, Morton TG, Lowit A, & Reaves E. to Andreasen J. Dated 3 January 2008; US EPA (2008b) Carbofuran: proposed

from three studies (Tyl *et al*., 2005; Moser *et al*., 2007; and Hoberman, 2007a).[10] A safety factor of 25 was considered to be appropriate because the acute toxic effects of carbofuran are dependent on C_{max} rather than the area under the curve of concentration–time (AUC) and data indicated that the sensitivity of acetylcholinesterase activity to inhibition by carbofuran was similar in humans and laboratory animals (rats, dogs) (Annex 5, reference *113*, p.7). The ARfD was considered to be adequately protective of infants and children since it was based on the NOAEL identified in studies in pups aged 11 days.

The 2008 JMPR noted that this ARfD was lower than the ADI of 0–0.002 mg/kg bw. This is plausible in view of the toxicological characteristics of inhibition of acetylcholinesterase activity by carbofuran, which shows very rapid recovery; long-term exposure can thus be likened to a series of acute exposures. The 2008 JMPR therefore concluded that the ADI and ARfD for carbofuran should be based on the same NOAEL and revised the ADI to 0–0.001 mg/kg bw based on the overall NOAEL of 0.03 mg/kg bw from the new studies of acute toxicity in rats and using a safety factor of 25.

Evaluation of carbofuran by the EC

The EC also considered the studies of acute toxicity in rats, except for the study by Moser *et al*. (2007), as key studies for establishing reference doses. However, the EC emphasized that they did not consider either the ARfD of 0.001 mg/kg bw or the ADI of 0–0.001 mg/kg bw to be sufficiently protective for neurotoxicity in children. On the basis of the information provided by the EC, the concerns raised by the EC centred on the following issues:

- In the study of Hoberman (2007a), the lowest dose of 0.03mg/kg bw was considered to be a lowest-observed-adverse effect level (LOAEL) rather than a NOAEL, since brain acetylcholinesterase activity in female pups aged 11 days was inhibited by 20% ($p < 0.01$).
- On the basis of the studies from Tyl (2005) and Hoberman (2007a), the EC calculated a BMD_{10} of 0.014–0.016 mg/kg bw. This BMD_{10} was considered to be supportive of an extra two-fold safety factor to extrapolate the LOAEL for pups (0.03 mg/kg bw) to a NOAEL (0.015 mg/kg bw).
- The EC noted that a safety factor of 100 should be maintained to derive the ADI and ARfD for carbofuran. EC considered it insufficiently proven that a lower safety factor should be applied based upon the assumption that N-methyl carbamate toxicity, which is dependent on a C_{max} rather than an AUC effect, would exhibit lower inter- or intraspecies variability.

In conclusion, the EC concluded that an ADI of 0–0.00015 mg/kg bw and an ARfD of 0.00015 mg/kg bw should be established, based on an extrapolated NOAEL of 0.015 mg/kg bw and a safety factor of 100.

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tolerance revocations. Federal Register 73(148):44863–44892.

[10] Hoberman AM (2007a) Cholinesterase depression in juvenile (day 11) and adult rats following acute oral (gavage) dose of carbofuran technical. Unpublished report No. A2006-6137 dated 31 May 2007 from Charles River Laboratories Preclinical Services, Horsham, PA, USA. Submitted to WHO by FMC Corporation, Agricultural Products Group, Philadelphia, PA, USA.

Moser VC, McDaniel KL, Phillips PM (2007) Report on cholinesterase comparative sensitivity study of carbofuran: adult and PND11. Unpublished report dated 14 November 2007 from Neurotoxicology Division, National Health and Environmental Effects Research Laboratory, Office of Research and Development, US EPA, Research Triangle Park, North Carolina 27711. Submitted to WHO by Office of Pesticide Programs, US EPA, Washington, DC, USA.

Tyl RW, Marr M, Myers CB (2005) Acute dose-response study of carbofuran technical administered by gavage to adult and postnatal day 11 male and female CD (Sprague-Dawley) rats. Unpublished report No. A2005-5981 dated 7 November 2005 from RTI International, Center for Life Sciences and Toxicology, Research Triangle Park, NC, USA. Submitted to WHO by FMC Corporation, Agricultural Products Group, Philadelphia, PA, USA.

Comments by the JMPR

After consideration of the EC concerns and after reviewing the conclusions of the 2008 JMPR, the present Meeting highlighted the following points:

- In one study (Hoberman, 2007a), inhibition of brain acetylcholinesterase activity was 20% in female pups at a dose of 0.03 mg/kg bw. In male pups, however, inhibition was only 13% and data indicated no evidence for a sex-specific difference in sensitivity to inhibition of brain acetylcholinesterase activity by carbofuran. Also, in the corresponding dose range-finding study (Hoberman, 2007b),[11] inhibition of brain acetylcholinesterase activity at a dose of 0.03 mg/kg bw was only 10% or 11% in male and female pups, respectively. Thus, based on data from both studies and for both sexes, the present Meeting considered the dose of 0.03 mg/kg bw to be an overall NOAEL for pups aged 11 days, since inhibition of brain acetylcholinesterase activity was clearly less than 20%.
- The overall NOAEL of 0.03 mg/kg bw is supported by the benchmark-dose analysis of data on brain acetylcholinesterase activity from the three studies in rat pups aged 11 days (Tyl et al., 2005; Hoberman, 2007a; Moser *et al.*, 2007). The estimated BMD_{10} for brain acetylcholinesterase activity was 0.04 mg/kg bw, while the $BMDL_{10}$ was 0.03 mg/kg bw. The Meeting considered that the BMD_{10} used by the JMPR was more reliable than that calculated by the EC as it used data from three studies (Moser *et a*l., 2007; Tyl *et al*., 2005; Hoberman, 2007a) rather than two (Tyl *et al*., 2005c; Hoberman, 2007a).
- For carbofuran, the acute toxic effects are dependent on C_{max} rather than AUC and data indicated that the sensitivity of humans and laboratory animals (rats, dogs) to inhibition of acetylcholinesterase activity was similar. Thus the Meeting considered that a safety factor of 25 was appropriate. A detailed rationale for this position is included in the report of the 2008 JMPR (Annex 5, reference *113*, p.7: Safety factors for acute C_{max}-dependent effects: specific considerations with respect to carbamates such as carbofuran).

Therefore, the Meeting reaffirmed both the ARfD of 0.001 mg/kg bw and the ADI of 0–0.001 mg/kg bw based on an overall NOAEL of 0.03 mg/kg bw for inhibition of brain acetylcholinesterase activity in rat pups aged 11 days and with a safety factor of 25. Also, the Meeting confirmed that both the ADI and the ARfD are adequately protective of infants and children.

3.3 CHLORANTRANILIPROLE (230)

Background

At the Forty-first Session of the CCPR, the Delegation of the USA raised concerns regarding the reasoning for the maximum residue levels for chlorantraniliprole in grapes and leafy vegetables (spinach) differing from estimates made using the NAFTA calculator.[12] A concern form was submitted.

The Meeting noted there were many approaches to estimating MRLs, including experience, modelling and the use of statistics to evaluate sets of numbers. Experience takes into account the crop varieties used in residue trials and their potential for residues, the number of trials, distribution of trial locations, size of trial plots, timing of spray applications, spray volumes, use of spray additives

[11] Hoberman AM (2007b) Acute oral (gavage) dose range-finding study of cholinesterase depression from carbofuran technical in juvenile (day 11) rats. Unpublished report No. A2006-6135 dated 31 May 2007 from Charles River Laboratories Preclinical Services, Horsham, PA, USA. Submitted to WHO by FMC Corporation, Agricultural Products Group, Philadelphia, PA, USA.

[12] Codex Alimentarius Commission (2009) Report of the Forty-first Session of the Codex Committee on Pesticide Residues, Beijing, China, 20–25 April 2009 (ALINORM 09/32/24), para 126.

such as adjuvants, range of half-times for residue decline and the large database of residue of data for other pesticides on the same or similar crops. These factors cannot be taken into account by the NAFTA calculator (see General consideration 2.1).

Statistical methods use well-established mathematical approaches to estimate a number. The NAFTA calculator used by the JMPR uses a decision-tree approach to estimate one of the following:

- The upper 95% confidence limit for the 95th percentile residue
- The point estimate of the 99th percentile residue
- The mean plus three-times the standard deviation.

The JMPR has previously suggested in the report of its meeting in 2008 that more than 15 datapoints are required for application of the statistical approaches described above, although the NAFTA White Paper[13] acknowledges that the accuracy of NAFTA estimates for smaller datasets diminishes as sample size decreases. The JMPR considered a combination of experience of historical data and statistical methods to arrive at the MRL recommendations.

Grapes

Data from seventeen residue trials matching GAP were available with a highest residue of 0.52 mg/kg. The estimate derived from use of the NAFTA calculator was 1.4 mg/kg; however, the Meeting noted that the data in the Q-Q plot depart from the trend line at the high end of the plot, where extrapolation to provide the NAFTA calculator derived estimate occurred. The Meeting could not conclude that the data follow a lognormal distribution. The range of estimates provided by the different options in the NAFTA calculator, before rounding, were:

- Assuming the data follow a normal distribution:
    - 95% upper confidence level for the 95th percentile 0.61 mg/kg
    - 99th percentile (point estimate) 0.59 mg/kg
- Assuming the data follow a lognormal distribution:
    - 95% upper confidence level for the 95th percentile 1.64 mg/kg
    - 99th percentile (point estimate) 1.39 mg/kg
    - Upper prediction level for the 95th percentile assuming a coefficient of variation of 1 0.77 mg/kg
- Non-parametric methods
    - Mean plus 3 times the standard deviation 0.70 mg/kg
    - EU method II 0.66 mg/kg.

The 2008 JMPR took into account experience of likely high residues at the day of the last spray and use of decline half-lives obtained from the reported residue decline trials (assuming a DT_{50} of 34 days). Noting the above and the complete range of estimates derived from the NAFTA calculator, the Meeting recommended a value of 1 mg/kg for grapes.

The Meeting confirmed its previous recommendation of 1 mg/kg for grapes.

[13] Statistical Basis of the NAFTA method for calculating pesticide maximum residue limits from field trial data. http://www.regulations.gov/search/Regs/home.html#documentDetail?R=090000648026e8d0

Leafy vegetables (spinach)

The 2008 JMPR estimated a maximum residue level for leafy vegetables based on a dataset of seven residue trials for spinach with a highest observed residue of 8.9 mg/kg. The NAFTA calculator estimated 15 mg/kg. Visual inspection of the Q-Q plot in the NAFTA calculator did not enable the Meeting to conclude the data follow a log-normal distribution. The range of estimates provided by the different options in the NAFTA calculator, before rounding, were:

- Assuming the data follow a normal distribution:
    - 95% upper confidence level for the 95th percentile 13.1 mg/kg
    - 99th percentile (point estimate) 11.31 mg/kg
- Assuming the data follow a lognormal distribution:
    - 95% upper confidence level for the 95th percentile 19.98 mg/kg
    - 99th percentile (point estimate) 14.5 mg/kg
    - Upper prediction level for the 95th percentile assuming a coefficient of variation of 1 64 mg/kg
- Non-parametric methods:
    - Mean plus three-times the standard deviation 12.7 mg/kg
    - EU method II 16.6 mg/kg.

As with grapes, the 2008 JMPR took into account experience of likely high residues at the day of the last spray the decline half-lives obtained from the reported residue decline trials (DT_{50} time of 14 days). Noting the range of estimates available from use of the NAFTA calculator, the small dataset and the results based on an estimate from the day of the last spray, the 2008 JMPR estimated a maximum residue level of 20 mg/kg.

The Meeting confirmed its previous recommendation of 20 mg/kg for leafy vegetables.

The present Meeting also reiterated the statement of the 2008 JMPR that, for small datasets, the NAFTA White Paper and reviews of the performance of the calculator suggest a large uncertainty in such estimates of high percentiles. Use of other tools and experience is needed to ensure that the maximum residue level estimates are realistic.

3.4 CYFLUTHRIN (157)/BETA-CYFLUTHRIN (228) – ALTERNATIVE GAP

Cyfluthrin and beta-cyfluthrin were evaluated for toxicology by the 2006 JMPR and for residues by the 2007 JMPR under the CCPR periodic review programme, and maximum residue levels for cyfluthrin, arising from the use of either cyfluthrin or beta-cyfluthrin on a number of commodities, were recommended.

The 2007 JMPR estimated short-term intakes for children that exceeded the ARfD of 0.04 mg/kg bw for broccoli and head cabbage and noted that there were insufficient data to support an estimation of lower maximum residue levels based on alternative GAPs for these commodities.

At the Forty-first Session of the CCPR in 2009, the Committee agreed that if no data were available to support lower MRLs for broccoli and head cabbage (based on alternative GAP), the draft MRLs would be considered for withdrawal at the 2010 session.[14]

[14] Codex Alimentarius Commission (2009) Report of the Forty-first Session of the Codex Committee on Pesticide Residues, Beijing, China, 20–25 April 2009 (ALINORM 09/32/24), paras 106–107.

Information on current GAP and new supervised trials data from Indonesia were provided to the 2009 JMPR for cabbages, but no new residue data or information were available for broccoli.

Results of supervised trials on crops

Based on US GAP and residue data for cyfluthrin, the 2007 JMPR estimated a maximum residue level of 4 mg/kg, an STMR of 0.25 mg/kg and an HR of 2.1 mg/kg for cyfluthrin in cabbage (head) but estimated that the short-term intake for children was 240% of the ARfD (0.04 mg/kg bw).

Cabbages, Head – beta-cyfluthrin

Residue trials conducted in Germany matching the GAP of Sweden and Poland (10 g ai/ha; PHI of 7 days) and evaluated by the 2007 JMPR, reported residues of < 0.01, < 0.01, 0.06 and 0.08 mg/kg.

New trials with beta-cyfluthrin reported to the Meeting from Indonesia (GAP, 15 g ai/ha; PHI of 7 days) reported residues of < 0.01, 0.02 and 0.05 mg/kg.

The Meeting agreed that the data were insufficient to estimate a maximum residue level to support an alternative GAP for beta-cyfluthrin on cabbage (head).

Cabbages, Head – cyfluthrin

Residue trials with cyfluthrin conducted in Portugal and Spain, matching the GAP of Italy (25 g ai/ha; PHI of 3 days) reported residues of 0.01 and 0.09 mg/kg.

Trials conducted in Germany, matching the GAP of Belgium (maximum of 2 applications, 25 g ai/ha, PHI of 14 days) reported residues of < 0.01, 0.02 and 0.06 mg/kg.

The Meeting agreed that the data were insufficient to estimate a maximum residue level to support an alternative GAP for cyfluthrin on cabbage (head).

Alternative GAP was considered by the present Meeting, but the previous HR recommendation was confirmed because of insufficient residue data. Hence, a refinement of the international estimate of short-term dietary intake (IESTI) was not possible with the current data. The Meeting established a group ARfD for cyfluthrin and beta-cyfluthrin in 2006 on the basis of acute neurotoxicity observed in a 4-week study in rats and a safety factor of 25, and it is unlikely that it could be refined.

3.5 FENTHION (39)

Background

Fenthion is an insecticide that has been used since 1957 for the control of a wide range of insect pests on fruit, vines, olives, vegetables, cotton, tea, sugar-cane, sugar-beet, and rice. The use pattern also includes the postharvest disinfestation of fruit, the control of insect pests (e.g., mosquitoes, fleas) for public health purposes and animal houses and for the control of animal ectoparasites.

Evaluation of fenthion by the JMPR

Fenthion was first evaluated by the JMPR in 1971 and has been reviewed several times since, most recently in 1995 within the periodic review programme of the CCPR. An ADI of 0–0.007 mg/kg bw was established.

The 2000 JMPR could not evaluate studies of residues in peaches, cherries and olives, since the trials were performed in EU Member States and the related GAP in those countries was pending.

Consideration of fenthion by CCPR and by the EC

The CCPR at its Thirty-fourth Session in 2003 noted that the current Codex MRLs are mainly based on EU uses, and that fenthion was under evaluation in the EU.[15]

In 2004, the EU decided not to include fenthion in Annex I of Directive EC/ 91/414, implying that all uses of fenthion within the EU would stop. Since the current Codex MRLs are based on European use labels and European supervised field trials, CCPR considered revoking all existing Codex MRLs.

The CCPR at its Fortieth Session in 2008 noted that GAP information for cherries, citrus fruit and olives would be provided by Australia and decided to maintain the Codex MRLs for cherries, citrus fruits, olives and olive oil, virgin, for 4 years under the periodic review programme. The Committee also decided to delete the proposed MRLs for olive oil, virgin, mandarins and orange, sweet, sour, since they were based on European uses.[16]

Comments by JMPR

The present Meeting did not receive any data to evaluate, and noted that fenthion was not scheduled for periodic re-evaluation until 2017.

3.6 METHOMYL (094)

Background

The CCPR at its Forty-first Session[17] noted the concerns expressed by the EC and Norway regarding acute dietary intake for grape and tomato, based on the ARfD established by the EC. The delegation of the EC informed the Committee that they would submit a concern form for apple.

Evaluation of methomyl by the JMPR

Methomyl is a carbamate insecticide that is registered throughout the world for foliar application on numerous agricultural crops. JMPR has evaluated the compound several times since 1978. In 1989, an ADI of 0–0.03 mg/kg bw was established and in 2001, the Meeting was requested to establish an ARfD. The Meeting at that time established an ARfD of 0.02 mg/kg bw based on the results of a study in human volunteers. The Meeting noted that this ARfD was lower than the ADI, and concluded that the ADI and ARfD should be based on the same NOAEL. The ADI was accordingly revised to 0–0.02 mg/kg bw.

Methomyl was evaluated for residues under the periodic review programme of the CCPR in 2001. Maximum residue levels for methomyl, arising from the use of either methomyl or thiodicarb, were recommended for a number of crops. The 2001 JMPR estimated short-term intakes that exceeded the ARfD of 0.02 mg/kg bw for apples, broccoli, Brussels sprouts, head cabbage, cauliflower, celery, water melon, grapes, kale, head lettuce, leaf lettuce, spinach, sweet corn and tomato.

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[15] Codex Alimentarius Commission (2003) Report of the Thirty-fourth Session of the Codex Committee on Pesticide Residues, The Hague, The Netherlands 13–18 May 2002 (ALINORM 03/24), paras 80–81.

[16] Codex Alimentarius Commission (2008) Report of the Fortieth Session of the Codex Committee on Pesticide Residues, Hangzhou, China, 14–19 April 2008 (ALINORM 08/31/24), paras 50–51.

[17] Codex Alimentarius Commission (2009) Report of the Forty-first Session of the Codex Committee on Pesticide Residues, Beijing, China, 20–25 April 2009 (ALINORM 09/32/24), para 78.

The CCPR at its Thirty-eighth Session[18] requested JMPR to consider using alternative GAPs to recommend lower MRLs for apples, brassica vegetables, celery, fruiting vegetables, cucurbits, grapes, leafy vegetables and pears. The 2008 JMPR was able to recommend maximum residue levels for apple, pear, cucurbits (cucumbers, courgettes and melons), grapes, lettuce and tomatoes. Most of the recommendations were based on European data. No new residue data or information was available for brassica vegetables and celery and the 2008 JMPR withdrew its previous recommendations for those commodities.

The international estimated daily intakes (IEDI) in the 13 GEMS/Food Consumption Cluster Diets, based on the STMRs estimated by the 2008 JMPR were in the range of 0% to 3% of the maximum ADI of 0.02 mg/kg bw. The IESTI varied from 0% to 50% of the ARfD (0.02 mg/kg bw) for the general population. The IESTI varied from 0% to 100% of the ARfD for children aged 6 years and younger. The highest percentages (50% of the ARfD for the general population, 100% of the ARfD for children) were found for tomatoes. The Meeting concluded that neither the long-term nor the short-term intake of residues of thiodicarb and methomyl from uses that had been considered by the JMPR was unlikely to present a public health concern.

Evaluation of methomyl by the EC

The present Meeting received the EC concern form, together with the results of the EU dietary-intake calculation. The following information was presented: "Using EC endpoints (ARfD 0.0025 mg/kg bw/day) and risk assessment methodologies (EFSA model PRIMo rev2), apples are 666% of the ARfD[19], using an HR value of 0.17 mg/kg (15 trials). It is acknowledged that a higher ARfD of 0.01 mg/kg bw/day is accepted by JMPR, based on a human volunteer study. Even using the JMPR ARfD with EC risk assessment methodologies, apples are 167% of the ARfD."

Comments by JMPR

The present Meeting noted that the ARfD established by JMPR is 0.02 mg/kg bw, not 0.01 mg/kg bw, as was incorrectly reported in the EC concern form. Furthermore, the Meeting noted that using the JMPR ARfD with the EC risk-assessment methodologies, the short-term intake (children, large portion for UK infant, 180 g/person) for apples was 83% when using a variability factor of 7, while it was 61% of the ARfD when using a variability factor of 5. The Meeting, using a variability factor of 3, calculated a short-term intake of 60% of the ARfD for children, based on a children's large portion from the USA of 680 g/person.

The Meeting confirmed that the short-term intake of residues of thiodicarb and methomyl from uses on apple is unlikely to present a public health concern.

3.7 PHORATE (112)

Phorate is a systemic organophosphate contact insecticide and acaricide that inhibits acetylcholinesterase activity. Residue and analytical aspects of phorate were evaluated by the JMPR in 1977, 1984, 1990, 1991, 1992, and 2005. The evaluation in 2005 was a periodic review. The toxicological periodic review was conducted in 2004, when an ADI of 0–0.0007 mg/kg bw and an ARfD of 0–0.003 mg/kg bw were established.

The residue definition for phorate, both for enforcement and for risk assessment for animal and plant commodities, is: the sum of the parent, its oxygen analogue, and their sulfoxides and

[18] Codex Alimentarius Commission (2006) Report of the Thirty-eighth Session of the Codex Committee on Pesticide Residues, Fortaleza, Brazil, 3– 8 April 2006 (ALINORM 06/29/24), paras 80– 81.

[19] For children.

sulfones, expressed as phorate. The analytical methodology available relies on the oxidation of all phorate-related residues to the common moiety metabolite, phoratoxon sulfone.

The 2005 JMPR noted that the acute dietary intake of potato by children aged up to 6 years amounted to 120% of the ARfD. The value of 120% represents the IESTI for potato, microwaved with peel. The CCPR in 2006 therefore decided not to advance the maximum residue level in the Codex step system. The CCPR in 2007 was informed that the manufacturers would provide additional data for processed potato in 2008 for evaluation by the 2009 JMPR.

The present Meeting received a new study of processing in potatoes to facilitate a refinement of the risk assessment.

Methods of analysis

Total phorate-related residues (oxidizable to phoratoxon sulfone) were determined by gas chromatography with flame photometric detection (GC-FPD), following method M-1620 (see 2005 JMPR). The reported LOQ was 0.049 mg/kg eq, the LOD was 0.003 mg/kg eq. Method verification recoveries at 0.049, 0.25 and 2.0 mg/kg eq were for each fortification level above 90% (n=3, RSD, < 4%).

Fate of residues in storage and during processing

The Meeting received new information on the fate of incurred residues of phorate during washing and microwave cooking of potatoes. The samples from the field studies were analysed twice, owing to the variable results of the first experiment. The reason for this was considered to be as follows. The application of phorate in this study was as an in-furrow granule. As a result, it is possible that potatoes formed directly in the furrow accumulated more phorate, both on the surface, including adhered soil, and internally, than potatoes formed outside the treated furrow. In order to get a representative field sample, the potatoes were sampled from directly in the row (in the furrow where the insecticide was applied) as well as from the sides of the row. Each collected treated sample contained randomly selected potatoes from both areas, with potentially great variability in residue content between potatoes used in each processing step. The Meeting considered this to be a plausible explanation for the variable results.

The second experiment was modified to reduce this potential variability between potatoes used in each processing step, by direct pairing of potatoes/potato parts across the unwashed versus washed and cooked samples. For the second processing set, the frozen whole potato retained samples held by the processing facility were used for processing.

Mean weight loss for the potatoes during cooking in processing experiment 2 (66%, mean of treated samples) was significantly higher than the weight loss in processing experiment 1 (15%). For microwaving, 15–20% is the commercial norm. Projected residues at 15% weight loss to correct for excess weight loss due to frozen storage of potatoes before processing were reported by the study director.

The Meeting decided that the experiment in which frozen potatoes with peel were microwaved does not reflect common practices. The Meeting could not confirm that the extensive weight loss did not result in an unusual loss of phorate residues. The Meeting decided not to use the results of the new processing study, and confirmed its previous recommendations.

Using the HR for potato (0.27 mg/kg,) the 2005 JMPR estimated highest residues for the processed commodities (HR-Ps) as listed below. Furthermore, using the STMR for potato (0.05 mg/kg), the Meeting estimated STMR-Ps for these commodities.

Table 2 Estimation of highest concentrations of phorate residues in processed potato commodities

Commodity	Processing factor (median or best estimate)	STMR-P (mg/kg)	HR-P (mg/kg)
Potatoes boiled with peel	0.13	0.0065	0.0351
Potatoes boiled without peel	0.11	0.0055	0.0287
Potatoes baked with peel	0.28	0.014	0.0756
Potatoes baked without peel	0.27	0.0135	0.0729
French fries	0.38	0.019	0.1026
Potatoes microwaved with peel	0.36	0.018	0.0972

HR-P, highest residue in a processed commodity calculated by multiplying the HR of the raw commodity by the corresponding processing factor; supervised trials median residue in a processed commodity calculated by multiplying the STMR of the raw commodity by the corresponding processing factor

The 2005 JMPR decided to use the HR-P and STMR-P for potatoes, microwaved with peel, in the calculations of dietary intake for potatoes since this represented the worst-case situation. The present Meeting noted that the dietary intake of French fries would also be critical.

DIETARY RISK ASSESSMENT

Long-term intake

Conclusion of the 2005 JMPR:

The IEDIs of phorate, based on the STMRs estimated for 18 commodities, for the five GEMS/Food regional diets were in the range of 9% to 20% of the maximum ADI (0–0.0007 mg/kg bw/d). The Meeting concluded that the long-term intake of residues of phorate resulting from uses that have been considered by the JMPR was unlikely to present a public health concern.

Short-term intake

The IESTI for phorate was calculated for potatoes, both by using the HR for potatoes, microwaved with peel, and for French fries, the latter based on new consumption data. The results of which can be found in Annex 4.

The IESTI represented 70% of the ARfD (0.003 mg/kg bw) for the general population (both for potatoes, microwaved with peel, and for French fries) and 170% and 180% of the ARfD for children, from consumption of potatoes, microwaved with peel, and French fries, respectively. The information provided to the JMPR precludes an estimate that the dietary intake of potatoes by children aged 6 years and younger would be below the ARfD.

The Meeting noted that the dietary intake estimation was already based on residues in processed potatoes, leaving little room for refinement. Furthermore, the ARfD was based on a single-dose study and it was unlikely that it could be refined.

3.8 PROCYMIDONE (136)

Background

At the Fortieth Session of the CCPR, the Delegation of the EC raised concerns regarding the ADI and ARfD for procymidone established by the JMPR in 2007, which were higher than those established by the EC.[20]

Evaluation of procymidone by the JMPR

In 2007, the Meeting established an ADI of 0–0.1 mg/kg bw for procymidone based on the overall NOAEL of 12.5 mg/kg bw per day identified on the basis of hypospadias and alterations in testes, prostate and epididymis weights in two studies of reproductive toxicity in rats and a study of developmental toxicity in rats, with a safety factor of 100. The ADI was supported by NOAELs of 14 mg/kg bw per day in a long-term study in rats and 17 mg/kg bw per day in a long-term study in mice. An ARfD of 0.1 mg/kg bw was established based on the NOAEL of 12.5 mg/kg bw per day identified on the basis of hypospadias in a study of developmental toxicity in rats, with a safety factor of 100. The 2007 JMPR concluded that the effects on organ weights seen in studies of reproductive toxicity were largely a consequence of postnatal exposure over a period of time and therefore not appropriate for the establishment of an ARfD.

Evaluation of procymidone by the EC

The concern raised by the EC, as stated on the concern form, was that procymidone and its metabolite (PCM-CH_2OH) bind to the human androgen receptor in vitro, indicating that procymidone has antiandrogenic activity in humans. Since data on toxicokinetics in humans still do not exist, it was concluded that it cannot be excluded that human exposure to procymidone would not lead to teratogenic effects. The EC also noted that procymidone is classified as "Repr. Cat. 2 R61"[21] in the EC.

The documentation submitted by the EC cited two sets of reference doses for procymidone. The first set of reference doses was agreed following an expert toxicology meeting and are the agreed values cited in the "Review Report" supporting the authorization of procymidone.[22] These values comprise an ADI of 0.025 mg/kg bw based on a NOAEL of 2.5 mg/kg bw per day from a study of reproductive toxicity in rats, with a safety factor of 100, and an ARfD of 0.035 mg/kg bw based on the NOAEL of 3.5 mg/kg bw from a study of developmental toxicity in rats, with a safety factor of 100.

The second set of reference doses was proposed in an addendum produced by the rapporteur member state (France) in 2007, which had not been discussed by EC toxicologists at any peer review meetings. The ADI of 0.0028 mg/kg bw was based on a LOAEL of 2.5 mg/kg bw per day from a study of reproductive toxicity in rats, with a safety factor of 900 (3 for moving from a LOAEL to a NOAEL; 3 for interspecies variability; 10 for intraspecies variability and 10 for severity of effect). The ARfD of 0.012 mg/kg bw based on the NOAEL of 3.5 mg/kg bw from a study of developmental toxicity in rats, with a safety factor of 300 (3 for interspecies variability; 10 for intraspecies variability and 10 for severity of effect).

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[20] Codex Alimentarius Commission (2008) Report of the Fortieth Session of the Codex Committee on Pesticide Residues, Hangzhou, China, 14–19 April 2008 (ALINORM 08/31/24), para 73.

[21] May cause harm to the unborn child. Toxic to reproduction, Category 2, i.e.,likely to be relevant to humans.

[22] European Commission (2006) Review report for the active substance procymidone. Finalized in the Standing Committee on the Food Chain and Animal Health at its meeting on 27 January 2006 in view of the inclusion of procymidone in Annex 1 of Directive 91/414/EEC. SANCO/4064/2001 rev 1, dated 19 January 2006. European Commission Health and Consumer Protection Directorate-General. Draft working document.

The available information provided by the EC gave no detailed rationale for:

- The effects seen at the LOAELs used in the first evaluation;
- Changing from a NOAEL to a LOAEL in the study of reproductive toxicity;
- The reduction of the default interspecies safety factor;
- The additional safety factor for severity.

Comments by the JMPR

In order to respond as thoroughly as possible to the concerns raised, the 2009 JMPR went to considerable lengths to obtain more detailed information on the basis for the EC concerns, as these were not clearly described or justified on the concern form or submitted documents. The Meeting requested that any future concerns submitted to JMPR are accompanied by comprehensive and transparent supporting information.

The 2007 JMPR and 2007 EC appear to have had access to the same supporting databases. The 2007 JMPR discussed the reproductive effects of procymidone in great depth (performing its own benchmark-dose calculations for some end-points) and concluded that procymidone was a reproductive toxicant and could bind to the human androgen receptor in vitro. The 2007 JMPR also considered in depth the data on the toxicity of procymidone metabolites and the data on toxicokinetics in rats, rabbits and monkeys and their relevance to human exposures.

The main differences between the evaluations made by the 2007 JMPR and the EC were the NOAELs identified, and in the 2007 EC proposals, the safety factors chosen. The present Meeting reviewed tabulated data on a number of end-points, including all those identified in additional EC documents as being the basis for identifying the NOAELs used to set the EC reference doses. These end-points included anogenital distances, testes, prostate, epididymis and seminal vesicle weights, hypospadias, undescended testes and histopathology of testes, epididymides, coagulating glands, prostate and seminal vesicles. The present Meeting also reviewed the publications describing the 2007 JMPR decisions.

The present Meeting noted that the monograph produced by the 2007 JMPR described some effects at the intermediate dietary concentration of 250 ppm (17 mg/kg bw per day), which would give a NOAEL of 3.0 mg/kg bw per day (50 ppm) identified in the first study of reproductive toxicity. However, these findings were not evident at the NOAEL of 14 mg/kg bw per day in the long-term study in rats, for the parental effects, nor at the NOAEL of 12.5 mg/kg bw per day in the subsequent study of reproductive toxicity, for the pup effects. The present Meeting confirmed that the overall NOAEL from the studies of reproductive toxicity in rats was 12.5 mg/kg bw per day based on the NOAELs that were between the LOAEL and NOAEL for the first study of reproductive toxicity. The present Meeting noted that most of the findings mentioned in EC documents were not seen below doses of 37 mg/kg bw per day.

In the study of developmental toxicity in rats, the only finding at 12.5 mg/kg bw per day was a statistically significant (but < 10%) change in anogenital distance in male fetuses removed by caesarean section. However, in the part of this study where dams were allowed to deliver naturally, there were no significant effects on anogenital distance at postnatal days 1 or 21 in the group at 12.5 mg/kg bw per day. The present Meeting confirmed that the findings at 12.5 mg/kg bw per day were not adverse and identified this dose as the NOAEL.

The EC addendum gave no explanation for the choice of the non-default safety factors for interspecies (3) and severity (10). The 2007 JMPR discussed the use of a data-derived safety factor when deriving the ARfD for procymidone, but concluded that the uncertainties were such that this was not justifiable. The 2007 JMPR considered that the findings at the LOAELs were such that no additional safety factors were needed to derive the ARfD and ADI. The present Meeting confirmed that a safety factor of 100 was appropriate for deriving both the ADI and the ARfD for procymidone.

The present Meeting reaffirmed the ADI for procymidone of 0–0.1 mg/kg bw based on the overall NOAEL of 12.5 mg/kg bw per day from two studies of reproductive toxicity in rats and an ARfD for procymidone of 0.1 mg/kg bw based on the NOAEL of 12.5 mg/kg bw per day in a study of developmental toxicity in rats, both with a safety factor of 100.

3.9 SPIROTETRAMAT (234)

Background

At the Forty-first Session of the CCPR, the Delegation of the USA expressed concern over the maximum residue level estimation of 0.5 mg/kg made by the 2008 JMPR and submitted a concern form. The USA noted that there were 11 trials in the USA and that use of the NAFTA calculator produced an estimate of 0.3 mg/kg in the USA, from the same dataset. An explanation of the derivation of the JMPR estimate was requested and a request was made to consider 0.3 mg/kg as a revised estimate.

Consideration and response

The supervised field trial data were from USA trials conducted on almonds and pecans. The results in ranked order were: 0.020 (3), 0.031, 0.048, 0.054, 0.082, 0.089, 0.094, 0.13, 0.25 mg/kg (Annex 5, reference *113*, p.333).

The HR is 0.25 mg/kg, and thus the MRL would be somewhat greater than 0.25 mg/kg. The median was 0.05 mg/kg. All values exceed the limit of quantitation.

The Meeting noted that only 11 sample values were available for combined almond and pecan field trial sample results. The value of 0.5 mg/kg was based upon the consideration of a relatively small number of trials, meaning that one or more high residue values may have been missed in the limited crop field trials conducted, and on the need to cover possible residues from nut varieties of the tree nut group that were not included in the limited trials on pecans and almonds only.

The Meeting considered the results of the NAFTA statistical calculation spreadsheet. It provided estimates in the range of 0.3–0.6 mg/kg, depending on the distribution selected. The spreadsheet selected UPL median 95th value (0.3 mg/kg). This reflects the spreadsheet decision that the distribution is log-normal, but due to the small number of datapoints a diversion from the log normal 99 estimate (0.4 mg/kg) and the log-normal 95/95 value (0.6 mg/kg) is made.

The Meeting also noted that while the JMPR used the same dataset as the USA, there are differences in the treatment of that data that could lead to different estimates from the NAFTA calculator. The USA would have 22 residue values because of the procedure of using two datapoints per trial location. This inclusion of duplicate points would no doubt result in the use of the log-normal 99 or log-normal 95/95 value. The Meeting has rejected this approach, as it believes that samples from the same plot at the same site are not independent, and uses the highest residue from each trial site.

Furthermore, the Meeting decided that statistical methods may not be appropriate for datasets of fewer than 15 values (Annex 5, reference *113*, General consideration 2.8, p. 40). Examples show the uncertainty of the estimation based on a small number of residue datapoints, and this uncertainty and likelihood of underestimating the maximum residue level is clearly explained in the Canada/US White Paper for the NAFTA calculator[23].

[23] Statistical Basis of the NAFTA method for calculating pesticide maximum residue limits from field trial data. http://www.regulations.gov/search/Regs/home.html#documentDetail?R=090000648026e8d0

The Meeting considered that given the small dataset with HR of 0.25 mg/kg and the need to extrapolate pecan and almond data to all nuts, the maximum residue level should be estimated at 0.5 mg/kg. The lowest possible estimate could not be 0.3 mg/kg, as this was seen as too restrictive based on the few trial results available and the extrapolation to nut varieties with no trial data.

The Meeting confirmed its previous recommendation of 0.5 mg/kg for spirotetramat on tree nuts.

3.10 TRIADIMEFON (133) AND TRIADIMENOL (168)

Background

Triadimefon and triadimenol have been evaluated by the JMPR several times between 1978 and 2007. These compounds were re-evaluated as part of the periodic review programme of CCPR in 2007 for residues and in 2004 for toxicology. The Meeting recommended a number of maximum residue levels and established an ADI of 0–0.03 mg/kg bw and an ARfD of 0.08 mg/kg bw for both compounds. In 2008, the Fortieth Session of the CCPR, due to dietary intake concerns, requested JMPR to consider the alternative GAP approach to assess whether a lower maximum residue level recommendation for grapes was possible.

Information on current GAPs submitted to the 2009 JMPR included a company's statement that the GAP from Taiwan, China, is no longer supported.

Results of supervised residue trials on crops

For triadimefon and triadimenol, GAP information on grapes submitted to the present Meeting was similar to the GAPs on which the re-evaluation for periodic review in 2007 was based. Although the GAP from Taiwan, China, no longer supported by the company was available in 2007, the evaluation of supervised residue trial data was based on uses reported from Belarus, Croatia, Kazakhstan, Russia, South Africa, the former Yugoslav Republic of Macedonia, and the USA (triadimefon) as well as Australia, Bulgaria, Cyprus, France, Georgia, Italy, Moldavia, New Zealand, South Africa and the Ukraine (triadimenol). None of these GAPs have been revised to allow a re-evaluation in view of an alternative GAP approach.

The 2007 JMPR considered all supervised field trials available for grapes and decided to combine all residue data, since due to the high variability within the crop field trial, data could not be attributed to one specific GAP. Residue data selected in 2007 were: < 0.02(3), 0.03, < 0.04, < 0.04, 0.04(3), < 0.05(5), 0.05, 0.05, 0.06, 0.06, 0.07(4), 0.08, 0.08, 0.09(3), 0.1, 0.1, 0.11, 0.11, 0.15(4), 0.16, 0.17, 0.18, 0.21, 0.25, 0.27, 0.27, 0.28, 0.3, 0.32, 0.33, 0.36, 0.37, 0.43, 0.46, 0.54, 0.58, 0.59, 0.6, 0.6, 0.69, 0.78, 0.78, 0.8, 1.4, 1.7, 1.9 and 3.2 mg/kg (sum of triadimefon and triadimenol).

The HR of 3.2 mg/kg was based on one supervised field trial conducted with triadimefon according to the GAPs reported for Croatia and the former Yugoslav Republic of Macedonia using an application rate of 0.0025 kg ai/hL with a PHI of 35 days. This GAP represents the lowest application rate in combination with the highest PHI reported for all uses of triadimefon and triadimenol on grapes.

The second highest residue of 1.9 mg/kg found in grapes followed the use of triadimenol according to GAP reported from South Africa using 0.12 kg ai/ha (0.0075 kg ai/hL) with a PHI of 14 days.

The third highest residue of 1.7 mg/kg is based on a supervised field trial conducted with triadimefon according to the GAP reported from Belarus and Kazakhstan (0.0075 kg ai/hL; PHI, 30 days).

In view of this consideration, the 2007 JMPR concluded that an alternative GAP approach was not applicable to uses of triadimefon and triadimenol on grapes. Based on the uses of both

triadimefon and triadimenol, the Meeting confirmed its previous recommendation and estimated an STMR value of 0.15 mg/kg, an HR value of 3.2 mg/kg and a maximum residue level of 5 mg/kg for the sum of triadimefon and triadimenol in grapes.

Comment by the JMPR

The present Meeting concluded that an alternative GAP approach for the use of triadimefon and triadimenol on grapes was not possible since high residues would arise from all available GAPs, and confirmed the dietary risk assessment already presented in the re-evaluation in 2007.

The Meeting noted that the IESTI calculation for grapes at the HR level of 3.2 mg/kg, as well as the consumption of grapes at a level of 1.9 mg/kg and 1.7 mg/kg would lead to an exceedance of the ARfD.

The Meeting noted that although the ARfD is based on a study of acute neurotoxicity in rats given triadimefon and a safety factor of 25, the large dose spacing between the NOAEL and the LOAEL suggests the possibility that the ARfD may be refined (e.g., by benchmark-dose calculations).

4. DIETARY RISK ASSESSMENT

Assessment of risk from long-term dietary intake

At the present Meeting, compounds with recommended maximum residue levels and estimated STMRs were assessed for risks associated with long-term dietary intake. International estimated daily intakes (IEDIs) were calculated by multiplying the concentrations of residues (STMRs and STMR-Ps) by the average estimated daily per capita consumption for each commodity on the basis of the 13 GEMS/Food Consumption Cluster Diets.[24] IEDIs are expressed as a percentage of the ADI for a 55 kg or 60 kg person, depending on the cluster diet.

The percentages are rounded up to one whole number up to nine and to the nearest 10 above that. Percentages above 100 should not necessarily be interpreted as giving rise to a health concern because of the conservative assumptions used in the assessments.

Bifenthrin, cadusafos, chlorothalonil and cycloxydim were evaluated for toxicology at the current Meeting under the Periodic Re-evaluation Programme and ADIs were allocated. The long-term dietary risk assessment for these compounds will be considered during the periodic review for residues at subsequent Meetings.

The outcome of the evaluations of carbofuran, chlorantraniliprole, cyfluthrin/beta-cyfluthrin, fenthion, methomyl, paraquat, phorate, prochloraz, procymidone, triadimefon/triadimenol and spirotetramat performed at this Meeting was such that the long-term dietary intake assessment were considered unnecessary.

A summary of the long-term dietary risk assessments conducted by the present meeting is shown on Table 3. The detailed calculations of long-term dietary intakes are given in Annex 3. Calculations of dietary intake can be further refined at the national level by taking into account more detailed information, as described in the Guidelines for predicting intake of pesticide residues[25].

Table 3 Summary of long-term dietary of risk assessments conducted by the 2009 JMPR

CCPR code	Compound Name	ADI (mg/kg bw)	Range of IEDI, as % of maximum ADI
155	Benalaxyl	0-0.07	0-1
221	Boscalid	0-0.04	9-30
173	Buprofezin	0-0.009	1-50
090	Chlorpyrifos-methyl	0-0.01	20-140
118	Cypermethrin (includes alpha and zeta cypermethrin)	0-0.02	7-30
197	Fenbuconazole	0-0.03	0-2
235	Fluopicolide 2,6-dichlorobenzamide (M-01)	0-0.08 0-0.02	1-10 0-1
194	Haloxyfop and haloxyfop P	0-0.0007	20-80
176	Hexythiazox	0-0.03	0-2
216	Indoxacarb	0-0.01	1-30
236	Metaflumizone	0-0.1	0-1
209	Methoxyfenozide	0-0.1	0-8

[24] http://www.who.int/foodsafety/chem/gems/en/index1.html

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

CCPR code	Compound Name	ADI (mg/kg bw)	Range of IEDI, as % of maximum ADI
232	Prothioconazole[a]		
	Prothioconazole-desthio	0-0.01	0-2
237	Spirodiclofen	0-0.01	0-9
227	Zoxamide	0-0.5	0-0.3

[a] based on prothioconazole-desthio

Possible risk assessment refinement when IEDI exceeds the ADI

Chorpyrifos-methyl

The IEDI exceeded the ADI for the Cluster diets C (110% ofADI) and H (140% of ADI). The intake coming from the consumption of maize represented 42.7 and 72.8% of the total intake, respectively. The estimation of a STMR made by the Meeting considered the alternative GAP approach. A way of refining the long-term intake of chlorpyrifos-methyl is to have information on the expected residues in maize processed commodities, such as maize flour and cooked maize. The ADI for chlorpyrifos-methyl was established by the present Meeting on the basis of a NOAEL of 1 mg/kg bw/d from a 2-year study in rats and a safety factor of 100. However, two other studies had LOAELs of 3 mg/kg bw/d, therefore it is considered unlikely that the ADI could be refined.

Assessment of risk from short-term dietary intake

Available consumption data was used at the present Meeting to assess the risks associated with short term dietary intake for compounds with STMR and HR estimated values and established acute reference doses (ARfDs). The procedures for calculating the short-term intake were defined primarily in 1997 at an FAO/WHO Geneva Consultation[26] refined at the International Conference on Pesticide Residues Variability and Acute Dietary Risk Assessment sponsored by the Pesticide Safety Directorate and at subsequent JMPR Meetings.

Data on the consumption of large portions were provided to GEMS/Food by the governments of Australia, France, The Netherlands, Japan, South Africa, Thailand, the UK and the USA. Data on unit weights and per cent edible portions were provided to GEMS/Food by the governments of Belgium, France, Japan, Sweden, the UK and the USA. The body weights of adults and children aged $\leq$ 6 years were provided to GEMS/Food by the governments of Australia, France, the Netherlands, South Africa, Thailand, 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[27]. The documents are dated April, 2008 (large portions and body weights) and May, 2003 (unit weights). The procedures used for calculating the International estimated short-term intake (IESTI) are described in detail in Chapter 3 of the 2003 JMPR report. Detailed guidance on setting ARfD is described in Section 2.1 of the 2004 JMPR report[28].

On the basis of data received by the present or previous Meetings, JMPR considered the establishment of an ARfD to be unnecessary for boscalid, chlorantraniliprole, hexythiazox, metaflumizone, spirodiclofen and zoxamide. Therefore, it was not necessary to estimate the short-term intakes for these compounds.

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

[27] http://www.who.int/foodsafety/chem/acute_data/en/

[28] Pesticide Residues in Food–2004. Report of the JMPR 2004, FAO Plant Production and Protection Paper 178. Rome, Italy, 20–29 September 2004

Bifenthrin, cadusafos, chlorothalonil and cycloxydim were evaluated for toxicology at this Meeting under the Periodic Re-evaluation Programme and ARfDs were allocated. The short-term dietary risk assessment for these compounds will be considered during the periodic review for residues at subsequent Meetings.

The outcome of the evaluation of fenthion, methomyl, prochloraz, procymidone and spirotetramat performed at this Meeting was such that it was not necessary to undertake short-term dietary intake assessments.

The short-term intake of fenbuconazole was estimated by the present Meeting, however the need of an ARfD has yet not been considered by the JMPR. Therefore, the risk assessment for this compound was not finalised.

The short-term intakes as percentages of the ARfDs for the general population and for children are summarized in Table 4. The detailed calculations of short-term dietary intakes are given in Annex 4.

Table 4 Summary of short-term dietary risk assessments conducted by the 2009 JMPR

CCPR code	Compound Name	ARfD (mg/kg bw)	Commodity	Percentage of ARfD	
				General population	Children aged ≤ 6 years
155	Benalaxyl	0.1 [a]	all	0-4 [a]	NR
173	Buprofezin	0.5	all	0-30	0-50
096	Carbofuran	0.001	Banana Mandarin Orange	80 20 30	150 40 60
090	Chorpyrifos-methyl	0.1	all	0-10	0-30
157/228	Cyfluthrin/beta-cyfluthrin**	0.04	Cabbages, Head	100	240
118	Cypermethrin (includes alpha and zeta cypermethrin)	0.04	all	0-20	0-40
194	Haloxyfop & Haloxyfop-P	0.08	all	0-10	0-10
216	Indoxacarb	0.1	Lettuce, Leaf Others	60 0-10	150 0-20
235	Fluopicolide 2,6-dichlorobenzamide (M-01)	0.6 [a] 0.6	All all	0-70[a] 0-1	NR 0-2
209	Methoxyfenozide	0.9	all	0-2	0-6
057	Paraquat	0.006	rice	0	0
142	Prochloraz	0.1	Mushrooms	7	10
112	Phorate	0.003	Potatoes	80	190
232	Prothioconazole Prothioconazole- desthio	1 0.01 [a]	all all	0-0.2 0-20[a]	0-0.2 NR
133/168	Triadimefon/triadimenol**	0.08	Grapes	80	220

[a] For women of childbearing age;

** from previous meeting

NR: not required

Possible risk assessment refinement when IESTI exceeds the ARfD

Carbofuran in banana

The Meeting noted that the short-term dietary risk assessment of bananas could be refined if a metabolism study on bananas or residue trials employing a very sensitive analytical method were

available. The ARfD was reviewed by the present Meeting due to a request by the CCPR (Chapter 3.2). The ARfD of 0.001 mg/kg bw was confirmed and it is unlikely that it could be refined

Cyfluthrin/beta-cyfluthrin in head cabbages

Alternative GAP was considered by the present Meeting, but the previous HR recommendation was confirmed due to insufficient residue data. Hence, a refinement of the IESTI was not possible with the current data. The Meeting established a group ARfD for cyfluthrin and beta-cyfluthrin in 2006 based on acute neurotoxicity observed in a 4 week study in rats and a safety factor of 25 and it is unlikely that this could be refined.

Indoxacarb in leaf lettuce

The Meeting noted that leaf lettuce is consumed as a raw commodity and there is no alternative GAP available for this crop. Hence, a refinement of the IESTI is not possible with the current data. Furthermore, the ARfD was set based on a single-dose study by the JMPR in 2005 and it is unlikely that it could be refined.

Phorate in potato

The Meeting noted that the intake estimation is already based on residues in processed potatoes, leaving little room for refinement. Furthermore, the ARfD established by the 2004 Meeting was based on a single-dose study in rats and therefore it is unlikely that it could be refined.

Triadimefon/triadimenol in grapes

Alternative GAP was reconsidered by the present Meeting, with the previous HR recommendation confirmed. As a consequence, a refinement of the IESTI assessment was not possible with the current data. The Meeting noted that although the ARfD is based on a study of acute neurotoxicity in rats given triadimefon and a safety factor of 25, the large dose spacing between the NOAEL and the LOAEL suggests possibility of a refinement of the ARfD (e.g., by benchmark dose calculations).