CONTENTS

[1] T, toxicological evlauation; R, residue and analytical aspects; D, dietary risk assessment
* New compound
** Evaluated within the periodic review programme of the Codex Committee on Pesticide Residues

List of participants

2001 Joint FAO/WHO Meeting on Pesticide Residues
Geneva, 20–29 September 2001

WHO Members[2]

Professor Alan R. Boobis, Section on Clinical Pharmacology, Division of Medicine, Faculty of Medicine, Imperial College, Hammersmith Campus, Ducane Road, London W12 0NN, United Kingdom *(WHO Rapporteur)*
Tel: (44 20) 8383 3221; Fax: (44 20) 8383 2066; E-mail: a.boobis@ic.ac.uk

Professor Bingheng Chen, School of Public Health, Shanghai Medical University, 138 Yixueyuan Road, Shanghai, 200032 China
Tel: (86 21) 641 63 061 (home); Fax: (86 21) 641 63 061 (home); E-mail: bhchen@shmu.edu.cn / bhchen98@yahoo.com

Dr Angelo Moretto, Dipartimento Medicina Ambientale e Sanità Pubblica, Università di Padova, via Giustiniani 2, 35128 Padova, Italy *(Chairman)*
Tel: (39 049) 821 1377 / 2541; Fax: (39 049) 821 2550; E-mail: angelo.moretto@unipd.it

Dr Brian G. Priestly, Scientific Director, Chemicals & Non-Prescription Medicines Branch, Therapeutic Goods Administration, Commonwealth Department of Health and Aged Care, PO Box 100, Woden, ACT 2606, Australia
Tel: (61 2) 6270 4301; Fax: (61 2) 6270 4411; E-mail: brian.priestly@health.gov.au

FAO Experts

Dr Ursula Banasiak, Federal Biological Research Centre for Agriculture and Forestry, Stahnsdorfer Damm 81, D-14532 Kleinmachnow, Germany
Tel: (49 33203) 48338; Fax: (49 33203) 48425; E-mail: u.banasiak@bba.de

Dr Eloisa Dutra Caldas, Central Laboratory of Public Health of the Federal District, SGAN ad 601 Bl. O/D, 70.830-010 Brasilia / DF, Brazil *(FAO Rapporteur)*
Tel: (55 61) 316 9824 / 316 9825; Fax: (55 61) 321 9995; E-mail: eloisa@unb.br

Dr Stephen Funk, Health Effects Division (7509C), Environmental Protection Agency, 1200 Pennsylvania Avenue, NW, Washington, DC 20460, USA
Tel: (1 703) 305 5430; Fax: (1 703) 305 5147 / 5529; E-mail: funk.steve@epa.gov

Mr Denis J. Hamilton, Animal and Plant Health Service, Department of Primary Industries, Ann Street, Brisbane, QLD 4001, Australia *(Vice-Chairman)*
Tel: (61 7) 3239 3409; Fax: (61 7) 3211 3293; E-mail: hamiltdj@dpi.qld.gov.au

[2] Unable to attend: Dr Helen Häkansson, Institute of Environmental Medicine, Karolinska Institutet, Division of Risk Assessment and Organohalogen Pollutants, Box 210, S-171 77 Stockholm, Sweden
Tel: (46 8) 728 75 27; Fax: (46 8) 33 44 67; E-mail: Helen.Hakansson@imm.ki.se

Dr Bernadette C. Ossendorp, Centre for Substances and Risk Assessment, National Institute of Public Health and the Environment (RIVM), Antonie van Leeuwenhoeklaan 9, PO Box 1, 3720 BA Bilthoven, The Netherlands
Tel: (31 30) 274 3970; Fax: (31 30) 274 4401; E-mail: bernadette.ossendorp@rivm.nl

Secretariat

Dr Arpàd Ambrus, Head, Agrochemicals Unit, Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture, International Atomic Energy Agency, Wagramer Strasse 5, PO Box 100, 1400 Vienna, Austria
Tel: (43 1) 2600 28395; Fax: (43 1) 26007 28222; E-mail: a.ambrus@iaea.org

Dr Maria Cristina Alonzo Romanelli, Departamento de Salud Ambiental y Seguridad Quimica, Ministerio de Salud Publica, Avenida 18 de Julio 1892, 4to piso, Anexo B, Montevideo, Uruguay (*WHO Temporary Adviser)*
Tel: (598 2) 409 8302; Fax: (598 2) 409 7230; E-mail: aloncris@adinet.com.uy

Dr Andrew Bartholomaeus, Therapeutic Goods Administration, Commonwealth Department of Health and Aged Care, PO Box 100, Woden, ACT 2602, Australia (*WHO Temporary Adviser)*
Tel: (61 2) 62 70 43 72; Fax: (61 2) 62 70 43 53; E-mail: andrew.bartholomaeus@health.gov.au

Dr Ian C. Dewhurst, Pesticides Safety Directorate, Mallard House, King's Pool, 3 Peasholme Green, York YO1 7PX, United Kingdom (*WHO Temporary Adviser)*
Tel: (44 1904) 455 890; Fax: (44 1904) 455 711; E-mail: ian.dewhurst@psd.defra.gsi.gov.uk

Dr Wim H. van Eck, Chairman, Codex Committee on Pesticide Residues, Division of Public Health, Ministry of Health and Welfare and Sport, PO Box 20350, 2511 VX Den Haag, The Netherlands (*WHO Temporary Adviser)*
Tel: (31 70) 340 69 66; Fax: (31 70) 340 55 54; E-mail: wh.v.eck@minvws.nl

Dr Hend Galal-Gorchev, Environmental Health Inc., 4701 Willard Avenue, Suite 506, Chevy Chase, MD 20815-4613, USA (*WHO Temporary Adviser)*
Tel: (1 301) 951 8305; Fax: (1 301) 951 8307; E-mail: Galalgorch@aol.com

Dr John L. Herrman, International Programme on Chemical Safety, World Health Organization, 1211 Geneva 27, Switzerland *(WHO Joint Secretary)*
Tel: (41 22) 791 3569; Fax: (41 22) 791 4848; E-mail: herrmanj@who.int

Mrs Elisabeth. Heseltine, Communication in Science, Lajarthe, 24290 Saint-Léon-sur-Vézère, France *(Editor)*
Tel: (33 553) 50 73 47; Fax: (33 553) 50 70 16; E-mail: heseltin@club-internet.fr

Mrs Paula H. van Hoeven-Arentzen, Centre for Substances and Risk Assessment, National Institute of Public Health and the Environment, Antonie van Leeuwenhoeklaan 9, PO Box 1, 3720 BA Bilthoven The Netherlands (*WHO Temporary Adviser)*
Tel: (31 30) 274 32 63; Fax: (31 30) 274 4401; E-mail: paula.van.hoeven@rivm.nl

Mrs Fatoumata Jallow-NDoye, National Environment Agency, PMB 48, Banjul, The Gambia (*WHO Temporary Adviser)*
Tel (220) 223 206 / 228 056 / 224 867; Fax: (220) 229701; E-mail: nea@gamtel.gm / fjndoye@qanet.gm

Dr Dugald MacLachlan, Australian Quarantine and Inspection Service, Department of Agriculture, Forestry and Fisheries, Australia, Edmond Barton Building, Kingston, ACT 2604, Australia *(FAO Consultant)*
Tel: (61 2) 6272 3183; Fax: (61 2) 6272 3551; E-mail: dmaclach@affa.gov.au

Dr Timothy C. Marrs, Food Standards Agency, Room 504C, Aviation House, 125 Kingsway, London WC2B 6NH, United Kingdom (*WHO Temporary Adviser)*
Tel: (44 207) 276 8507; Fax: (44 207) 276 8513; E-mail: tim.marrs@foodstandards.gsi.gov.uk

Dr Jeronimas Maskeliunas, Food Standards Officer, Joint FAO/WHO Food Standards Programme, Food and Nutrition Division, Food and Agriculture Organization of the United Nations (FAO), viale delle Terme di Caracalla, 00100 Rome, Italy *(FAO Food Standards Officer)*
Tel: (39 06) 510 3967; Fax: (39 06) 570 54593; E-mail: Jeronimas.Maskeliunas@fao.org

Dr Gerald Moy, Food Safety Programme, World Health Organization, 1211 Geneva 27, Switzerland
Tel: (41 22) 791 3698; Fax: (41 22) 791 4807; E-mail: moyg@who.int

Dr Samuel W. Page, International Programme on Chemical Safety, World Health Organization, 1211 Geneva 27, Switzerland
Tel: (41 22) 791 3573; Fax: (41 22) 791 4848; E-mail: spage@who.int

Dr Roland Solecki, Pesticides and Biocides Division, Federal Institute for Health Protection of Consumers and Veterinary Medicine, Thielallee 88-92, D-14195 Berlin, Germany (*WHO Temporary Adviser)*
Tel: (49 188) 8412 3827; Fax: (49 188) 8412 3260; E-mail: r.solecki@bgvv.de

Dr Atsuya Takagi, Department of Toxicology, National Institutes of Health Sciences, 1-18-1, Kamiyoga, Setaga, Tokyo 158, Japan (*WHO Temporary Adviser)*
Tel: (81 3) 3700 1141 (ext 406); Fax: (81 3) 3700 9647; E-mail: takagi@nihs.go.jp

Dr Amelia Tejada, Pesticide Management Group, Plant Protection Service, Plant Production and Protection Division, Food and Agriculture Organization of the United Nations (FAO), Viale delle Terme di Caracalla, 00100 Rome, Italy (*FAO Joint Secretary)*
Tel: (39 06) 570 54010; Fax: (39 06) 570 56347; E-mail: Amelia.Tejada@fao.org

Dr Gero Vaagt, Pesticide Management Group, Plant Protection Service, Plant Production and Protection Division, Food and Agriculture Organization of the United Nations (FAO), Viale delle Terme di Caracalla, 00100 Rome, Italy
Tel: (39 06) 570 55757; Fax: (39 06) 570 56347; E-mail: Gero.Vaagt@fao.org[1]

Dr Christiane Vleminckx, Toxicology Division, Scientific Institute of Public Health, Ministry of Social Affairs, Public Health and Environment, Rue Juliette Wytsman, 16, B-1050 Brussels, Belgium (*WHO Temporary Adviser)*
Tel: (32 2) 642 5351; Fax: (32 2) 642 5224; E-mail: c.vleminckx@iph.fgov.be

Dr Yukiko Yamada, Director for International Affairs (Food Research), Research Planning and Coordination Division, National Food Research Institute, 2-1-12 Kannondai, Tsukuba 305-8642 , Japan *(FAO Consultant)*
Tel: (81 298) 38 8017; Fax: (81 298) 38 8005; E-mail: yamadayk@nfri.affrc.go.jp

[1] Attended the pre-meeting of the FAO Panel of the JMPR on 16 September 2001

Abbreviations

*	at or about the limit of quantification
ADI	acceptable daily intake
ai	active ingredient
AUC	area under the curve for concentration–time
bw	body weight
CCN	Codex classification number (for compounds or commodities)
CCPR	Codex Committee on Pesticide Residues
CXL	Codex level
2,4-D IPE	(2,4-dichlorophenoxy)acetic acid isopropyl ester
DT_{50}	time to 50% decomposition
DT_{90}	time to 90% decomposition
ECD	electron capture detection
F	fat
F_1	first filial generation
F_2	second filial generation
FAO	Food and Agricultural Organization of the United Nations
GAP	good agricultural practice
GC	gas chromatography
GLC	gas–liquid chromatography
GPC	gel-permeation chromatography
GEMS/Food	Global Environment Monitoring System–Food Contamination Monitoring and Assessment Programme
GSH	glutathione
HPLC	high-performance liquid chromatography
HR	highest residue in the edible portion of a commodity found in trials used to estimate a maximum residue level in the commodity
HR-P	highest residue in a processed commodity calculated by multiplying the HR of the raw commodity by the corresponding processing factor
IARC	International Agency for Research on Cancer
IEDI	international estimated daily intake
IESTI	international estimate of short-term dietary intake
JECFA	Joint Expert Committee on Food Additives
JMPR	Joint Meeting on Pesticide Residues
LC	liquid chromatography
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
MDL	method detection limit
MLD	minimum level of detection
MRL	maximum residue limit
MS	mass spectrometry
MS/MS	tandem mass spectrometry
NOAEL	no-observed-adverse-effect level
NPD	nitrogen–phosphorus detector
OECD	Organization for Economic Co-operation and Development
PF	processing factor

PHI	pre-harvest interval
P_{ow}	octanol–water partition coefficient
RfD	reference dose
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
TRR	total radiolabelled residue
TMDI	theoretical maximum daily intake
UV	ultraviolet radiation
W	the previous recommendation is withdrawn
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 owener of the data submitted for the JMPR review or has received the dat 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 2001 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 17 to 26 September 2001. The FAO Panel of Experts had met in preparatory sessions from 12 to 16 September.

The Meeting was opened by Dr R. Helmer, Director of the WHO Department of Protection of the Human Environment, on behalf of the Directors General of FAO and WHO. Dr Helmer noted that the Meeting will be considering a number of important issues, among the most important being acute risk assessment, in addition to the evaluation of a large number of pesticides. He also noted that FAO and WHO were initiating a project to update and consolidate the principles of risk assessment for the toxicity, intake, residues, and specifications, as appropriate, for pesticides, veterinary drugs, food additives, and contaminants. This will be a comprehensive project that will provide an opportunity to harmonize approaches across all classes of chemicals in food. Dr Helmer also reminded the participants that they were invited to the Meeting in their personal capacities as international experts, with the responsibility of serving and advising the two specialized agencies of the United Nations, and *not* as representatives of their governments, institutes, or any other organizations.

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 ADIs where possible.

The Meeting evaluated 26 pesticides, including four new compounds and seven compounds that were re-evaluated within the periodic review programme of the Codex Committee on Pesticide Residues (CCPR) for toxicology 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).

2. GENERAL CONSIDERATIONS

2.1 Further issues related to establishing an acute reference dose

The Joint Meeting has considered on several occasions how and when to establish an acute reference dose (RfD) and has established such values for a number of pesticides since 1995. The basic principle, that the establishment an acute RfD should be considered on a case-by-case basis for all compounds evaluated by the JMPR, was reaffirmed at the current and at previous Meetings.

Guidelines for assessing acute dietary risks, including guidelines on establishing acute RfDs, are being developed concurrently in a number of regulatory jurisdictions. The current Meeting considered a national Dutch guidance document[1] and a draft guidance document, which is being jointly developed by all Member States of the European Union[2], accompanied by brief informative presentations, which summarized recent developments in Europe for the establishment of acute RfDs for pesticides. It was noted that the European guidance documents acknowledged the work done by the JMPR and that there is much commonality in the guidelines being developed. The Meeting stressed the importance of continuing to work cooperatively with such agencies in developing a common approach to establishing acute RfDs.

The current Meeting considered further issues related to establishing acute RfDs.

Toxicological alerts and criteria for not establishing an acute RfD

The 2000 Joint Meeting developed guidance on the types of toxicological alerts that would suggest the need for establishing an acute RfD. By inference, the absence of such alerts in adequately conducted studies should be considered justification for not establishing an acute RfD, although the Meeting has always recognized that the basis for such a decision must be explicitly stated.

The current Meeting addressed the issue of whether specific cut-off values can be applied to relevant NOAELs in assessing whether a pesticide is of sufficiently low toxicity to justify a decision not to establish an acute RfD. It considered that this approach has merit, but that there should be extensive consultation on what constitutes acceptable cut-off values.

The Meeting reaffirmed its previous position that the estimated potential intake of relevant residues should not influence a decision on whether to set an acute RfD. However, the draft European Union guidance document and the present Meeting raised the issue that an acute RfD might not be necessary for some pesticide uses (e.g. soil fumigation, rodenticide), even for acutely toxic pesticides, because of the minimal potential for residues to be left in food.

Suitability of databases

In recognition of the fact that current toxicological databases may not include studies that are particularly suitable, or relevant, for establishing an acute RfD, the 2000 Meeting developed draft guidance for testing and interpreting the results of tests, when necessary. The current Meeting also noted that the European guidance documents generally address the types of studies and end-points that might be suitable for allocating an acute RfD.

The Meeting further noted that the nature of the database available for a particular pesticide may result in the establishment of an acute RfD on the basis of relatively conservative assumptions. For

---

[1] M.T.M. van Raaij (2001) *Guidance document for setting an Acute Reference Dose in Dutch national pesticide evaluations*. RIVM report no. 620555002. National Institute of Public Health and the Environment (RIVM), Bilthoven, the Netherlands (document can be ordered or downloaded from www.rivm.nl/bibliotheek/rapporten/620555002.html).

[2] European Commission (2001) *Guidance for the setting of an Acute Reference Dose (ARfD).* Draft guidance document (7199/VI/99 rev. 5 of 05/07/2001), DG SANCO.

example, certain toxicological end-points such as haematotoxicity and hepatotoxicity observed at the end of a 28-90-day study might conceivably be observed after acute exposure. In such cases, and in the absence of any early or interim observations, the NOAEL identified in the study might be used to establish an acute RfD, even though it may not be appropriate for an acute effect. The value of the acute RfD for chlorpropham established by the 2000 JMPR illustrates the conservatism that can be introduced by such considerations. The Meeting reaffirmed that conservatism is necessary in such cases, but a statement should be made that the assessment of acute dietary risk might require refinement of the acute RfD by new studies that more appropriately address the end-point of concern.

Human studies

The implications of using an end-point from an appropriately conducted study in humans was considered. The Meeting reaffirmed the principle that such studies could be used if they had been conducted in accordance with relevant ethical guidelines. However, it was recognized that the designs of human studies have some limitations in comparison with those in experimental animals, and that their use should always be considered in the context of the total toxicological database. For example, it was recognized that studies involving only men or only women might be inappropriate for establishing an acute RfD that would protect the whole population if the available data from experimental animals suggested that significant sex differences in toxicity exist. The consideration given to the allocation of an acute RfD for diazinon at the current Meeting is a case in point.

The Meeting also reaffirmed that acute RfDs, and ADIs, based on studies in humans should provide a sufficient margin of safety for toxicological end-points that cannot readily be addressed by such studies (e.g. developmental toxicity), and that the descriptions of the experimental studies should indicate where such potential exists.

Safety factors

Both the European guidance documents and the JMPR have recognized that the default safety factor of 100 may not always be the most suitable for application to the NOAEL in studies of single doses. The Meeting also concluded that use of smaller safety factors may be appropriate for pesticides whose acute toxicity is likely to be related to peak concentration (C_{max}), rather than to the area under the curve (AUC) of blood concentration versus time. This principle was followed when the JMPR considered acute RfDs for methomyl and carbaryl at its current Meeting, and for thiodicarb at the 2000 Meeting. The scientific principles that underpin the selection of safety factors other than the default 100 were outlined in detail in Annex 5 to the 2000 JMPR report and in an IPCS report (IPCS, 2001).[1] The key assumption is that acute toxic effects which are associated with rapid absorption and/or elimination and which are rapidly reversible (as with some carbamates) is likely to depend on the C_{max} achieved in blood, and that this shows less inter-species and inter-individual variation than clearance or the AUC.

Should an ADI be established at a level higher than the acute RfD?

The Meeting addressed the conceptual problem posed when the NOAEL for the relevant end-point for acute toxicity results in a derived acute RfD which is lower than the ADI for that pesticide. For example, for two of the carbamates evaluated by the current Meeting, the NOAELs for the same toxicological end-point (brain acetylcholinesterase inhibition) in rodents were higher after repeated dietary intake (possible basis for establishing the ADI) than after a single gavage (possible basis for establishing the acute RfD). This is due to both the rapid reversibility of the inhibition of acetylcholinesterase activity by carbamates (i.e. inhibition does not increase with repeated doses) and the rapid absorption and elimination of these compounds. For these reasons, the same daily dose of a carbamate may inhibit brain acetylcholinesterase activity when it is given as a single bolus dose (gavage)

[1] IPCS (2001) Guidance document for the use of data in development of chemical-specific adjustment factors for interspecies difference and human variability. Available online at http://www.ipcsharmonize.org/index.html.

but may have no effect when administered either in the diet, where intake occurs over many hours, or in several doses. After gavage, the C_{max} in plasma and brain is high enough to inhibit acetylcholinesterase, the AUC being the same as after dietary intake. Although the Meeting was aware of the toxicological plausibility of these findings, it considered that, when NOAELs from studies in rodents are used, those seen after gavage are the most appropriate for establishing both the ADI and the acute RfD for carbamates with rapid toxicokinetics, when inhibition of acetylcholinesterase is the end-point of concern.

The Meeting noted that a further complication arises from differences in the way that acute and long-term dietary intakes are estimated. The pattern of human food intake is characterized by two to three short periods of intake per day, but the data used to calculate acute dietary intake cover a single day's intake and it is impossible to separate the contribution of a given meal. The Meeting therefore noted that the current definition of the acute RfD, which envisages comparison with consumption either at a single meal or over a whole day, should be re-addressed in the light of this problem.

Taking all these factors into account, the present Meeting established the ADI for methomyl at the same level as the acute RfD, although the toxicological data might have allowed the ADI to be set at a higher level.

Further guidance

For further consideration of these issues and to continue making progress, the Meeting recommended that WHO establish a working group, consisting of scientists who have developed the concepts of the acute RfD at JMPR, in national governments, and in the European Commission.

The working group should develop a working paper for consideration by the 2002 JMPR. The working paper should build on the experience that has been gained, emphasize the general agreement that has been reached among the various groups involved, and provide proposals for further guidance.

The issues which may need to be considered include the following:

- definition of the acute RfD;
- the types of end-points (effects relevant for a single exposure) that suggest the need for establishing an acute RfD;
- consideration of a cut-off value for not establishing an acute RfD and the appropriate size of the cut-off value;
- consideration of an upper limit for an acute RfD;
- development of a decision tree (to promote consistency);
- establishment of the size of default safety factors, including the situation in which acute toxicity is more likely to be related to peak concentration than to the AUC;
- possible intake scenarios and relevant toxicity tests to mimic them;
- strategies for developing test guidelines and improving databases for assessing acute intake;
- proposals for interim measures to be used until relevant toxicity studies have been performed;
- appropriate use of human studies;
- appropriateness of establishing the ADI at a level higher than the acute RfD, and the risk management and risk communication implications
- the risk assessment, risk management, and risk communication implications of establishing more than one acute RfD for sensitive subgroups; and
- an inventory of acute RfDs that have been established by JMPR and other scientific bodies and their bases, which will highlight areas in which harmonization can be improved.

2.2 Sharing the work of agricultural pesticide reviews

Governments invest significant resources in evaluating agricultural pesticides before they are marketed, to ensure that they do not pose unacceptable risks to human health and the environment. They also re-

evaluate pesticides that have been in use for many years to be sure that they meet current scientific and safety standards. International organizations like FAO and WHO are also involved in assessing the safety of pesticides, and other compounds, for the purpose of setting Codex standards for the protection of consumer health and the promotion of fair practices in international trade. Governments and international organizations have recognized the substantial benefits that can in principle accrue if the task of pesticide evaluation is shared, rather than work being duplicated. Improved efficiency in pesticide evaluations is important in light of limited, ever-diminishing resources, while at the same time there is increased pressure on governments and international organizations to speed up the process of reviewing pesticides and to make their decisions more quickly.

Background

A workshop on sharing the work of agricultural pesticide reviews, organized by the OECD and co-hosted by the Commission of the European Union and the Environmental Protection Agency of the USA, was held in Brussels on 12–14 February 2001. The participants were unanimous that work was already occasionally being shared and that the process had improved both the consistency and the quality of reviews. Now is the time to change work sharing and to identify specific projects and goals so that active progress can be made. Efficient communication, planning and commitment are essential to establishing work sharing. Thus, the schedules and proposed activities of the various groups must be shared, and a proactive approach should be taken to work sharing.

In this context, 'work sharing' means dividing the work of reviewing a submission on a pesticide among two or more reviewers in different national or regional authorities or international organizations, each referring to the other's evaluation in making its review, while respecting the right of each country or organization to finalize its own risk assessment and to make its own regulatory decision. The objective of work sharing is to reduce the workload. It should result in an assessment of similar or higher quality. The ultimate goal of work sharing is globalization of pesticide reviews.

Countries of the OECD, through the OECD Working Group on Pesticides, have been working together since 1992 to harmonize regulatory approaches to pesticide registration. The work has included the development and implementation of common formats for submissions of data from industry ('dossiers') and reviews from governments ('monographs')[1] as well as harmonization of data requirements, test guidelines and risk assessment methods. As a result, there is now a basis for countries and organizations to share work on evaluating submissions on new and existing active substances of pesticides.

The Meeting welcomed the activities of the OECD and took note of the conclusions and recommendations of the above-mentioned workshop. It recognized the value of work sharing as a means of reducing the workload of FAO and WHO Panel Members. Nevertheless, the Meeting considered that, before work sharing could be accepted on a routine basis in the work of JMPR, technical, scientific and political conditions would have to be elaborated.

The Meeting recognized that harmonization of procedures between JMPR, OECD and national governments is a prerequisite for successful implementation of the principle of work sharing at the international level.

[1] Guidance documents are available on the OECD website at http://www.oecd.org/ehs/PestGD01.htm

Pilot project

The availability of national and regional evaluations in a standard format should facilitate the work of the expert groups that make up the FAO/WHO Joint Meeting on Pesticide Residues. The JMPR cannot, however, accept a national or regional pesticide evaluation uncritically. Moreover, an evaluation of data on residues at the international level inevitably follows different rules from a review at the national level. The JMPR considers worldwide data derived from Good Agricultural Practice (GAP) and on residues, and establishes MRLs, STMRs and HRs that may be different from those established in regional or national reviews. The parts of an evaluation that should in principle not pose problems for general or mutual use include those on toxicology, plant and animal metabolism, animal feeding, physico-chemical data and processing. Work sharing should focus on these components of an evaluation.

The Meeting welcomed the implementation of a formal pilot project on work sharing at the international level, in which differences and similarities between current procedures and approaches to toxicological and residue evaluations used by JMPR, OECD and national governments should be identified. It should include comparisons of formats, data requirements and risk assessment methods. Attention should be given to data confidentiality and its consequences for work sharing. Due attention should also be given to the question of whether work sharing should rely on officially approved evaluations only. The aim of the pilot project should be to identify any potential problems that would require further harmonization and to estimate the practical costs and the saving of time that could be expected. The Meeting recommended that one or two active substances be identified for evaluation as a test of work sharing and that the pilot project should be carried out as soon as possible, preferably in 2002. Experts from JMPR, OECD and national governments should be invited to participate in the project.

The Meeting was aware of experiences in work sharing at bilateral and regional levels during the past several years. It considered that formalization of work sharing at the international level would not be an easy exercise from which quick results could be expected. The proposed pilot project and subsequent steps should therefore be carefully planned. The pilot project should not be funded from the budgets available for regular JMPR activities.

The Meeting noted that not only technical and scientific aspects but also political issues are associated with the formalization of work sharing. It considered that the the CCPR should reflect at an early stage on the consequences of work sharing for the elaboration and adoption of Codex standards for pesticide residues in the long run.

The Meeting considered that harmonization of data requirements and standardization of formats would also facilitate the submission of dossiers by industry and ultimately make it easier for national governments to accept the assessments underlying the recommendations of JMPR.

The Meeting looked forward to publication of the final OECD Minimum Data Requirements for Establishing Maximum Residue Limits, to facilitate work sharing between JMPR and national governments or regional organizations. JMPR will follow with interest the discussions on items that are still in abeyance, such as the climate zoning project and extrapolation of the behaviour of residues between crops, and will contribute to such discussions in order to achieve agreement at the international level.

Coordination of evaluation programmes

A further point of concern is coordination of the timing of reviews. Improved coordination is needed in setting priorities for compounds to be reviewed. The scheduling of national and regional

evaluations and the availability of data to be submitted by their owners should be taken into consideration by the CCPR in setting priorities and by JMPR in scheduling the evaluation of new compounds and those for periodic review. Currently, data owners probably have the best view of the scheduling of reviews of pesticides by governments and at the regional or international level.

Recommendations

- The Meeting recommended that FAO and WHO implement a pilot project on work sharing in the evaluation of pesticides at the international level in close cooperation with the OECD, national governments and regional and sub-regional authorities.
- The Meeting recommended that the CCPR examine the implications of work sharing for the elaboration and adoption of MRLs for pesticide residues.
- The Meeting recommended that the CCPR, when setting priorities for review of pesticides by JMPR, take account of the scheduling of compounds for review at the national and regional levels.

2.3 Numerical expression of residue limits

The JMPR[1] in 1988 provided guidelines on the expression of residue limits and proposed to adopt the following scale for the numerical expression of the limits: 0.01, 0.05, 0.1, 0.2, 0.5, 1, 2, 3, 5, 10, 15, 20 and 30 mg/kg. The *FAO Manual* (FAO, 1997) expanded the scale to: 0.01, 0.02, 0.05, 0.1, 0.2, 0.5, 1, 2, 3, 5, 10, 15, 20 30, 50 and 100 mg/kg, and stated that other values could be used if necessary for special reasons.

The scale has generally been followed since, but experience has shown the need to insert other values on occasion, when 'rounding up' to the standard scale appears excessive. In particular, there has been the need to use 0.03, 0.3 and 7 mg/kg.

The Meeting recommended the adoption of a standard 1, 2, 3, 5, 7 system for residue values up to 10 mg/kg, i.e. 0.01, 0.02, 0.03, 0.05, 0.07, 0.1, 0.2, 0.3, 0.5, 0.7, 1, 2, 3, 5, 7 and 10 mg/kg. For higher values, recommendations of 15, 20 and 25 mg/kg have been found useful, and, above these values, rounding to the next 10, i.e. 30, 40, 50, etc, is preferred. The option to use other values as necessary should be maintained.

2.4 JMPR requirements for certain components of periodic re-evaluations

At its 33rd Session (ALINORM 01/24a, 2001, para 217), the CCPR requested JMPR to review its requirements for periodic re-evaluation when certain components of the re-evaluation have not changed (such as analytical methods or studies on metabolism). The Meeting understood that the intention of the request was to suggest that studies that have been reviewed recently need not be re-evaluated during a periodic review if they have been found satisfactory, in order to reduce the workload of JMPR.

JMPR attempts to do this when practical. For example, when folpet was reviewed in 1997, the review included information on metabolism, analytical methods and stability under freezer storage. When folpet was reviewed in the periodic review programme in 1998, it was agreed that the 1997 review would be included in the 1998 periodic review for the sake of completeness.

Reviews made many years previously are generally not particularly useful, because JMPR practices have evolved over time: more information is now extracted, and the evaluations are more detailed. The

[1] JMPR 1988. 2.7 Expression of residue limits.

importance and relevance of studies may also differ with time; for example, analytical methods for residues in animal commodities are unimportant until MRLs for those commodities are needed.

The Meeting agreed that in some circumstances recent reviews of studies could be carried over to periodic reviews, but it requested data submitters to provide all relevant studies unless they had prior written permission from the FAO and WHO Secretaries to withhold studies that had already been reviewed.

2.5 Estimation of maximum residue levels and supervised trials median residue values for commodities of animal origin

Residues in animal commodities (meat, milk and eggs) may arise from consumption by farm animals of feed items containing residues or from direct application of a pesticide onto the animal to control pests such as ectoparasites. Methods for estimating maximum residue levels in animal commodities have recently been improved, and the explanations in reports have become more detailed. The data can be used in many ways, and the procedure used may depend on the availability of data. The procedures described in this report are based on recent cases and particularly on the data on compounds reviewed in 2001. The Meeting anticipated that other cases will occur in which of the current procedures will have to be amended.

Residues arising from consumption of feed items

In 1986, JMPR[1] explained the use of data from studies of animal transfer (farm animal feeding studies) in the estimation of MRLs in foods of animal origin. It emphasized that judgement should be used in establishing the expected level of ingestion. The Meeting in 1986 considered that it was unrealistic to assume that the theoretical maximum residue level would be achieved and maintained in the rations of food-producing animals receiving feeds produced on a farm or mixed feeds produced from commercially available ingredients.

The 1997[2] and 1998[3] Meetings elaborated the principles of estimating maximum residue levels and STMR values for commodities of animal origin. The 1997 Meeting made a distinction between situations in which the plateau of residue levels in milk or eggs is reached rapidly and those in which it is reached slowly in a study with repeated doses, and recommended the following procedure for estimating maximum residue levels and STMR values:

	Residue reaches plateau rapidly		Residue reaches plateau slowly	
	Maximum residue level	STMR	Maximum residue level	STMR
Feed item residue level	MRL	STMR	STMR	STMR
Feed incorporation rate	Maximum	Maximum	Maximum	Maximum
Feeding study residue level[a]	Highest	Mean	Highest	Mean

[a] Highest and mean refer to residue levels in the tissues and milk of the relevant group of animals in the feeding study.

[1] JMPR Report 1986. 2.7 Animal transfer studies and the estimation of MRL values in foods of animal origin.
[2] JMPR Report 1997. 2.4 The estimation of maximum residue and STMR levels for products of animal origin when residues are transferred from feed items.
[3] JMPR Report 1998. 2.5 The estimation of STMRs and maximum residue levels for commodities of animal origin - worked examples.

The 1998 JMPR prepared a worked example for estimation of residues in milk and applied the highest transfer factor, obtained from the highest feeding level, representing about nine times the calculated maximum daily intake of dairy cows. (Transfer factor = residue concentration in milk or tissue ÷ residue concentration in diet.)

In the evaluations made by the 1998, 1999 and 2000 Meetings, the principle was applied on a case-by-case basis to consolidate the procedure for estimation of residues. The present Meeting evaluated the experience gained and agreed on application of the following procedure for estimating maximum residue levels and STMR values. The procedure is demonstrated in a worked example.

***Estimation of dietary burden of animals*:**

(a) The maximum percentage of various commodities in animal feed is taken from Appendix IX of the *FAO Manual*.
(b) All feed items and their corresponding residue levels, expressed on a dry weight basis, are listed.
(c) The list of feed items that contribute to the dietary burden of residues in farm animals are chosen in such a way as to give the highest dietary burden.
(d) For compounds that reach the residue plateau in milk or eggs rapidly, the residue contribution of a feed commodity to the maximum residue level is calculated from the percentage of the diet and the estimated MRL, or the highest residue when no MRL is recommended, for raw agricultural commodity feed items. For processed commodities, e.g. apple pomace, that are likely to originate from a number of farms, the STMR of the processed commodity (STMR-P) is chosen as the highest residue that would probably occur in practice.
(e) For compounds that reach the residue plateau in milk or eggs slowly, the contribution of the residue to the MRLs in commodities of animal origin is calculated from the percentage of the diet and from the STMR or STMR-P values for residues in animal feed items.

***Use of the results of studies of animal transfer (farm animal feeding) and dietary burden to estimate maximum residue levels and STMR values for commodities of animal origin*:**

(a) When the feeding level in a transfer study matches the dietary burden, the residue levels from the transfer study may be used directly as estimates of residues in tissues, milk and eggs resulting from the dietary burden.
(b) When the feeding levels in a transfer study are different from the dietary burden, the resulting residues in tissues, milk and eggs can be estimated by interpolation between the closest feeding levels.
(c) When the dietary burden is lower than the lowest feeding level in the transfer study, the resulting residues in tissues, milk and eggs can be estimated by applying the transfer factor at the lowest feeding level to the dietary burden.
(d) When the dietary burdens of beef and dairy cattle are different, the higher one should be used to calculate the residues in muscle, liver and kidney.
(e) For estimating maximum residue levels and HR values in meat, fat, liver, kidney and eggs, the highest residue in an animal in the relevant feeding group of the transfer study is used.
(f) For estimating STMR values in meat, fat, liver, kidney and eggs, the mean residue value in the animals in the relevant feeding group of the transfer study is used.
(g) For estimating maximum residue levels and STMR values in milk, the mean residue value in the animals in the relevant feeding group of the transfer study is used.

Example: Spinosad

The residues of spinosad in milk reached a plateau after approximately 6 days, i.e. relatively rapidly. The maximum residue levels in animal commodities are derived from the feed commodity MRLs, as stated by the 1997 JMPR[2].

Estimation of maximum dietary burden of farm animals:

Commodity	Group	Residue (mg/kg)	Basis	Dry matter (%)	Residue, dry weight (mg/kg)	Choose diets (%)			Residue contribution (mg/kg)		
						Beef cattle	Dairy cows	Poultry	Beef cattle	Dairy cows	Poultry
Apple pomace wet	AB	0.064	STMR-P	40	0.16	10			0.016		
Citrus pulp	AB	0.12	STMR-P	91	0.13						
Maize forage	AF	5	MRL	100	5.0	40	50		2.0	2.5	
Maize fodder	AS	5	MRL	100	5.0						
Wheat straw and fodder, dry	AS	1	MRL	100	1.0						
Sorghum	GC	1	MRL	86	1.2	40	40	80	0.47	0.47	0.93
Almond hulls	AM	2	MRL	90	2.2	10	10		0.22	0.22	
Cotton seed hulls		0.0020	STMR-P	90	0.0022						
Cotton seed meal		0.0017	STMR-P	88	0.0019			20			0.0004
					Total	100	100	100	**2.7**	**3.2**	**0.93**

Estimation of STMR dietary burden of farm animals

Commodity	Group	Residue (mg/kg)	Basis	Dry matter (%)	Residue, dry weight (mg/kg)	Choose diets (%)			Residue contribution (mg/kg)		
						Beef cattle	Dairy cows	Poultry	Beef cattle	Dairy cows	Poultry
Apple pomace, wet	AB	0.064	STMR-P	40	0.16	10			0.016		
Citrus pulp	AB	0.12	STMR-P	91	0.13						
Maize forage	AF	0.70	STMR	100	0.70	40	50		0.28	0.35	
Maize fodder	AS	0.46	STMR	100	0.46						
Wheat straw and fodder, dry	AS	0.215	STMR	100	0.22						
Sorghum	GC	0.165	STMR	86	0.19	40	40	80	0.08	0.08	0.15
Almond hulls	AM	0.56	STMR	90	0.62	10	10		0.062	0.062	
Cottonseed hulls	SO	0.0020	STMR-P	90	0.0022						
Cottonseed meal	SO	0.0017	STMR-P	88	0.0019			20			0.00039
					Total	100	100	100	**0.43**	**0.49**	**0.15**

The dietary burdens of poultry will not be discussed further in this example.

As the maximum dietary burdens of beef and dairy cattle are 2.7 and 3.2 mg/kg, respectively, the levels of residues in tissues and milk were taken directly from the feeding level of 3 ppm in the transfer study, without interpolation. As the STMR dietary burdens (0.43 and 0.49 mg/kg) are lower than the lowest feeding level, 1 ppm, the resulting residues in tissues and milk were calculated by applying the transfer factors at the lowest feeding level to those STMR dietary burdens.

The highest individual tissue residue from the relevant feeding group was used in conjunction with the highest dietary burden of residue to calculate the probable highest residue level in animal commodities. The mean concentration of residue in the tissues of animals in the relevant feeding group was used in conjunction with the STMR dietary burden to estimate the STMR values for animal commodities. For milk, the mean plateau concentration of residue in the relevant feeding group was used to estimate both the maximum residue level and the STMR.

Value	Feeding level (ppm) *Interpolated* / Actual	Spinosad residues (mg/kg) [a]								
		Milk (mean)	Fat		Muscle		Liver		Kidney	
			High [b]	Mean [c]	High	Mean	High	Mean	High	Mean
MRL beef cattle	*2.7*/ 3									
MRL dairy cows	*3.2*/ 3	*0.13*/ 0.13	*1.7*/ 1.7		*0.069*/ 0.069		*0.44*/ 0.44		*0.26*/ 0.26	
STMR beef cattle	*0.43*/ 1									
STMR dairy cows	*0.49*/ 1	*0.022*/ 0.044		*0.32*/ 0.65		*0.010*/ 0.020		*0.064*/ 0.13		*0.032*/ 0.065

[a] Residue values in italics are interpolated from the dietary burden, feeding levels in the transfer study and the residue found in the transfer study.
[b] Highest individual tissue residue in animals in the relevant feeding group.
[c] Mean residue in animal tissue (or milk) in the relevant feeding group.

As the STMR burden for dairy cows exceeds that for beef cattle, it is used as the estimated maximum residue level and STMR in fat, muscle, liver and kidney.

The highest concentrations of residues expected in tissues and milk are: 1.7 mg/kg in fat, 0.26 mg/kg in kidney, 0.44 mg/kg in liver and 0.13 mg/kg in milk. The recommended MRLs (rounded suitably) are then: 2 mg/kg in cattle meat (fat), 0.5 mg/kg in cattle kidney, 0.5 mg/kg in cattle liver and 0.2 mg/kg in milk. The proposed STMR values are: 0.010 mg/kg in cattle meat, 0.032 mg/kg in cattle kidney, 0.064 mg/kg in cattle liver and 0.022 mg/kg in milk.

Residues arising from direct application to farm animals

Pesticides may be applied directly to farm animals for the control of lice, flies, mites and ticks. The application may be in the form of dips, sprays, pour-ons and jetting. If residues are likely to occur in animal commodities, residue trials are needed in which the correct methods of application, dosage and withdrawal times are used. The number of supervised trials on animals is, of necessity, far fewer than for crops.

The conditions of a supervised residue trial on farm animals should meet the maximum conditions described on the label of the pesticide container. If more than one application method is permitted (e.g. dip or pour-on treatment), data should be available for each method. The evaluation should give the highest residue found in individual animal tissues resulting from the approved method and dose. The highest concentration will form the basis for the recommended MRL. The evaluation should record the average residues in milk each day in the treated group. The recommended MRL will depend on the highest average value in milk achieved within the conditions described on the label.

The STMR concept is designed for supervised field trials on crops to obtain the typical residue value when a pesticide is used at maximum GAP. The method is not directly applicable to a trial of a

single direct treatment of an animals. Nevertheless, the Meeting agreed that, when a pesticide is used directly on animals (at maximum label conditions), a typical residue value would be useful in estimating long-term dietary intake. For this purpose, the median concentration of residues in the tissues of animals slaughtered at the shortest interval after treatment (or later if the residue concentrations were higher later) would be taken to represent that typical value.

Reconciliation of recommended maximum residue limits resulting from direct treatment and from residues in animals feed

When the recommended maximum residue levels for the two sources of residues do not agree, the higher recommendation will prevail. Similarly, the estimates for typical residues (from direct use at maximum label conditions) or STMR values derived from the dietary burden of farm animals and animal feeding studies, whichever is the higher, should be adopted for estimating long-term intake.

The Meeting recommended that the contents of this report be referred to the Joint Expert Committee on Food Additives (JECFA) for information and comment if necessary.

2.6 Application of statistical methods for evaluating residue data

Use of statistical methods for estimating maximum residue levels and in the evaluation of experimental results was considered by the Meeting in 1999, when it recommended use of statistical calculations as a tool in the estimation of maximum residue levels and re-examination of the situation when more practical experience had been gained. The 2001 Meeting considered the distribution pattern of pesticide residues derived from supervised field trials and the applicability of various tests for their evaluation.

Treatment of apparent outliers

As the distribution of residues among trials (fields) is not normal, statistical tests in which normal distribution is assumed, such as the Dixon or Grubb outlier test, cannot be used. As the number of trials is not sufficient to apply non-parametric methods for testing outliers, residue values above those of the majority of the population must be treated individually and should be disregarded only if the experimental evidence raises doubt about their reliability. When results are evaluated, therefore, utmost care must be taken in deciding that a result is not valid (but not a statistical outlier). Rejection of such results must be justified by agricultural practice or other evidence from the experimental set-up or analytical conditions.

Comparison of residue populations

Different patterns or conditions of use often result in somewhat different concentrations of residues in the same crop. The Meeting has to decide which data sets for a given commodity or commodity group should be combined for estimating an STMR. A decision that two residue populations are similar or not can substantially influence the estimated STMR values. The Meeting considered that the Mann-Whitney U-test was suitable for verifying whether residue populations resulting from different GAP and/or climatic conditions or derived from different crops have similar median values.

The basic principle involved is that, if one type of pesticide use gives results that appear to be higher than those resulting from another type of use, there should be few instances in which individual results from the ‘higher’ population are exceeded by results from the ‘lower’ population. The sum of such cases is calculated, and the smaller is compared with the tabulated critical value. In making this comparison, the critical region, i.e. that in which the null hypothesis (the two median values are not different) can be rejected, is that in which the test statistic is *less than or equal to* the tabulated value; this

is contrary to the criterion of many significance tests (e.g. Student t test, F test, χ^2 test). With the appropriate statistical table, a two-tailed test ($\alpha_2 = 5\%$) is usually applied and it is assumed that $n_1 \leq n_2$, where n_1 and n_2 are the numbers of data points in populations 1 and 2, respectively. The test statistics, U_1 and U_2, are calculated as:

$$U_1 = n_1 n_2 + [n_1(n_1+1)]/2 - \sum R_1$$
$$U_2 = n_1 n_2 + [n_2(n_2+1)]/2 - \sum R_2$$

where $\sum R$ is the sum of ranks of the corresponding values. The correctness of a calculation can be checked from:

$$U_1 + U_2 = n_1 n_2$$

The calculation is illustrated by comparing the residue populations of tebufenozide in mandarin and orange flesh from Italy and Spain. The U test is suitable for deciding whether the residue populations in citrus flesh deriving from use of the pesticide on oranges and mandarin in trials in Italy and Spain are similar or different. The stepwise procedure is the following:

Residues in mandarin flesh: 0.069, 0.076, 0.082, 0.092, 0.14, 0.18 mg/kg

Residues in orange flesh: 0.021, 0.03, 0.04, 0.04, 0.05, 0.053, 0.11, 0.13, 0.13, 0.15 mg/kg

1. Use bold or colour fonts to distinguish one of the two sets of samples.
2. Combine and rank the measurements for both set of samples from lowest to highest.
3. Place the corresponding ranks next the measurements under the appropriate columns. The quantities n_1 and $\sum R_1$ are assigned to the smaller when the sample sizes are different. For similar values, assign the average of the ranks (e.g. for 0.04, 0.04, the ranks are 3.5 and 3.5 instead of 3 and 4).
4. Calculate the sum of the ranks for each data set. A useful check for correct assignment of ranks is that the sum of the ranks should be equal to the sum of the natural numbers $n_1 + n_2$.
5. Insert the appropriate values in the equations: We obtain $U_1 = 17$ $U_2 = 43$).
6. Take the lower value and compare it with the tabulated value. The critical value is 11 for $n_1 = 6$ and $n_2 = 10$ at $\alpha_2 = 5\%$.

As U_1 is greater than 11, we can conclude that the samples probably come from populations with the same median.

Residues (mg/kg)	**Ranks**	
	Mandarin	**Orange**
0.021		1
0.03		2
0.04		3.5
0.04		3.5
0.05		5
0.053		6
0.069	7	
0.076	8	
0.082	9	
0.092	10	

0.11		11	
0.13		12.5	
0.13		12.5	
0.14	14		
0.15		15	
0.18	16		
∑Rank	64		72
U_1	**17**		
U_2			43
Critical value (n_1 = 6, n_2 = 10, α_2 = 5%)			**11**
U_1 > 11	**Populations similar**		

As the lower of U_1 and U_2 is greater than the critical value of 11, we conclude that the populations have similar distributions, and the populations can be combined for the purposes of estimating an STMR. This conclusion affects calculation of the long-term intake of residues, as the median values for the individual populations were 0.087 mg/kg for mandarin flesh and 0.0515 mg/kg for orange flesh instead of 0.079 mg/kg for the combined population.

The Meeting agreed to combine residue populations when the *U* test suggested that their medians were similar and to use the combined population for estimating maximum residue levels and STMR values. For populations that are different, the Meeting agreed to use only that population which had the highest valid residue value for both estimates. The test should be applied with caution for residues below the LOQ in the populations to be compared.

The Meeting reiterated its view that evaluation of data from trials of pesticide residues is complex and includes consideration of factors such as metabolism and rate of disappearance. It cannot be based only on calculations, and therefore statistical methods can only support an expert judgement.

3. DIETARY RISK ASSESSMENT FOR PESTICIDE RESIDUES IN FOOD

Assessment of risk of long-term dietary exposure

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

Long-term dietary intakes in the GEMS/Food diets are expressed as a percentage of the ADI for a 60-kg person, with the exception of the Far Eastern diet, in which a body weight of 55 kg is used. The estimates are summarized in Table 1. The percentages up to and including 100% are rounded to one significant figure and values above 100% to two significant figures. When the percentages for the compounds for which IEDIs are calculated are greater than 100%, the information provided to JMPR does not allow estimation that the dietary intake would be below the ADI. These compounds are identified by a footnote in the Table. The detailed calculations of long-term dietary intake are given in Annex 3.

The Meeting drew attention to the use of residue levels in muscle tissue for estimating dietary intake of residues in meat of fat-soluble compounds. Previously, residue levels in trimmable fat, with adjustment by a default factor, were used to estimate dietary intake from meat.

In response to requests from the 2001 CCPR, the JMPR calculated the dietary intakes of clethodim and mevinphos. The estimated dietary intake of clethodim ranged from 3 to 30%, and the TMDI of mevinphos ranged from 0 to 3% (Annex 3). The Meeting concluded that dietary intake of clethodim and mevinphos is unlikely to present a public health concern.

Calculations of dietary intake can be further refined at the national level by taking into account more detailed information on food consumption, data from monitoring and surveys, on total diet or reliable data on the percentage of a crop treated and the percentage of the crop imported.

Table 1. Summary of risk assessments of long-term dietary intake conducted by the 2001 JMPR

Code	Name	ADI (mg/kg bw)	Exposure range (% of ADI)	Type of assessment
117	Aldicarb	0-0.003	6-20	DIE
008	Carbaryl	0-0.0008	300-560	TMDI
201	Chlorpropham	0-0.03	2-50	IEDI
187	Clethodim	0-0.01	4-30	IEDI

[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

Code	Name	ADI (mg/kg bw)	Exposure range (% of ADI)	Type of assessment
020	2,4-D	0- 0.01	3-20	IEDI
130	Diflubenzuron	0-0.02	3-20	TMDI
151	Dimethipin	0-0.02	3-20	IEDI
087	Dinocap	0-0.008	0-2	IEDI
030	Diphenylamine	0-0.08	0-4	IEDI
202	Fipronil	0-0.0002	20-60	IEDI
194	Haloxyfop	0-0.0003	50-440[a]	IEDI
110	Imazalil	0-0.03	10-100	TMDI
111	Iprodione	0-0.06	3-50	IEDI
199	Kresoxym-methyl	0-0.4	0	IEDI
094	Methomyl	0-0.02	3-20	IEDI
147	Methoprene (S) Methoprene (R,S)	0-0.05 0-0.09	20-70 10-40	IEDI IEDI
053	Mevinphos	0-0.0008	0 - 4	TMDI
062	Piperonyl butoxide	0-0.2	20-40	IEDI
142	Prochloraz	0-0.01	30-140 [a]	TMDI
203	Spinosad	0-0.02	2-30	IEDI
196	Tebufenozide	0-0.02	1- 20	IEDI

[a] The information provided to JMPR precludes an estimate that the long-term dietary intake of residues would be below the ADI.

Assessment of risk of short-term dietary exposure

Risks associated with short-term dietary intake were assessed for compounds for which MRLs were recommended and STMR values estimated at the present Meeting and for which an acute reference dose (acute RfD) has been established, in commodities for which data on consumption were available. The procedures for calculating the short-term intake were defined primarily at the Geneva Consultation (WHO, 1997b) and refined at subsequent meetings[1] (Annex 5, reference 89). Data on the consumption of large portions were provided by Australia, France, The Netherlands, Japan, the United Kingdom and the USA. Data on unit weight and per cent edible portion were provided by France, the United Kingdom and the USA. The body weights of adults and children aged ≤ 6 were provided by Australia, France, the Netherlands, the United Kingdom and the USA.

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 described below. The following definitions apply to all equations:

[1] Pesticide Safety Directorate 1998. *Pesticide Residues Variability and Acute Dietary Risk Assessment*. York.

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 data from supervised trials data 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 of the whole portion is < 25 g).

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

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). The variability factors, v, shown below are applied in the equations. When sufficient data are available on residues in single units to calculate a more realistic variability factor for a commodity, the calculated value should replace the default value.

Commodity characteristic	v
Unit weight of whole portion is > 250 g	5
Unit weight of whole portion is ≤ 250 g	7
Unit weight of whole portion is ≤ 250 g, from granular soil treatment	10
Leafy vegetables with unit weight of whole portion is ≤ 250 g	10

When data are available on residues in a single unit and thus allow estimation of the highest residue in a

single unit, this value should be used in the first part of the equation for case 2a, with no variability factor, and the HR value derived from data on composite samples should be used in the second part of the equation. 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.

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

Case 2b

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

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

Case 3

When a processed commodity is bulked or blended, the STMR-P value represents the probable highest concentration of residue.

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

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 (Table 2). If the percentage is greater than 100%, the information provided to the JMPR does not allow an estimation that the short-term dietary intake of the residue in that commodity would be below the acute RfD. These compound–commodity combinations are identified by a footnote in the Table.

The Meeting concluded that acute RfDs might be necessary for iprodione and haloxyfop, but these have not yet been established. The IESTIs were calculated, but the acute risk assessment could not be finalized. The Meeting recommended that these compounds be evaluated for establishment of acute RfD in a near future.

Earlier Meetings concluded that acute RfD are unnecessary for diphenylamine, imazalil, kresoxim-methyl and pyriproxyfen. On the basis of data received by the present Meeting, the establishment of acute RfDs was considered to be unnecessary for chlorpyrifos-methyl, diflubenzuron, methoprene and spinosad. The Meeting concluded, on the basis of previous evaluations, that acute RfD are unnecessary for 2,4-D and piperonyl butoxide, because the compounds are unlikely to present acute toxicological hazards. Therefore, as residues are unlikely to present an acute risk to consumers, intake of these compounds was not estimated.

The IESTIs and/or percentage of the acute RfD for the general population and for children are summarized in Table 2. The percentages of the acute RfD are rounded to one significant figure for values up to and including 100% and to two significant figures for values above 100%. The detailed calculations of short-term dietary intake are given in Annex 4.

Table 2. Summary of risk assessments of short-term dietary intake conducted by the 2001 JMPR

Code	Compound	Acute RfD (mg/kg bw)		IESTI (mg/kg bw per day)		Percentage of acute RfD	
				General population	Children	General population	Children
117	Aldicarb	0.003	banana:	0.00428	0.00981	140[1]	330[1]
			potato:	0.00681	0.01693	230[1]	560[1]
			microwaved potato:	0.00481	0.01189	160[1]	400[1]
201	Chlorpropham	0.03	potato:	0.46716	1.38305	1600[1]	4600[1]
			potato, cooked:	0.15437	0.45692	510[1]	1500[1]
			Other commodities:	0.00001-0.00406	0.00001-0.01202	0-10	0-40
022	Diazinon	0.03		0.0008-0.0088	0.00171-0.02784	3-30	6-90
151	Dimethipin	0.02		0-0.00229	0.0001-0.0012	0-10	0-10
087	Dinocap	0.03		0.00012-0.00636	0.00012-0.00636	20	60
				0.00012-0.00636		80	(for women of childbearing age)
188	Fenpropimorph	1.0		0.0002-0.0161	0.0003-0.0422	0-2	0-4
202	Fipronil	0.003		0-0.00073	0.00001-0.00239	1-20	0-80
094	Methomyl	0.02	apple	0.05194	0.15365	260[1]	770[1]
			broccoli	0.16212	0.30660	810[1]	1500[1]
			Brussels sprout	0.4015	0.08909	200[1]	450[1]
			Cabbages, head	0.06382	0.24976	320[1]	1200[1]
			Cauliflower	0.11791	0.34468	590[1]	1700[1]
			Celery	0.05040	0.06250	250[1]	310[1]
			Watermelon		0.02713		140[1]
			Grapes	0.094548	0.32417	470[1]	1600[1]
			Kale	0.13375	0.21850	670[1]	1100[1]
			lettuce, head	0.40875	0.61500	2000[1]	3000[1]
			lettuce, leaf	0.30125	0.7500	1500[1]	3800[1]
			spinach	0.563107	1.43647	2800[1]	7200[1]
			sweet corn	0.028338	0.08318	140[1]	420[1]
			tomato		0.03748		190[1]
			other commodities:	0-0.01125	0-0.02030	0 - 60	0 - 100
060	Phosalone	0.3		0.0001-0.0355	0.00002-0.11830	0 - 10	0 - 40
196	Tebufenozide		apple		0.10564		210[1]
			cabbage		0.20516		600[1]
			kale		0.7079		140[1]
			grapes		0.09351	190[1]	
			spinach	0.22100	0.601820	440[1]	1220[1]
			lettuce, head	0.13244	0.19926	260[1]	400[1]
			lettuce, leaf		0.24300		490[1]
			pear		0.08992		180[1]
			other commodities	0-0.05242	0- 0.04467	0-100	0-90

[1] The information provided to the JMPR precludes an estimate that the short-term dietary intake of residues in this commodity would be below the acute reference dose

References

WHO 1997b. *Guidelines for predicting dietary intake of pesticide residues.* 2nd revised edition, GEMS/Food Document WHO/FSF/FOS/97.7, World Health Organization, Geneva

WHO 1997b. *Food consumption and exposure assessment of chemicals*. Report of a FAO/WHO Consultation. Geneva, Switzerland, 10-14 February 1997. World Health Organization, Geneva

PSD 1998. *Pesticide Residues Variability and Acute Dietary Risk Assessment*. York, United Kingdom, 1-3 December 1998. The Pesticide Safety Directorate, York.

4. EVALUATION OF DATA FOR ACCEPTABLE DAILY INTAKE FOR HUMANS, MAXIMUM RESIDUE LEVELS AND SUPERVISED TRIALS MEDIAN RESIDUE VALUES

4.1 ALDICARB (117)

Residue and analytical aspects

Aldicarb was last evaluated for residues in 1994 by the JMPR within the CCPR periodic review programme. The 1994 Meeting estimated maximum residue levels for a wide range of commodities and estimated a temporary maximum residue level of 0.5 mg/kg for potato, pending the submission of data from supervised trials corresponding to current use patterns; it withdrew the MRL for banana. In 1996, new data on residues in banana and potato were evaluated, and the MRL of 0.5 mg/kg on potatoes was confirmed. At its Thirtieth Session, the CCPR noted that new data on banana and potato based on amended GAP use would become available (ALINORM 99/24). At the present Meeting, data on residues in trials on banana and potato, residues in individual units of banana and potato, a study on processing of potato, and an estimate of short-term dietary intake by a probabilistic method were provided.

Stability of residues in stored analytical samples

Aldicarb and its metabolites were relatively stable at a concentration of 0.1 mg/kg in banana and in processed fractions stored for up to 5 months in a freezer. After storage, 64–87% of the added compounds remained in banana pulp, 56–80% in peel, 61–98% in purée and 57–71% in banana chips. No new studies were provided on potato samples.

Results of supervised trials

In Guadeloupe, Martinique and Côte d'Ivoire, the GAP for banana is 2 g ai/plant. The labels either states that a period of 180 days is necessary between the last treatment and the expected harvesting date or specifies a PHI of 180 days. The Meeting agreed that, if bananas were treated with aldicarb with the intention of harvesting 180 days later, the use would be considered at GAP if the bananas were harvested at maturity.

Twenty-four trials were conducted in these countries, with 1 x 2 g/plant applied to the first and/or the second generation, on bagged and/or unbagged bananas (PHI, 134–286 days). The concentrations of residues of aldicarb in bagged banana were 0.01 (4), 0.02, < 0.03 (3) and 0.12 mg/kg, and those in bagged banana pulp were 0.01 (4), 0.02, < 0.03 (2), 0.03 and 0.10 mg/kg. The concentrations in unbagged banana fruit were 0.01 (9), 0.02 (2), < 0.03 (3) and 0.10 mg/kg, and those in unbagged banana pulp were 0.01 (9), 0.02 (2), < 0.03 (3) and 0.09 mg/kg, as aldicarb. Residues after culture by GAP on bagged and unbagged banana applied to a single population, and were combined. The residue concentrations in fruit, in ranked order (median underlined), were: 0.01 (13), 0.02 (3), < 0.03 (6), 0.10 and 0.12 mg/kg, and those in pulp were 0.01 (13), 0.02 (3), < 0.03 (5), 0.03, 0.09 and 0.10 mg/kg, as aldicarb.

On the basis of the concentrations in the fruit, the Meeting estimated a maximum residue level of 0.2 mg/kg for aldicarb in banana. On the basis of the concentrations in pulp, the Meeting estimated a STMR of 0.01 mg/kg, and a HR of 0.10 mg/kg for aldicarb in banana.

Individual pulp units from four trials (12 units per trial from four bunches) conducted in Guadeloupe (first-generation; PHI, 134 days for bagged and 161 days for unbagged bananas) and from

two trials conducted in Martinique (second-generation; PHI, 167 and 136 days for bagged banana) were analysed. The distribution of residues in the 12 units did not represent the expected distribution of residues among plants on a treated field. Aldicarb is a systemic insecticide, which is taken up by the plant from the soil. The residues are equally distributed in the peel and the pulp, and there is no difference between the concentrations in bagged and unbagged banana. Futhermore, the main source of variation in concentrations is differences in uptake. The sampling plan used, in which only four bunches were selected from the treated area, would not indicate the probable variation in concentrations, and, consequently, no variability factor could be estimated. The Meeting agreed that a default variability factor of 5 should be used to estimate short-term dietary intake of aldicarb from banana; the unit weight of the whole portion includes more than one finger and is > 250 g (see section 3).

Overall, 29 trials were conducted with aldicarb on potato in Europe (three in Greece, four in The Netherlands, two in Italy, four in Spain and 16 in the United Kingdom). GAP in The Netherlands involves furrow application of a dose of 12.8 g/100 m, equivalent to 1.7 kg ai/ha, or broadcast application of 3.36 kg/ha and a PHI of 90 days. The residue concentrations in four trials conducted in The Netherlands according to GAP were 0.10, 0.17, 0.20 and 0.27 mg/kg. Seventeen trials conducted in the United Kingdom according to GAP in The Netherlands gave concentrations of < 0.03 (3), 0.03, 0.07, 0.08, 0.09, 0.10 (2), 0.11 (2), 0.12 (2), 0.14, 0.18 and 0.36 mg/kg. In Greece, Italy and Spain, critical GAP is furrow application of 2.5 kg ai/ha and a PHI of 90 days. The concentrations in trials conducted according to GAP were 0.04, 0.03 and 0.06 mg/kg in Greece, 0.04 and 0.03 mg/kg in Italy and 0.45, 0.06, 0.27 and 0.04 mg/kg in Spain.

In the USA, 16 trials were conducted according to the GAP rate of 3.36 kg ai/ha, a PHI of 100 or 150 days and positive displacement application, in Colorado, Idaho, Michigan, North Dakota, South Dakota and Washington. The concentrations of aldicarb residues in tubers after 120 days were < 0.02, 0.02 (2), 0.03 (3), 0.04 (3), 0.05, 0.06 (2), 0.10, 0.11, 0.13 and 0.20 mg/kg.

The concentrations of residues in trials conducted in Europe and the USA were considered to apply to a single population and were combined, in ranked order, as follow: < 0.02, 0.02 (2), < 0.03 (3), 0.03 (6), 0.04 (5), 0.05, 0.06 (4), 0.07, 0.08, 0.09, 0.10 (3), 0.11 (3), 0.12 (2), 0.13, 0.14, 0.18, 0.20, 0.27, 0.36 and 0.45 mg/kg, as aldicarb equivalents. The Meeting confirmed the previous recommended MRL of 0.5 mg/kg and estimated a STMR values of 0.06 mg/kg and a highest residue of 0.45 mg/kg for aldicarb in potato, as aldicarb equivalents.

The Meeting considered the database from 26 supervised field trials on potato submitted to the 1996 JMPR that had been carried out in the USA with the recommended positive displacement application of aldicarb. In each trial, 30–100 individual potato tubers were analysed. The observed maximum concentrations of residues in individual tubers in each trial were, in rank order, 0.045 (2), 0.046, 0.048, 0.063, 0.065, 0.072, 0.11, 0.17 (2), 0.20, 0.22, 0.23, 0.25, 0.26, 0.27, 0.29, 0.31, 0.32, 0.34, 0.51, 0.61, 0.94, 1.1 and 1.2 (2) mg/kg. Data on individual tubers were submitted to the present Meeting from 11 supervised trials conducted in Europe according to GAP, with furrow application. In each trial, 27–50 individual potato tubers were analysed. The observed maximum concentrations of residues in individual tubers in each trial were, in rank order, 0.05, 0.051, 0.065, 0.10 (2), 0.11, 0.138, 0.262, 0.34, 0.426 and 1.07 mg/kg. The Meeting agreed that the maximum residue levels in individual tubers in Europe and the USA comprised a single population and could be combined, in ranked order, as follow: 0.045 (2), 0.046, 0.048, 0.05, 0.051, 0.063, 0.065 (2), 0.072, 0.1 (2), 0.112, 0.11, 0.14, 0.17 (2), 0.2, 0.22, 0.23, 0.25, 0.26, 0.262, 0.27, 0.29, 0.31, 0.32, 0.34 (2), 0.43, 0.51, 0.61, 0.94, 1.1 (2) and 1.2 (2) mg/kg.

The Meeting agreed that the highest residue in this data set (1.2 mg/kg) could be used to estimate short-term intake of aldicarb from consumption of potato. When this value is used, no variability factor need be applied to the first part of the equation for calculation of the IESTI in case 2a (see section 3). The HR value estimated from the composite sample, 0.45 mg/kg, was used in the second part of the equation.

Fate of residues during storage

A study of the fate of residues of aldicarb and its metabolites present at 0.1 mg/kg in banana pulp and peel at room temperature showed that 36–82% of the residues remained after 6 days.

Fate of residues during processing

A study was conducted on processing of potato obtained from three fields in Spain that had been commercially treated with aldicarb at the time of planting. Samples taken 67–88 days after treatment (average size of tubers, 3–4 cm) contained residues of total aldicarb, expressed as aldicarb, at concentrations of 0.06, 0.15 and 0.45 mg/kg. After microwave boiling, the tubers contained an average of 70% of the residues present before cooking (processing factors, 0.72, 0.72 and 0.65). On the basis of the average processing factor for microwaved potato (0.7), the estimated STMR of 0.06 mg/kg and a HR of 0.45 mg/kg for potato, the Meeting estimated a STMR-P of 0.042 and a HR-P of 0.315 mg/kg for aldicarb in microwaved potato.

On the basis of the highest residue of 1.2 mg/kg for potato, the Meeting estimated a highest residue of 0.84 mg/kg for aldicarb in microwaved potato. This value can be used to estimate short-term intake of aldicarb from the consumption of microwaved potato, and no variability factor need be applied to the first part of the equation for calculation of the IESTI in case 2a (see section 3). The HR-P value estimated for the composite sample (0.315 mg/kg) was used in the second part of this equation.

In processing studies submitted to the 1996 JMPR, the average processing factors were 0.75 for potato flakes, 0.48 for chips, 0.29 for frozen fries and 0.39 for cooked fries. On the basis of the estimated STMR and HR values for potato, the Meeting estimated a STMR-P value for aldicarb in potato flakes of 0.045 mg/kg and a HR-P value of 0.338 mg/kg; a STMR-P value for potato chips of 0.0288 mg/kg and a HR-P value of 0.216 mg/kg; a STMR-P value for frozen fries of 0.0174 mg/kg and a HR-P value of 0.131 mg/kg; and a STMR-P value for cooked fries of 0.0234 mg/kg and a HR-P value of 0.176 mg/kg for aldicarb in potato.

The Meeting received the result of use of a probabilistic method for estimating short-term dietary intake. The model and data applied only to the situation in the United Kingdom.

Dietary risk assessment

Long-term intake

Currently, the ADI for aldicarb is 0–0.003 mg/kg bw. The dietary intake was calculated of the 21 commodities for human consumption for which CXLs exist and for banana and potato on the basis of the STMRs estimated in this evaluation. The results are shown in Annex 3. The estimated dietary intake of aldicarb ranged from 6% of the ADI in the African diet to 20% in the Middle Eastern diet. The Meeting concluded that the intake of residues of aldicarb resulting from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

An acute RfD of 0.003 mg/kg bw for aldicarb was established by the 1999 JMPR. The IESTI for aldicarb was calculated for banana and potato (Annex 4). For banana, it was 140% of the acute RfD for the general population and 330% of the acute RfD for children. For potato, it was 230% of the acute RfD for the general population and 560% of the acute RfD for children. The IESTI for microwaved potato was 160 and 400% of the acute RfD for the general population and children, respectively. The information provided to the Meeting precluded a conclusion that the acute dietary intake of banana and potato by children and adults would be below the acute RfD.

4.2 CARBARYL (008)

Toxicology

Carbaryl was evaluated for toxicological effects by the Joint Meeting in 1963, 1965, 1966, 1967, 1969, 1973, and 1996. An ADI of 0–0.02 mg/kg bw was established in 1963 on the basis of a 1-year study in dogs, and this ADI was confirmed in 1965, 1966, and 1967. In 1969, a temporary ADI of 0–0.01 mg/kg bw was established, which incorporated an extra safety factor because of concern about effects on the male reproductive system in a 1-year study in rats treated by gavage, with a NOAEL of 2 mg/kg bw per day, and because a dose of 0.12 mg/kg bw per day may have affected renal function in a 6-week study in volunteers. In 1973, the Meeting established an ADI of 0–0.01 mg/kg bw. In 1996, carbaryl was reviewed as part of the periodic review programme of the CCPR. The Meeting established an ADI of 0–0.003 mg/kg bw on the basis of a LOAEL of 15 mg/kg bw per day in a study of carcinogenicity in mice and a safety factor of 5000, which included an extra safety factor of 50 to account for the presence of vascular tumours in male mice at all doses tested. The Meeting stated that the resulting ADI provided an adequate margin of safety, taking into account the LOAEL (3.1 mg/kg bw per day for maternal toxicity) in the study of developmental toxicity in dogs and the uncertainties about the effects on the male reproductive system.

The following information was available to the present Meeting: new studies on metabolism in mice and rats; a 14-day study of effects on some enzyme activities in rats; a 6-month study in the *p53* knockout mouse model; (re-)evaluation of the incidence of bladder tumours in the 2-year study of toxicity and carcinogenicity in rats; (re-)evaluation of all slides from the 2-year study of carcinogenicity in mice and the 2-year study of toxicity and carcinogenicity in rats; and an extended and updated epidemiological study. Furthermore, additional studies were available on the neurotoxicity, developmental toxicity, and reproductive toxicity of carbaryl.

To elucidate the role of metabolism in the formation of tumours in the long-term studies in mice and rats, metabolite profiles were determined in mice and 15-month-old rats. The kinetics and metabolism of carbaryl in mice and rats were found to be comparable in studies evaluated by the 1996 JMPR. Some evidence was obtained that mice formed more metabolites via epoxidation and conjugation at a high, probably toxic, dietary concentration of carbaryl (about 8000 ppm). In the study in 15-month-old rats, no convincing evidence was found for a shift in the urinary metabolite pattern at the high (toxic) dietary concentration of 7500 ppm.

The 1996 Meeting could not identify a NOAEL for vascular tumours (haemangiomas and haemangiosarcomas) in male mice. The highest dose in this 2-year study also increased the incidence of renal tubular-cell adenomas and carcinomas in males and the incidences of vascular tumours and of hepatocellular adenomas and carcinomas in females. Re-evaluation of the histological slides from the 2-year study in mice confirmed the original findings of the study pathologists, namely, increased incidences

of vascular tumours in males at all doses. Although the incidence of vascular tumours found at the lowest dietary concentration of 100 ppm, equal to 15 mg/kg bw per day, in this study was within the range of incidences in some control groups in 104-week studies performed in other laboratories, it was not possible to exclude the possibility that the incidences were outside the range of values for control groups in similar studies performed in the same laboratory, in the absence of data on such studies.

In 1996, the Meeting concluded that carbaryl is not genotoxic. Some support for a non-genotoxic mechanism of vascular tumour formation by carbaryl in mice was found in a newly available 6-month study in the *p53* knockout mouse model, in which tumours are induced readily by genotoxic compounds. In this model, carbaryl did not induce vascular tumours, whereas the genotoxic carcinogen urethane, used as a positive control in the validation study, did.

The Meeting concluded that the increased incidence of vascular tumours was likely to be species- and sex-specific, but, in view of the rarity and malignancy of these tumours, they could not be discounted in human risk assessment.

In 1996, the Meeting concluded that carbaryl is carcinogenic in rats only at doses that exceed the maximal tolerated dose. Increased incidences of tumours were observed in the thyroid in males, the liver in females, and the urinary bladder in males and females at the highest dietary concentration of 7500 ppm. Re-evaluation of the histological slides from the 2-year study in rats confirmed the original findings of the study pathologist that increased incidences of tumours in the thyroid (follicular-cell adenomas and carcinomas in males), liver (hepatocellular adenoma in females), and urinary bladder (transitional-cell papillomas and carcinomas in males and females) occurred at the highest dietary concentration of 7500 ppm. The finding of extensive hyperplasia in the urinary bladder without associated necrosis, inflammation, or regeneration suggested that the tumorigenic response was due to cell proliferation associated with a mitogenic effect of carbaryl or one of its metabolites, which appears to be an effect specific to rats. On the basis of this new information, the Meeting reaffirmed the conclusion of the 1996 JMPR.

In 1996, the Meeting recommended that a new two-generation study of reproductive toxicity be carried out in rats, with special attention to the male reproductive tract, as effects on this system were observed in some long-term studies of toxicity in rats at doses given by gavage that were significantly lower than those given in the diet in studies of reproductive toxicity (which suffered from various shortcomings in study design). In the newly available two-generation study of reproductive toxicity, treatment with carbaryl had effects on the offspring at maternally toxic doses. No effects on reproductive parameters were found in animals of either sex at any dietary concentration up to the highest dose equal to 92 mg/kg bw per day. At a concentration of 300 ppm, equal to 21 mg/kg bw per day, effects were seen on the weights of the body and liver of parental animals and on the mortality rate of pups of the F_2 generation. The NOAEL for parents and offspring was 75 ppm, equal to 4.7 mg/kg bw per day. On the basis of this new study, and taking into account that all the previously evaluated studies were of limited significance and validity for evaluating reproductive effects, the Meeting concluded that carbaryl does not impair fertility or reproduction and has no adverse effects on the male or female reproductive system.

In 1996, the Meeting concluded that carbaryl has developmental toxicity, manifested as deaths *in utero*, reduced fetal weight, and malformations, but only at doses that are overtly maternally toxic. The shortcomings of these studies were such that NOAELs for developmental toxicity that could be used for risk assessment could not be identified. In the newly available studies of developmental toxicity in rats and rabbits, treatment with carbaryl caused fetal effects only at maternally toxic doses**.** In a study in rats, the highest dose of 30 mg/kg bw per day resulted in maternal toxicity and reduced fetal body weights and delayed ossification. The NOAEL for maternal, embryo-, and fetotoxicity was 4 mg/kg bw per day. Effects on cholinesterase activity were not determined. In a study in rabbits, doses ≥ 50 mg/kg bw per day were maternally toxic (inhibition of erythrocyte acetylcholinesterase activity). Fetotoxic effects (reduced

fetal body weight per litter) were seen at 150 mg/kg bw per day, the highest dose tested. The NOAEL for maternal toxicity was 5 mg/kg bw per day, and that for embryo- and fetotoxicity was 50 mg/kg bw per day. The compound did not induce irreversible structural effects in either rats or rabbits at doses up to 30 and 150 mg/kg bw per day, respectively. On the basis of the new studies and taking into account that the previously evaluated studies were of limited significance and validity for evaluating developmental effects, the Meeting concluded that carbaryl is not teratogenic.

In studies of neurotoxicity in rats, a single dose ≥ 30 mg/kg bw or repeated administration of doses ≥ 10 mg/kg bw per day for 13 weeks by oral gavage resulted in dose-dependent clinical effects, including decreased pupil size, tremors, salivation, reduced body temperature, and fur staining. A single oral dose of 500 or 1000 mg/kg bw was lethal. Single oral doses ≥ 10 mg/kg bw (lowest dose tested) induced marked, dose-dependent reductions in cholinesterase activity in plasma, erythrocytes, whole blood, and brain, which returned to pretreatment values within 4**,** 24, and 48 h after doses of 10, 30, and 90 mg/kg bw, respectively. A NOAEL could not be identified in these studies with single doses. The LOAEL was 10 mg/kg bw. In the 13-week study of neurotoxicity, cholinesterase activity was significantly decreased by more than 20% in erythrocytes, whole blood, plasma, whole brain, and individual brain structures at doses of 10 and 30 mg/kg bw at weeks 4, 8, and 13 in a dose-related fashion. The NOAEL was 1 mg/kg bw per day.

In a study of developmental neurotoxicity, treatment of pregnant rats from day 6 of gestation to day 10 *post partum* at a dose of 10 mg/kg bw per day induced clinical effects and reductions in erythrocyte and brain cholinesterase activity. Treatment of the dams had no effect on clinical, developmental, or behavioural parameters in offspring up to 4 months of age. The NOAEL for offspring was 10 mg/kg bw per day, the highest dose tested. The NOAEL for neurotoxic effects in the dams was 1 mg/kg bw per day.

Two epidemiological studies of carbaryl production workers employed between 1978 and 1994 showed no increase in the mortality rate from cancer when compared with that of unexposed workers. After re-evaluating a 6-week study in volunteers (which was reported in the evaluations of the 1973 and 1996 JMPR), the Meeting concluded that an increased ratio of amino acid nitrogen to creatinine in urine observed at a dose of 0.13 mg/kg bw per day was an equivocal, inconsistent effect and was not relevant for risk assessment.

The Meeting concluded that the existing database on carbaryl was adequate to characterize potential hazards to fetuses, infants, and children.

The critical effect of carbaryl is inhibition of brain acetylcholinesterase activity. This is a rapidly reversible effect (recovery within 4 h in rats at the lowest single dose of 10 mg/kg bw), which is driven by the peak concentration in plasma rather than by the area under the plasma concentration-time curve (AUC). Therefore, in terms of brain acetylcholinesterase activity, the ADI could be established at the same value as the acute RfD. However, carbaryl was considered to be a non-genotoxic carcinogen in mice, causing vascular tumours in one sex (males) at all doses tested. The Meeting established an ADI of 0-0.008 mg/kg bw on the basis of the LOAEL of 100 ppm, equal to 15 mg/kg bw per day, and a safety factor of 2000, which incorporated an extra safety factor of 20 in view of the occurrence of this rare and malignant type of tumour, for which a no-effect level could not be identified.

Carbaryl is moderately toxic to rats after a single oral dose (LD_{50} = 220-720 mg/kg bw). In studies with single and repeated oral doses, the critical effect of carbaryl was of an acute nature, i.e. inhibition of acetylcholinesterase activity. A NOAEL could not be identified for this effect in studies with single doses in rats; the lowest effective dose was 10 mg/kg bw, at which no clinical signs were observed. As dogs and rats have been shown to be equally sensitive to cholinesterase inhibition by carbaryl in short-term and long-term studies, the Meeting established an acute RfD of 0.2 mg/kg bw, on the basis of the

NOAEL of 125 ppm, equal to 3.8 mg/kg bw per day, in a 5-week study in dogs. A safety factor of 25 was used because the effects were rapidly reversible and were driven by the peak concentration in plasma.

An addendum to the toxicological monograph was prepared.

Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment
Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Mouse	2-year study of carcinogenicity[a]	Carcinogenicity	-	100 ppm, equal to 15 mg/kg bw per day
Rat	2-year study of toxicity and carcinogenicity[a]	Toxicity	250 ppm, equal to 10 mg/kg bw per day	1500 ppm, equal to 60 mg/kg bw per day
		Carcinogenicity	1500 ppm, equal to 60 mg/kg bw per day	7500 ppm, equal to 350 mg/kg bw per day[b]
	13-week study of neurotoxicity[c]	Neurotoxicity	1 mg/kg bw per day	10 mg/kg bw per day
	Multigeneration study of reproductive toxicity[a]	Parental toxicity	75 ppm, equal to 4.7 mg/kg bw per day	300 ppm, equal to 21 mg/kg bw per day
		Offspring toxicity	75 ppm, equal to 4.7 mg/kg bw per day	300 ppm, equal to 21 mg/kg bw per day
	Study of developmental toxicity[c]	Maternal toxicity	4 mg/kg bw per day	30 mg/kg bw per day
		Embryo- and fetotoxicity	4 mg/kg bw per day	30 mg/kg bw per day
	Study of acute neurotoxicity[c]	Neurotoxicity	–	10 mg/kg bw
Rabbit	Study of developmental toxicity[c]	Maternal toxicity	5 mg/kg bw per day	50 mg/kg bw per day
		Embryo- and fetotoxicity	50 mg/kg bw per day	150 mg/kg bw per day
Dog	5-week study of toxicity[a]	Toxicity	125 ppm, equal to 3.8 mg/kg bw per day	400 ppm, equal to 10 mg/kg bw per day
Dog	1-year study of toxicity[a]	Toxicity	125 ppm, equivalent to 3.1 mg/kg bw per day	400 ppm, equal to 10 mg/kg bw per day

[a] Diet
[b] Above the maximum tolerated dose
[c] Gavage

Estimate of acceptable daily intake

0–0.008 mg/kg bw

Estimate of acute reference dose

0.2 mg/kg bw

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

- Study of carcinogenicity in mice
- Studies of the mechanism of formation of vascular tumours in mice[2]
- Further observations in humans

List of relevant end-points for setting guidance values for dietary and non-dietary exposure

Absorption, distribution, excretion, and metabolism in mammals

Rate and extent of oral absorption:	Up to 95% absorption within 24-48 h
Dermal absorption	Slow in rats, 16-34% at low doses, 1.2-4% at high doses within 24 h. In humans, 45% within 8 h after application in acetone
Distribution:	Uniformly distributed; highest concentrations of residues in carcass, kidney, and blood
Potential for accumulation:	None
Rate and extent of excretion:	Rapid and nearly complete within 24 h at low dose, within 48 h at high dose. Mainly via urine (90-95%)
Metabolism in animals	Extensive, with only 2.9% unchanged in urine. Three main metabolic pathways: (i) arene oxide formation with subsequent hydrolysis to dihydrodihydroxycarbaryl and conjugation via the mercapturic acid (ii) carbamate hydrolysis to form 1-naphthol (iii) oxidation of *N*-methyl moiety (alkyl oxidation) The metabolites formed via these pathways were conjugated with sulfate or glucuronic acid.
Toxicologically significant compounds	Parent compound

Acute toxicity

Rat, LD_{50}, oral	220-720 mg/kg bw (pretreatment with carbaryl increased LD_{50}); cats most sensitive species
Rat, LD_{50}, dermal	> 2000 mg/kg bw
Rat, LC_{50}, inhalation	No data
Skin irritation	Classification unknown
Eye irritation	Classification unknown
Skin sensitization	Classification unknown

Short-term toxicity

Target / critical effect	Cholinesterase inhibition; effects on liver
Lowest relevant oral NOAEL	3.8 mg/kg bw per day (5 weeks, dogs)
Lowest relevant dermal NOAEL	No data
Lowest relevant inhalation NOAEL	10 mg/m^3 (90 days, rats)

Genotoxicity	Weight of evidence suggests no genotoxic concern

Long-term toxicity and carcinogenicity

Target/critical effect	Cholinesterase inhibition; liver, kidney, urinary bladder Mice: vascular tumours Rats: thyroid, body weight
Lowest relevant NOAEL	< 15 mg/kg bw per day (2 years, mice, LOAEL) 10 mg/kg bw per day (2 years; rats)
Carcinogenicity	Mice: vascular tumours in males at lowest dietary concentration (15 mg/kg bw per day). At maximum tolerated dose: renal tubular cell-adenoma in males and hepatocellular carcinoma and vascular tumours in females Rats: Thyroid follicular-cell adenoma (males) hepatocellular carcinoma (females), urinary bladder transitional-cell carcinoma (both sexes) at maximum tolerated dose

Reproductive toxicity	
Reproduction target / critical effect	Deaths of pups in F_2 generation at parentally toxic doses (cholinesterase activity not examined) 4.7 mg/kg bw per day
Lowest relevant (reproductive) NOAEL	
Developmental target / critical effect	Rats: decreased fetal body weight, delayed ossification at maternally toxic dose (cholinesterase activity not examined) Rabbits: decreased fetal body weight at maternally toxic dose
Lowest relevant developmental NOAEL	4 mg/kg bw per day (rats)
Neurotoxicity / Delayed neurotoxicity	
Acute; NOAEL	< 10 mg/kg bw; inhibition of cholinesterase activity (rats, single dose) 3.8 mg/kg bw; inhibition of cholinesterase activity (5 weeks, dogs)
90-day; NOAEL	1 mg/kg bw per day; inhibition of cholinesterase activity (rats)
Delayed neuropathy	Negative
Other toxicological studies; observations in humans	No reliable data
Medical data	Several cases of poisoning dominated by symptoms of inhibition of cholinesterase activity

Summary	Value	Study	Safety factor
ADI	0-0.008 mg/kg bw	Mice, carcinogenicity (LOAEL)	2000
Acute reference dose	0.2 mg/kg bw	Dogs, 5 weeks	25

Dietary risk assessment

The theoretical maximum daily intakes from the five GEMS/Food regional diets, on the basis of existing MRLs, represented 300–560% of the ADI (Annex 3). The dietary intake estimates will be refined further during the periodic review of residues of carbaryl.

4.3 CHLORPROPHAM (201)

Residue and analytical aspects

Chlorpropham (isopropyl-3-chlorophenylcarbamate) was reviewed only for toxicology by the JMPR in 1963, 1965 and 2000. The compound was identified as a candidate for evaluation of residues as a new compound by the JMPR 2001 by the CCPR at its Thirtieth Session (1998) (ALINORM 99/24).

Chlorpropham is used as a growth regulator to suppress the post-harvest sprouting of ware potatoes during storage. As a herbicide, it controls a broad spectrum of annual weeds. Only information on its use as a growth regulator for ware potatoes was made available to the Meeting by the Chlorpropham Manufacturers Task Force in the USA. This comprised studies on metabolism in animals and plants, methods of residue analysis, stability of residues in stored analytical samples, uses, results of supervised residue trials under commercial storage conditions and processing data. Information on national trials conducted according to GAP was provided by the governments of Australia and Germany.

Pure chlorpropham is a cream-coloured, crystalline solid of moderate volatility. It has limited solubility in water but is highly soluble in certain organic solvents. The log P_{ow} of 3.4 suggests that bioaccumulation may occur.

The trials summarized below were based on post-harvest use of chlorpropham on stored potatoes only.

Metabolism

Animals

The metabolism of chlorpropham in rats, lactating goats and laying hens is qualitatively similar. In rats, chlorpropham was rapidly absorbed and essentially completely metabolized before excretion in urine and, in small amounts, in faeces. Within 24 h, 82–92% of the radiolabel was recovered in the urine and 3–5% in the faeces. Three major metabolic routes were proposed: (1) hydroxylation at the 4-position and subsequent conjugation with sulfate or glucuronide; (2) oxidation of the isopropyl side-chain to form isopropanol and subsequent formation of isopropionate moieties; and (3) decarbanilation to form 3-chloroaniline followed by *N*-acetylation, 4-hydroxylation and conjugation.

After administration of [^{14}C-ring]chlorpropham in capsules at a dose of 1.6–1.9 mg/kg bw (32–36 ppm in the feed) to two lactating goats for 7 days, rapid absorption and elimination *via* urine and faeces were seen (about 99%). About 1% was transferred to milk and liver, and one or two orders of magnitude less to fat and muscle. The goats metabolized chlorpropham readily. The main metabolic pathways included hydroxylation at the 4-position and subsequent formation of conjugates of sulfate or glucuronide. The main residue in the milk and kidney was the metabolite 4-hydroxy-chlorpropham-*O*-sulfonic acid (81% and 16% of TRR, respectively), while the main residue in fat tissues was chlorpropham (88% of TRR).

In laying hens receiving a daily dose of 6 mg [^{14}C-ring]chlorpropham by capsule (3.3–4.2 mg/kg bw or 50 ppm in the feed) for 7 days, 83% of the cumulative dose was recovered from excreta and only 0.03% from the egg production. The maximum concentrations of residues were 0.07 mg/kg in egg white and 0.23 mg/kg in egg yolk. The concentrations of TRR in tissues and organs were low (~0.5 mg/kg in liver and kidneys, ~0.2 mg/kg in fat and skin; 0.015 and 0.006 mg/kg in thigh and breast muscle, respectively). Chlorpropham was the main residue in hen fat and skin (92% and 68% of TRR, respectively), while the main residues in liver and kidney were 3-chloro-4-hydroxyaniline conjugates (25–64%). The *O*-sulfonic acid conjugate of 3-chloro-4-hydroxyaniline was the main compound in eggs (22% of TRR).

Plants: potato

Studies on metabolism and residues in crops other than potato were not provided. Translocation and formation of metabolites in potatoes were investigated after treatment by surface coating with [^{14}C-ring]chlorpropham and simulation of cold-storage conditions. Translocation was slow; approximately 86% of the TRR still being present in the surface methanol-wash fraction as chlorpropham after 52 weeks of storage. About 10% of TRR was recovered from the peel and about 3% from the pulp, mainly as unchanged chlorpropham.

The main metabolite in peel was an oligosaccharide of 4-hydroxy-chlorpropham. 3-Chloroaniline was the second main metabolite in peel. It was not identified as a free metabolite in pulp but in conjugated form, as 3-chloroaniline-*N*-glucosylamine (6% of TRR in pulp). The main metabolites in pulp,

both representing about 18% of TRR, were an oligosaccharide and an amino acid conjugate of 4-hydroxy-chlorpropham. About 10% of TRR in peel and pulp was not extractable. Three potential metabolic pathways in plants were proposed:

- hydroxylation and subsequent conjugation with glucose, oligosaccharides or amino acids at the 4-position (*para* to the amino moiety) or conjugation of 4-hydroxy-chlorpropham with a methyl moiety to *para*-methoxy-chlorpropham or to an *S*-cysteinyl-hydroxy-chlorpropham;
- decarbanilation to 3-chloroaniline, followed by conjugation with glucose and other biomolecules;
- oxidation of the isopropyl chain and subsequent conjugation with oligosaccharide(s).

Methods of analysis

Plant matrices: potato

Most of the methods submitted for the analysis of chlorpropham residues in potato involved homogenization with an organic solvent (e.g. methanol, petroleum ether/acetone, hexane/acetone) followed by partition into dichloromethane. For further purification of the extract, an adsorbent column (e.g. florisil) can be used. Chlorpropham is determined by GLC–NPD or after bromination as the bromo derivative by GLC–ECD. The LOQ was validated as 0.02 mg/kg.

Methods for the determination of chlorpropham and its three metabolites 3-chloroaniline, 4-hydroxy-chlorpropham and *para*-methoxy-chlorpropham in potato and potato products were submitted. They involved methanol/water as the primary extraction solvent, sometimes acid or alkaline hydrolysis and sonication for splitting conjugates, with subsequent clean-up by liquid–liquid partition with other organic solvents or phosphate buffer. For oil-processed samples, GPC clean-up follows. Determination was made by GLC–NPD. The methods have been validated for analysis of the parent compound and metabolites in whole potato, fresh peel and pulp, fries with and without skins, canola oil, potato chips with and without skins, processed dried peels, processed wet peels and dehydrated granules.

The recoveries of chlorpropham, 4'-hydroxy-chlorpropham and *para*-methoxy-chlorpropham were satisfactory. 3-Chloroaniline was recovered from fortified samples of varying consistency (40–70% from whole potato, pulp, peel with a fortification level of 0.4 mg/kg), as a large proportion of the aniline moiety can remain bound on biological material and occur as e.g. *N*-glucosyl or *N*-malonyl conjugates. Therefore, for each batch of samples from supervised trials, three untreated samples of each matrix were extracted, two of which were fortified with chlorpropham and the three metabolites to document recovery levels. The third sample served as a blank matrix to monitor contamination and interfering background matrix. Furthermore, matrix-based calibration standards were used. The method detection limits (MDL) and the LOQ for chlorpropham, 3-chloroaniline, *para*-hydroxy-chlorpropham and *para*-methoxy-chlorpropham (MDL / LOQ) were:

- 0.08 / 0.45 mg/kg in whole potato, fresh pulp, fresh peel and processed wet peel,
- 0.2 / 1.1 mg/kg in fries,
- 0.45 / 2.2 mg/kg in chips,
- 0.38 / 1.9 mg/kg in dehydrated granules and processed dried peel,
- 2.9 / 14 mg/kg in canola oil.

Animal matrices

The parent and the metabolite -hydroxy-chlorpropham-*O*-sulfonic acid cannot be determined together in ruminant matrices. The method for chlorpropham involves solid phase matrix dispersion followed by

GLC–MS detection. The recoveries of the lowest fortification level of 0.01 mg/kg in whole milk, liver, muscle, kidney and fat were about 200% in some cases. Therefore, the LOQ for chlorpropham achievable in whole milk, skim milk and cream should be 0.05 mg/kg and that for liver, muscle, kidney and fat should be 0.1 mg/kg.

4-Hydroxy-chlorpropham-*O*-sulfonic acid is determined in whole and skim milk by dilution with acetonitrile, selective precipitation of interfering substances and analysis by reversed-phase HPLC with UV detection. In tissues and cream, 4-hydroxy-chlorpropham-*O*-sulfonic acid is isolated by solid phase extraction and is determined by reversed-phase HPLC and UV detection. The achievable LOQ for this metabolite in whole milk, skim milk, cream, liver, muscle, kidney and fat is 0.05 mg/kg.

Stability of residues in stored analytical samples

Plant matrices: potato

A study of stability in freezer storage at –20 to –21 (C with fresh whole tubers, pulp and peel and processed potato products (chips, fries, dehydrated granules, processed wet and dried peel), fortified at two levels with chlorpropham or one of the metabolites 3-chloroaniline, 4-hydroxy-chlorpropham or *para*-methoxy-chlorpropham, showed that 3-chloroaniline and 4-hydroxy-chlorpropham were unstable in whole potatoes, potato pulp and potato peel after 90 days of storage. 3-Chloroaniline was also unstable in processed wet peels. The low initial recoveries of these analytes and their instability in fresh products may be due to bioreactivity with the potato matrix. An acceptable stability of 5–6 months' storage was found for chlorpropham and *para*-methoxy-chlorpropham.

Animal matrices

Cow liver, muscle and milk were fortified with 0.1 mg/kg chlorpropham and 4′-hydroxy-chlorpropham-*O*-sulfonic acid and stored at –20 °C. There was no significant degradation of either compound in any of the matrices over the storage period: chlorpropham, 28 days in liver, 59 days in muscle and 127 days in milk; 4-hydroxy-chlorpropham-*O*-sulfonic acid, 59 days in liver, 122 days in muscle and 133 days in milk.

Definition of the residue

Plant material

Studies of metabolism in stored potatoes established that most of the radiolabel was in the peel (10% of the applied amount after washing) and only a small proportion (3% of the applied amount) in the pulp. Most of the residue in the peel consisted of chlorpropham (85%) and only a minor part (3.5%) was 3-chloroaniline. Chlorpropham made up 42% of the residue in pulp.

In a supervised trial with stored potatoes, the only metabolite detected was 3-chloroaniline, less than 2% of the residue consisting of chlorpropham. Residues of *para*-methoxy-chlorpropham and (conjugates of) 4-hydroxy-chlorpropham were not detected.

The 2000 JMPR identified 3-chloroaniline as a toxicologically significant compound, apart from the parent chlorpropham. As 3-chloroaniline forms only a minor part of the residue, the Meeting agreed that residues in potatoes can be defined as chlorpropham *per se* for enforcement and risk assessment purposes.

Animal products

Studies of metabolism were carried out in rats, goats and hens. Chlorpropham was rapidly and virtually completely absorbed, extensively metabolized and rapidly excreted in both domestic animals and rats. As potatoes are a minor feed item for chicken (< 10% of feed, see *FAO Manual*, p. 125), the Meeting focused on the study of metabolism in goats.

The main residue in milk and kidney of goats was the low-fat-soluble metabolite 4-hydroxy-chlorpropham-*O*-sulfonic acid (81% and 16% of measured TRR), while the fat-soluble chlorpropham was the main residue in fat (88%). No methods of analysis are available to determine the two residues simultaneously. As the metabolite was considered to be of no toxicological significance by the 2000 JMPR, the Meeting agreed that the residue definition for animal products for compliance with the MRL and dietary risk assessment should be chlorpropham only.

The presence of chlorpropham in fat and cream but not in muscle or skim milk in the feeding study in dairy cows and its log P_{OW} of 3.4 imply solubility in fat. The Meeting agreed that the residue is fat-soluble.

Fate of residues during storage

Chlorpropham is registered in the USA for post-harvest treatment on potato as an emulsifiable concentrate used by direct spray of a 1% aqueous emulsion on potato tubers moving along a conveyor line or as an aerosol fog at a standard application rate of 0.015 kg ai/t. The rate should be adapted to the storage period and temperature. Re-treatments can be made with one of the following regimens:

- aerosol fog at 0.02 kg ai/t at each of two applications 90 days apart, followed by direct spray at 0.01 kg ai/t, or
- aerosol fog at 0.03 kg ai/t and a second aerosol fog at 0.015 kg ai/t 140 days later.

A withholding period in days was not identified.

Extensive data were provided from a supervised trial in the USA on various treatment schedules on ware potatoes stored in bins. Each bin had its own air ventilation, refrigeration unit and computer-controlled monitoring system for accurate measurement of sampling pile conditions. The bins, each containing approximately 63.5 t of potatoes, were designed to allow access for tuber sampling during storage. Industry standards for relative humidity and temperature with continuous air flow were followed. Each bin was fogged with aerosol separately. Each bin was therefore considered as a separate trial. Furthermore, applications carried out at different times and different rates were considered separate treatments and equal a separate trial. The residue values used for evaluation were selected as either the highest value of the six samples taken from each bin or, in the case of a decline study, only one value (the highest) was selected. The concentrations of residues of chlorpropham in whole unwashed tubers resulting from various treatments according to GAP were:

Treatment (kg ai/t potatoes)	Residues (mg/kg)	Time after initial treatment (days)
1 x EC direct spray 0.01	8.2	0
1 x aerosol fog 0.02 + 1 x EC direct spray 0.01	9.1, 9.3, 9.4, 11	5, 91, 96
1 x aerosol fog 0.02	8.7, 8.9	5
1 x aerosol fog 0.03	16, 23	5,
2 x aerosol fog 0.02	9.9, 18	96, 140
1 x aerosol fog 0.03 + aerosol fog 0.015	14, 16	145

2 x aerosol fog 0.02 + 1 x EC direct spray 0.01	8.2, 9.7, 11, 11, 13, 14	96, 140, 215

The concentrations, in ranked order (median underlined), were: 8.2 (2), 8.7, 8.9, 9.1, 9.3, 9.4, 9.7, 9.9, 11 (3), 13, 14 (2), 16 (2), 18 and 23 mg/kg.

Chlorpropham is registered in Belgium, France and Germany for spraying, dusting or hot fogging of ware potatoes at 0.01–0.02 kg ai/t without a withholding period in days. The same treatment rates are registered in The Netherlands, with a withholding period of 60 days. The potatoes can be stored in boxes or in bulk.

One trial carried out in France in 1998 (1 x 0.007 + 1 x 0.006 kg ai/t, pile from pallox) and one trial from Belgium in 1997 (1 x 0.015 kg ai/t, manual treatment of potatoes in paper bags) resulted in maximum residue concentrations of 8.8 and 13 mg/kg. The tubers were not washed before freezing of the analytical samples.

Treatment of potatoes stored in boxes was investigated in several trials, in which some of the potatoes were washed and some were washed and peeled after sampling. Seven trials in Belgium (1997) with hot fogging application of 1 x 0.007 kg ai/t plus 1 x 0.006 kg ai/t resulted in values of 0.61, 0.85, 0.89, 0.96, 1.1 and 1.2 (2) mg/kg. Seven trials in Germany in 1998 (dusting, 1 x 0.015 kg ai/t) resulted in concentrations of 0.06, 0.11, 3.5 (2), 3.8, 4.3 and 4.9 mg/kg. Four trials carried out in Germany in 1996 and 1999 with powdering of 1 x 0.01 kg ai/t, resulted in values of 1.7, 1.9, 2.0, 2.5, 2.5, 3.0, 3.0 and 3.2 mg/kg. The concentrations in washed whole potato tubers were, in ranked order (median underlined), 0.61, 0.85, 0.89, 0.96, 1.1, 1.2 (2), 1.7, 1.9, 2.0, 2.5 (2), 3.0 (2), 3.1, 3.2, 3.5 (2), 3.8, 4.3, 4.8 and 4.9 mg/kg.

The data on residues received from the European studies of box-stored, washed potatoes are different from those from the study of bin storage of unwashed tubers in the USA. The MRL, STMR and highest residues were derived from the USA data on unwashed potatoes and the two trials with unwashed potatoes in France and Belgium. The residue concentrations, in ranked order, were: 8.2 (2), 8.7, 8.8, 8.9, 9.1, 9.3, 9.4, 9.7, 9.9, 11 (3), 13 (2), 14 (2), 16 (2), 18 and 23 mg/kg.

The Meeting estimated a maximum residue level of 30 mg/kg, a STMR value of 11 mg/kg and a highest residue of 23 mg/kg for ware potatoes.

Fate of residues during processing

No information on the fate or nature of the residue after hydrolysis under cooking conditions was submitted.

Cooked potatoes were prepared from one fresh whole tuber sample containing 4.6 mg/kg chlorpropham. The concentration of residues decreased to 0.24 mg/kg in peeled fresh potatoes and to 0.08 mg/kg in peeled cooked potatoes after cooking for 20 min. Cooking reduced the value to 33% (processing factor, 0.33). From the STMR and the HR values for fresh ware potatoes of 11 and 23 mg/kg, an STMR-P value of 3.6 mg/kg and an HR-P value of 7.6 mg/kg were calculated for cooked potatoes with skin.

Cooked and peeled potatoes: The median processing factor for chlorpropham on raw peeled potatoes, based on 166 samples, was 0.027. Application of this factor to the STMR of 11 mg/kg and the HR of 23 mg/kg for raw ware potatoes provided a median value of 0.297 mg/kg and a highest residue of 0.62 for raw peeled potatoes. With the processing factor for cooking (0.33), a STMR-P value of 0.098 mg/kg and a HR-P value of 0.2 mg/kg were calculated for cooked potatoes without skin.

An adequate, extensive study of potato processing by standard industrial procedures provided information on the distribution of residues of chlorpropham and 3-chloroaniline in whole potato, pulp and peel, chips, and frozen and dehydrated products. Processing factors could be derived for fresh peeled potato and fresh peel, but not for chips, fries, dehydrated granules or processed peel, as different samples were used for the determination of residues in the raw agricultural commodity and in the processed product. For this reason, the concentrations used for evaluation of chips, fries, dehydrated granules and processed peel were selected from the data in trials conducted according to GAP.

Chips[1]: The concentrations of chlorpropham residues in chips with and without skin were 0.82, 1.2, 1.5 (2), 1.7, 1.9, 3.8, 4.0, 4.1, 4.2, 4.4, 4.6 (3), 5.0, 5.3, 6.3 (2), 6.4, 7.0, 7.1, 7.9 and 8.1 mg/kg and < 0.045 (11), 1.1, 1.2, 1.3, 1.4 (3), 1.5 (4), 1.6 and 1.8 mg/kg. The Meeting estimated STMR-P values of 4.6 and 1.1 mg/kg for chips with and without skin, respectively.

Fries[1]: The concentrations of chlorpropham residues in fries with and without skin were 0.97, 1.1, 1.2 (2), 1.3 (2), 1.4 (5), 1.5 (3), 1.6 (5), 1.7, 1.9, 2.0 (3), 2.1 (2), 2.2 (3), 2.3 (2), 2.6 (2), 2.7, 2.8 and 4.0 mg/kg and < 0.2 (20), 0.23, 0.28 (2), 0.29, 0.31, 0.32, 0.33, 0.34 (2), 0.35, 0.36, 0.37 (2), 0.4, 0.41 and 0.54 mg/kg, respectively. The Meeting estimated STMR-P values of 1.6 and 0.2 mg/kg for fries with and without skin, respectively.

Dehydrated granules[2]: The concentrations of residues in dehydrated granules were < 0.38 (3), 0.41, 0.57, 0.63, 0.64, 0.65, 0.67, 0.69 (2), 0.71, 0.75 (3), 0.76, 0.81, 0.82, 0.87 (2), 0.91, 0.95, 0.96, 1.0, 1.1, 1.2 (3), 1.3, 1.4, 1.5 (3), 1.6, 1.9 and 2.1 mg/kg. The Meeting estimated an STMR-P value for chlorpropham of 0.845 mg/kg in dehydrated granules.

Potato peel, processed[2]: The concentrations of residues in industrially produced wet peel were 10, 11, 12, 13, 14 (5), 15 (3), 17 (4), 19, 21, 26 (3), 30, 31 (3), 32, 33 (2), 34 (2), 35 (2), 41, 42, 43 and 45 mg/kg The Meeting estimated an STMR-P value of 23.5 mg/kg for processed potato wet peel.

Residues in animal commodities

The Meeting estimated the dietary burden of chlorpropham and 3-chloroaniline in farm animals on the basis of the feeds listed in Appendix IX of the *FAO Manual.* The Meeting agreed to use only the STMR value for calculation of the dietary burden from processed animal feed as wet potato peel. It is suitable for estimating MRLs and HRs for animal commodities.

Dietary burden of chlorpropham

Commodity	Residue (mg/kg)	Basis	Dry matter (%)	Residue, dry weight (mg/kg)	Choose diets (%)			Residue contribution (mg/kg)		
					Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cows	Poultry
Potato wet peel, processed	23.5	STMR-P	15	157	75	40	–	118	63	–

The dietary burden of chlorpropham in ruminant commodities (expressed as dry weight) used to estimate the MRL and STMR value was 118 mg/kg for beef cattle and 63 mg/kg for dairy cows.

In a 28-day study of cows given chlorpropham by capsule at a level equivalent to 0, 322, 955 or 3111 ppm in the feed (dry weight basis), only minor concentrations of chlorpropham residues (< 0.01–0.06 mg/kg) were found in milk at the highest level tested. The concentrations of the metabolite 4-hydroxy-chlorpropham-*O*-sulfonic acid (calculated as chlorpropham) were higher and roughly proportional to the feeding level, ranging from 0.1 to 0.61 mg/kg at the lowest level to 0.37–6.7 mg/kg at the highest level. Chlorpropham residues could not be detected in skim milk, but in cream the concentrations were 0.02–0.03 at the lowest level and 0.21–0.64 at the highest level. The residues of 4-hydroxy-chlorpropham-*O*-sulfonic acid were nearly equally distributed in skim milk and cream, the concentrations (calculated as chlorpropham) being 1.9–3.9 mg/kg and 1.7–3.6 mg/kg, respectively, in the group given the highest dose.

Minor concentrations of parent chlorpropham were found in muscle, liver and kidney. In the group at the highest level, the maximum values were 0.02 mg/kg in liver and kidney and 0.1 mg/kg in muscle. In fat, the chlorpropham residue values were 0.1–0.13, 0.19–0.39 and 0.15–2.8 mg/kg at the lowest, intermediate and highest level, respectively. Residues of 4-hydroxy-chlorpropham-*O*-sulfonic acid (calculated as chlorpropham) were found predominantly in kidney, with concentrations of 0.12–0.26 mg/kg, 0.76–1.2 mg/kg and 1.0–2.3 mg/kg at the three levels, respectively. No residues of the metabolite were detected (< 0.03 mg/kg) in muscle or fat. In liver, it was found only in cows at the highest level, at a maximum of 0.06 mg/kg.

The MRL and the STMR value for chlorpropham in milk were calculated from the interpolated dietary burden of 63 mg/kg (based on the STMR) for dairy cows; and the MRLs and the STMRs for meat, liver and kidney were derived from the dietary burden of 118 mg/kg for beef cattle. The interpolation is based on the actual concentration of residue in the group at the lowest level (322 ppm). As the compound is fat-soluble, the maximum residue level and the STMR value for milk were based on the concentrations of residue in cream. The following table shows the highest and the mean actual and interpolated residues used for estimating MRLs and STMR values for chlorpropham.

Feeding level (ppm) *Interpolated* / Actual	Chlorpropham residues (mg/kg)								
	Cream (mean)	Liver		Kidney		Muscle		Fat	
		High	Mean	High	Mean	High	Mean	High	Mean
MRL Beef cattle *118* / 322		*0.007* / 0.02		*< 0.004* / < 0.01		*0.004* / 0.01		*0.048* / 0.13	
STMR Beef cattle *118* / 322			*0.005* / 0.013		*< 0.004* / < 0.01		*< 0.004* / < 0.01		*0.04* / 0.11
MRL Dairy cows *63* / 322	*0.006* / 0.03								
STMR Dairy cows *63* / 322	*0.006* / 0.03								

The Meeting estimated maximum residue levels for chlorpropham of 0.0005* mg/kg F for milk, 0.01* mg/kg for edible offal of cattle and 0.1 mg/kg (fat) for cattle meat. The estimated STMR values are 0.0002 mg/kg for cattle milk, 0.005 mg/kg for edible offal of cattle and 0.004 mg/kg for cattle meat. The estimated highest residues are 0.007 mg/kg for edible offal of cattle and 0.004 mg/kg for cattle meat.

Further work or information

Desirable

1. A study on hydrolysis with radiolabelled chlorpropham to clarify the effect of cooking on the nature of residues (Annex 5, reference 86, pp. 12–15)
2. Processing studies on cooked potatoes with skin and for microwaved and oven-baked potatoes

Dietary risk assessment

Long-term intake

STMR or STMR-P values for chlorpropham were estimated by the Meeting for animal products, potatoes and six processed potato commodities. When data on consumption were available, these values were used to estimate dietary intake. The results are shown in Annex 3.

The IEDIs, based on the estimated STMR values, were 1–50% of the ADI for the five GEMS/Food regional diets. The Meeting concluded that long-term intake of residues of chlorpropham from use on potatoes is unlikely to present a public health concern.

Short-term intake

The IESTI for chlorpropham was calculated for animal products and for potatoes (and their processing fractions) for which maximum residue levels and STMR values were estimated and for which data on consumption were available. The results are shown in Annex 4.

The 2000 JMPR established an acute RfD of 0.03 mg/kg bw, on the basis of a NOAEL of 10 mg/kg bw per day in a 90-day study of toxicity in rats and a safety factor of 300. This value includes an additional safety factor of 3 to take account of inadequacies in the assessment of methaemoglobinaemia, the critical toxicological effect. The current Meeting stated that the assessment of acute risk might require refinement of the acute RfD by submission of new studies that more appropriately address the end-point of concern.

The IESTI represented 0–1600% of the acute RfD for the general population and 0–4600% of the acute RfD for children. The values of 510 and 1500% represent the estimated short-term intake of cooked potatoes with skin. Peeling and cooking of potatoes reduced the concentration of chlorpropham residue, resulting in IESTIs of 10% of the acute RfD for the general population and 40% of the acute RfD for children. The Meeting concluded that short-term intake of chlorpropham residues is unlikely to present a public health concern, when peeled potatoes are consumed.

4.4 CHLORPYRIFOS-METHYL (090)

Toxicology

Chlorpyrifos-methyl was evaluated by previous Joint Meetings, in 1975, 1991, and 1992. An ADI of 0–0.01 mg/kg bw was established in 1992 on the basis of a NOAEL of 0.1 mg/kg bw per day (the highest dose tested) in a 4-week study in volunteers, supported by a NOAEL of 1 mg/kg bw per day for inhibition of brain acetylcholinesterase activity and increased vacuolation of the adrenal zona fasciculata in a 2-year

study in rats at 50 mg/kg bw per day. The Codex Committee on Pesticide Residues recommended that chlorpyrifos-methyl be re-evaluated for possible establishment of an acute RfD.

Chlorpyrifos-methyl is a weak inhibitor of acetylcholinesterase in vivo, and its toxicologically relevant effects are associated with inhibition of nervous system acetylcholinesterase activity and vacuolation of the adrenal zona fasciculata. The latter effect was observed in rats and mice given repeated doses that also inhibited brain acetylcholinesterase activity. Chlorpyrifos-methyl was not acutely toxic, and, in the most recent studies, the LD_{50} in rats treated orally was ≥ 3000 mg/kg bw, with signs of cholinergic toxicity at doses ≥ 2000 mg/kg bw. WHO has classified chlorpyrifos-methyl as "unlikely to present acute hazard". With repeated (3 months to 2 years) dosing, inhibition of brain acetylcholinesterase activity not associated with cholinergic signs occurred at 41, 50, and 50 mg/kg bw per day in mice, rats, and dogs, respectively.

The Meeting also observed that dimethylphosphorylated acetylcholinesterase, resulting from interaction with the active metabolite chlorpyrifos-methyl-oxon, has a significant rate of spontaneous reactivation.

While chlorpyrifos-methyl is potentially neurotoxic, the Meeting concluded that, in view of its neligible acute toxicity and in the absence of other relevant acute end-points, including developmental toxicity, allocation of an acute RfD was unnecessary. The effects on brain acetylcholinesterase in studies with repeated doses were considered not relevant for establishing an acute RfD, because a number of doses were required to cause sufficient cumulative inhibition to result in a significant effect.

A toxicological monograph was not prepared.

4.5 2,4-D (20)

Residue and analytical aspects

2,4-D was evaluated for residues in a periodic review by the JMPR in 1998, and many MRLs were recommended. In the case of citrus fruits, the JMPR estimated a maximum residue level of 0.1 mg/kg for grapefruit and orange on the basis of four supervised trials conducted according to minor pre-harvest use as a plant growth regulator, and recommended withdrawal of the current CXL of 2 mg/kg for citrus fruit.

The CCPR at its Thirty-second session in 2000 decided to retain the CXL for citrus fruits, as the Delegations of South Africa, Uruguay and the USA preferred to do so in order to accommodate post-harvest use. The Delegation of Spain also preferred the CXL to MRLs for individual commodities. Spain and the USA informed the CCPR that the results of additional trials would become available for the JMPR. The Netherlands and South Africa disagreed with evaluation of data for the proposed separate MRLs for orange and grapefruit (ALINORM 01/24).

The 2001 JMPR received information on trials conducted in Uruguay and the USA on citrus fruit by GAP and on supervised trials for post-harvest use of 2,4-D on lemon and orange.

Residues of supervised trials

(2,4-Dichlorophenoxy)acetic acid isopropyl ester (2,4-D IPE) is currently registered and is applied after harvest to commercial citrus species in order to inhibit abscission of buttons on harvested fruit in Uruguay (grapefruit, orange, mandarin, lemon) and in the USA (lemon). The solutions of 2,4-D IPE can be applied as a treatment in a water–wax emulsion in packing houses or as a diluted flush or spray.

The 1998 JMPR evaluated two post-harvest trials on lemon in California conducted according to current GAP in Uruguay and the USA. The concentrations of residues in whole fruit were 0.54 and 0.61 mg/kg.

Post-harvest treatments were made to navel oranges (six trials) and lemons (four trials) with experimental packing-line equipment at a research centre in California in 2001. Applications were made in accordance with current label requirements in Uruguay and the USA at maximum rates. Commercial application and fruit handling practices were followed. The fruit was sprayed with 2,4-D IPE solution containing 0.05 kg ai/hl (2,4-D acid equivalent, 0.04 kg ai/hl). The concentrations of residues on whole orange fruit were, in ranked order (median underlined), 0.19, 0.2, <u>0.21</u> (2), 0.22 and 0.24 mg/kg. The concentrations on whole lemon fruit were, in ranked order, 0.37, 0.41, 0.44 and 0.6 mg/kg.

The Meeting acknowledged that the data for oranges (median, 0.21 mg/kg) and lemon (median, 0.49 mg/kg) were different. However, on the basis of Uruguayan use on orange, grapefruit, mandarin and lemon, the Meeting decided to recommend an MRL for citrus fruits based on the whole data set. The concentrations on whole fruit after post-harvest treatment of oranges and lemon were, in ranked order, 0.19, 0.20, 0.21 (2), 0.22, <u>0.24</u>, <u>0.37</u>, 0.41, 0.44, 0.54, 0.60 and 0.61 mg/kg. The Meeting estimated a maximum residue level of 1 mg/kg for citrus fruit. As no data were submitted for the edible portion, the Meeting estimated an STMR value of 0.3 mg/kg, based on the residues in whole fruit.

Fate of residues during processing

The 1998 JMPR estimated processing factors of 0.1 for citrus juice and < 1 for citrus oil. The Meeting applied these factors to the STMR value of 0.3 mg/kg for citrus fruit and estimated STMR-P values of 0.03 mg/kg for citrus juice and 0.3 mg/kg for citrus oil.

Dietary risk assessment

Long-term intake

STMR or STMR-P values for 2,4-D were estimated by the current Meeting for citrus fruits and the processed commodities citrus juice and oil. Further STMR or STMR-P values were estimated by the 1998 JMPR for 22 commodities. When data on consumption were available, these values were used to estimate dietary intake. The results are shown in Annex 3.

The IEDIs for the five GEMS/Food regional diets, based on the estimated STMRs, were 3–20% of the ADI. The Meeting concluded that long-term intake of residues of 2,4-D from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The 2001 JMPR concluded that it was unnecessary to establish an acute RfD for 2,4-D. The Meeting therefore concluded that the short-term intake of 2,4-D residues is unlikely to present a risk to consumers.

4.6 DIAZINON (022)

Toxicology

Diazinon was evaluated by the Joint Meeting in 1963, 1965, 1966 and 1970. In 1966, an ADI of 0–0.002 mg/kg bw was allocated on the basis of a NOAEL of 0.02 mg/kg bw per day in a study with volunteers and a 10-fold safety factor. Diazinon was last reviewed by the 1993 JMPR, when the ADI of 0–0.002 mg/kg bw was reaffirmed. The present review was undertaken to consider the need for establishing an acute RfD.

Diazinon is an organophosphate, and virtually all its toxicological effects are attributable to anticholinesterase activity.

The oral LD_{50} of diazinon in mice and rats was ≥ 200 mg/kg bw. Diazinon has been classified by the WHO as 'moderately hazardous'.

After preliminary studies to establish the time course of clinical signs and cholinesterase inhibition, a study of acute neurotoxicity in rats was undertaken. This study involved a two-phase protocol. In phase 1, clinical observations were made, but plasma, erythrocyte, and brain cholinesterase activity were not measured. The doses used were 100, 250, and 500 mg/kg bw for males and 25, 50, 100, 250 and 500 mg/kg bw for females. In phase 2, wider ranges of doses were used (0.05–500 mg/kg bw for males and 0.05–250 mg/kg bw for females), and plasma, erythrocyte, and brain cholinesterase activity were estimated. The NOAEL was 2.5 mg/kg bw in females and 100 mg/kg bw in males on the basis of inhibition of brain cholinesterase activity. The LOAELs were 25 mg/kg bw in females and 500 mg/kg bw in males.

A preliminary report was available of a study in male volunteers given ascending single doses of diazinon in gelatine capsules, both the volunteers and the investigators being unaware of who had received diazinon or placebo. Plasma cholinesterase activity was inhibited by > 20% at doses (0.12 mg/kg bw. Erythrocyte cholinesterase activity was not inhibited. The NOAEL was 0.21 mg/kg bw, the second highest dose studied; the highest dose was ignored as the group comprised a single volunteer.

After considering the previous evaluation of diazinon and the new data submitted, the Meeting established an acute RfD of 0.03 mg/kg bw. This was based on the NOAEL of 2.5 mg/kg bw in the studies of acute neurotoxicity in rats and a 100-fold safety factor. The study in male volunteers was considered of limited value in establishing the acute RfD, as the studies in rats provided evidence of a considerable sex difference in sensitivity to the inhibition of acetylcholinesterase activity by diazinon.

An addendum to the toxicological monograph was prepared.

Dietary risk assessment

Short-term intake

The IESTI for diazinon was calculated for the commodities for which MRLs have been recommended, for which STMR and highest residue values have been estimated and for which data on consumption of large portion sizes and unit weights were available. The results are shown in Annex 4.

The calculated short-term intakes were less than 100% of the acute RfD for children and for the general population. The Meeting concluded that the intake of residues of diazinon resulting from uses that have been considered by JMPR is unlikely to present a public health concern.

4.7 DIFLUBENZURON (130)

Toxicology

Diflubenzuron [1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl)urea] is an insecticide that acts by disrupting chitin synthesis and deposition. The toxicity of diflubenzuron was evaluated by the JMPR in 1981, 1984, and 1985; an ADI of 0–0.02 mg/kg bw was established at the latter Meeting. This ADI was maintained by a 1994 WHO Core Assessment Group that prepared Environmental Health Criteria 184. The present Meeting considered both studies performed since the last review and older re-submitted data.

Diflubenzuron administered orally is absorbed to a limited extent in mice, rats, and cats, the extent of absorption decreasing with increasing dose, from about 30% at 5 mg/kg bw to < 5% at 100 mg/kg bw in rats. The rate of absorption is rapid, with peak blood concentrations of radiolabel at about 4 h in rats given 5 mg/kg bw per day. The highest concentrations were found initially in liver and fat; at 7 days, significant concentrations of radiolabel remained in liver (170 ng equivalents/g) and erythrocytes (200 ng equivalents/g). The concentration of radiolabel in plasma of rats given 5 mg/kg bw fell from about 700 ng equivalents/g at 4 h to 3 ng equivalents/g on day 7. Excretion was rapid, 80-98% of the dose being excreted within 24 h. Absorbed diflubenzuron was excreted primarily in urine, with involvement of biliary excretion and enterohepatic circulation.

Studies of the metabolism of diflubenzuron in rats showed inconsistent results, the reasons being unclear. Unchanged diflubenzuron was the only component excreted in significant quantities in faeces. The results of urinary analyses indicated that absorbed diflubenzuron is metabolized extensively before excretion in the urine. The primary metabolic steps are hydroxylation of the anilino ring, cleavage of the ureido bridge, and conjugation, mainly with sulfate.

4-Chlorophenylurea, a residue of diflubenzuron that occurs in rice, has not been detected in significant quantities in studies of metabolism in rats. Its toxicity has thus not been assessed in the studies with diflubenzuron in mammalian systems. After oral administration, 4-chlorophenylurea is both absorbed to a greater extent (about 95%) and is more acutely toxic than diflubenzuron, with an LD_{50} of 1100 mg/kg bw. The Meeting considered that 4-chlorophenylurea should be considered for inclusion in the residue definition.

Another plant metabolite, diflurobenzoic acid, does occur in significant quantities in rats and has acute toxicity after oral administration similar to that of diflubenzuron (LD_{50}, 4600 mg/kg bw). Its toxicity was therefore considered to be assessed in studies with diflubenzuron.

4-Chloroaniline has been reported to be a minor metabolite of diflubenzuron in plants, but did not appear to be a metabolite in rats in the most recent study. 4-Chloroaniline has been reported to produce tumours in rats and mice at a dose of about 3 mg/kg bw per day and to give positive responses in some assays for genotoxicity in vitro (Environmental Health Criteria 184). The Meeting concluded that it had insufficient information to assess the toxicity of 4-chloroaniline.

The LD_{50} of diflubenzuron administered orally was > 4600 mg/kg bw in mice and rats; WHO has classified diflubenzuron as “unlikely to present an acute hazard in normal use”. Diflubenzuron also had little toxicity in rats exposed dermally, with an LD_{50} of > 10 000 mg/kg bw, or by inhalation, with an LC_{50} > 2.8 mg/l of air. No clinical signs were seen in these studies. A single dose of 10 000 mg/kg bw of a 25% w/w formulation of diflubenzuron given by gavage to mice and rats induced a slight (less than two-fold) but statistically significant increase in methaemoglobin concentration. Those of sulf-haemoglobin and Heinz bodies were unaffected. Diflubenzuron did not significantly irritate the skin or eyes of rabbits and did not irritate the skin of guinea-pigs exposed in a Magnusson and Kligman 'maximization' study.

Diflubenzuron showed a consistent profile of toxicity after repeated oral administration to mice, rats, and dogs. In agreement with the studies of the distribution of radiolabel, the primary target of the toxicity of diflubenzuron was erythrocytes. The mechanism of the haematotoxicity of diflubenzuron has not been elucidated, but haematotoxicity is a common finding with pesticides like diflubenzuron that are transformed to halogenated phenylamido derivatives. The most sensitive early end-point was increased concentrations of methaemoglobin and sulf-haemoglobin. The Meeting concluded that, because methaemoglobinaemia and sulf-haemoglobinaemia occurred only after saturation of reduction processes, it was more appropriate to use the statistical significance and dose-response relationships in a study rather than to set a numerical cut-off for adversity. The NOAELs for methaemoglobin and sulf-haemoglobin were dietary concentrations equal to 1.2 mg/kg bw per day for mice, equivalent to 2 mg/kg bw per day for rats, and 2 mg/kg bw per day for dogs. Reduced erythrocyte counts and volume fractions were associated with the increases in methaemoglobin and sulf-haemoglobin. Heinz bodies were seen at doses > 32 mg/kg bw per day in mice and > 50 mg/kg bw per day in dogs, but were not seen in rats. The haematological effects showed both time-related and dose-related trends, the NOAEL for methaemoglobinaemia in dogs being > 250 mg/kg bw per day at 4 weeks, 50 mg/kg bw per day at 13 weeks, and 2 mg/kg bw per day at 26 weeks. The only clinical sign of note was blue-grey extremities in mice after 1 week at dietary concentrations > 160 mg/kg bw per day and after 6 weeks at > 6.4 mg/kg bw per day.

The main gross and histological findings were associated with haematotoxicity. These comprised erythroid hyperplasia of the bone marrow of rats and dogs, enlarged spleens in all three species, and increased pigment deposition in the spleens of mice and rats. Increased pigmentation of a variety of cell types was seen in the liver. An increase in the severity of chronic hepatitis was seen in all groups in a 90-day study in rats, the LOAEL being equivalent to 8 mg/kg bw per day. The NOAELs for pathological findings were dietary concentrations equal to 6.4 mg/kg bw per day in mice and equivalent to 2 mg/kg bw per day in rats and a dose of 2 mg/kg bw per day given by capsule in dogs. In the 13-week study in dogs and a 91-week study in mice, increased total haemoglobin and reticulocyte counts, bone-marrow hyperplasia, and increased erythroid:myeloid ratios indicated that the haematopoietic stem cells were not affected, and that there had been a compensatory response to the effects of diflubenzuron.

The carcinogenic potential of diflubenzuron was investigated in one study in mice and two studies in rats. The incidences of tumours were not increased in any of these studies, at dietary concentrations equal to 840 mg/kg bw per day in mice and 470 mg/kg bw per day in rats.

The genotoxicity of diflubenzuron was investigated in an adequate battery of tests in vitro and in vivo. Negative results were obtained in all the studies. The Meeting concluded that diflubenzuron is unlikely to be genotoxic.

In view of the negative findings in assays for genotoxicity and carcinogenicity, the Meeting concluded that diflubenzuron is unlikely to pose a carcinogenic risk to humans.

In a two-generation study of reproductive toxicity in rats, no adverse effects were found on sperm quality or quantity, reproductive performance, litter size, or attainment of developmental landmarks at the highest dietary concentration. The NOAEL for reproductive toxicity was the highest dietary concentration, equal to an average intake of 3800 mg/kg bw per day for males and 4300 mg/kg bw per day for females. Reductions in pup weight gain during lactation were seen at the highest dose in the F_0 generation, with a NOAEL for toxicity equal to an average intake of 360 mg/kg bw per day. Adult animals showed toxic effects consistent with the findings in other studies with repeated doses, including alterations in erythrocyte parameters at all dietary concentrations; the LOAEL was equal to an average intake of 36 mg/kg bw per day. The absence of a clear NOAEL for general toxicity in adult animals was not considered in assessing diflubenzuron, as NOAELs for the same effects were available from other studies in adult animals.

The developmental toxicity of diflubenzuron was investigated in rats and rabbits. There was no evidence of overt maternal toxicity, fetotoxicity, or teratogenicity in either species at the highest dose of 1000 mg/kg bw per day. The Meeting concluded that diflubenzuron is not fetotoxic or teratogenic.

Samples from pups and weanling animals in the multigeneration study were not examined for haematological or histopathological end-points. However, the fact that young animals exposed at about 1000 times the overall NOAEL for haematological effects showed no overt evidence of toxicity provided a degree of reassurance that young animals are not significantly more sensitive to diflubenzuron than adults.

The Meeting concluded that the available database on diflubenzuron was adequate to characterize the potential hazards to fetuses, infants, and children

Routine medical monitoring (including haematology) of workers in the production and formulation of diflubenzuron over 25 years did not reveal any adverse effects attributable to the compound.

The Meeting re-confirmed the previously established ADI of 0-0.02 mg/kg bw, based on the NOAEL for haematological effects of 2 mg/kg bw per day in the 2-year studies in rats and the 52-week study in dogs.

The Meeting concluded that, although methaemoglobinaemia is potentially an acute effect, the overall toxicological profile of diflubenzuron indicates that establishment of an acute reference dose is unnecessary. The absorption of diflubenzuron declines with increasing doses, and its excretion is relatively rapid, which would tend to limit systemic concentrations after high acute doses. It is likely that a metabolite, rather than diflubenzuron *per se*, is responsible for the effects on erythrocytes. Diflubenzuron has very low acute toxicity when given by various routes (oral, dermal, and inhalation). Only marginal increases (less than doubling) in methaemoglobin concentrations were seen in mice and rats given 10 000 mg/kg bw of a formulation of diflubenzuron, equivalent to 2500 mg/kg bw diflubenzuron, which is above the limit doses normally used in toxicological tests. No developmental toxicity was seen when diflubenzuron was given at doses up to a limit dose of 1000 mg/kg bw per day. There was no evidence of neurotoxicity in routine studies of toxicity.

A toxicological monograph was prepared.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Mouse	91-week study of toxicity and carcinogenicity[a]	Toxicity	16 ppm (equal to 1.2 mg/kg bw per day)	80 ppm (equal to 6.4 mg/kg bw per day)
		Carcinogenicity	10 000 ppm[b] (equal to 840 mg/kg bw per day	–
Rat	104-week study of toxicity and carcinogenicity[a, c]	Toxicity	40 ppm (equivalent to 2 mg/kg bw per day)	160 ppm (equivalent to 8 mg/kg bw per day)
		Carcinogenicity	10 000 ppm[b] (equal to 470 mg/kg bw per day	–
	Two-generation study of reproductive toxicity[a]	Parental toxicity	–	500 ppm[d] (equal to 36 mg/kg bw per day)
		Reproductive toxicity	50 000 ppm[b] (equal to 3800 mg/kg bw per day)	–
		Offspring toxicity	5000 ppm (equal to 360 mg/kg bw per day)	50 000 ppm (equal to 3800 mg/kg bw per day)
	Study of developmental toxicity[e]	Maternal toxicity	1000 mg/kg bw per day[b]	–
		Embryo- and fetotoxicity	1000 mg/kg bw per day[b]	–
Rabbit	Developmental toxicity[e]	Maternal toxicity	1000 mg/kg bw per day[b]	–
		Embryo- and fetotoxicity	1000 mg/kg bw per day[b]	–
Dog	52-week study of toxicity[f]	Toxicity	2 mg/kg bw per day	10 mg/kg bw per day

[a]Diet
[b]Highest dose tested
[c]Two studies combined
[d]Lowest dose tested

[e]Gavage
[f]Capsule

Estimate of acceptable daily intake for humans
0–0.02 mg/kg bw

Estimate of acute reference dose
Unnecessary

Studies that would provide information useful for continued evaluation of the compound
Further observations in humans
Studies on 4-chlorophenylurea

Summary of critical end-points for diflubenzuron

Absorption, distribution, excretion, and metabolism in mammals	
Rate and extent of oral absorption:	Rapid, maximum plasma concentration of radiolabel at 4 h; limited, 30% of a 5 mg/kg bw dose in bile and urine; less absorption at 100 mg/kg bw
Distribution:	Extensive, highest concentrations in liver and erythrocytes
Potential for accumulation:	Generally low, but some potential in erythrocytes and liver
Rate and extent of excretion:	> 90% in 48 h
Metabolism in animals	Hydroxylation of anilino ring and cleavage of ureido bridge
Toxicologically significant compounds	Diflubenzuron; 4-chlorophenylurea (plant metabolite)
Acute toxicity	
Rat, LD_{50}, oral	> 4600 mg/kg bw
Rat, LD_{50} , intraperitoneal	Not applicable
Rat, LD_{50}, dermal	> 10 000 mg/kg bw
Skin sensitization	Negative, Magnusson and Kligman
Short-term toxicity	
Target/critical effect	Erythrocytes
Lowest relevant oral NOAEL	2 mg/kg bw per day (52-week study, dogs)
Genotoxicity	No genotoxic potential
Long-term toxicity and carcinogenicity	
Target/critical effect	Erythrocytes
Lowest relevant NOAEL	2 mg/kg bw per day (2-year study, rats)
Carcinogenicity	No carcinogenic potential
Reproductive toxicity	
Reproduction target/critical effect	None
Lowest relevant reproductive NOAEL	360 mg/kg bw per day; pup weight gain (rats)
Developmental target/critical effect	None
Lowest relevant developmental NOAEL	> 1000 mg/kg bw per day (rats and rabbits)
Neurotoxicity	No concern from other studies
Medical data	No adverse effects reported

Summary	Value	Study	Safety factor
ADI	0–0.02	2-year studies in rats and dogs	100
Acute RfD	Unnecessary		

Dietary risk assessment

The theoretical maximum daily intakes from the five GEMS/Food regional diets, on the basis of existing MRLs, represented 3–20% of the ADI (Annex 4). The Meeting concluded that intake of residues of diflubenzuron resulting from its uses that have been considered by the JMPR is unlikely to present a public health concern.

4.8 DIMETHIPIN (151)

Residue and analytical aspects

Dimethipin is a plant growth regulator used mainly as a defoliant and harvest aid to accelerate desiccation of plant material. Dimethipin was first evaluated in 1985. It was listed by the 1997 CCPR (ALINORM 95/24 A) for periodic re-evaluation and was scheduled for consideration by the FAO Panel of the 2001 JMPR. The Meeting received information on its physicochemical properties, metabolism, environmental fate, analytical methods, stability in storage, registered uses, and residues in supervised trials and processing studies.

The Meeting was provided with studies in which dimethipin radiolabelled at the 2 and 3 positions of the dithiin ring was used in order to follow its distribution and metabolism in animals and plants. The following abbreviations are used for the metabolites discussed below:

red-DMP, 2,3-dimethyl-1,1,4,4-tetraoxide-1,4-dithiane
acetyl dithiane, 2-acetyl-1,4-dithian-1,1,4,4-tetraoxide
DMP-S-cys, *S*-(2,3-dimethyl-1,1,4,4-tetraoxo-1,4-dithian-2-yl)-L-cysteine
glu-cys-S-DMP, *S*-(2,3-dimethyl-1,1,4,4-tetraoxo-1,4-dithian-2-yl)-L-cysteinyl-(-glutamic acid
DMP-S-acetate, 2-[(2,3-dimethyl-1,1,4,4-tetraoxo-1,4-dithian-2-yl)thio]ethanoic acid
DMP-GSH, *S*-(2,3-dimethyl-1,1,4,4-tetraoxo-1,4-dithian-2-yl)-L-glutathione
DMP-SH, 2-mercapto(2,3-dimethyl-1,1,4,4-tetraoxo-1,4-dithiane)
DMP-S-methyl, 2-methylmercapto-2,3-dimethyl-1,1,4,4-tetraoxo-1,4-dithiane
DMP-*tert*-OH, 2,3-dimethyl-1,1,4,4-tetraoxo-1,4-dithian-2-ol
DMP-*prim*-OH, 2,3-dimethyl-1,1,4,4-tetraoxo-1,4-dithian-8-ol
DMP-SO-methyl, 2-(methylsulfinyl)-2,3-dimethyl-1,1,4,4-tetraoxo-1,4-dithiane
hydroxy-DMP, 2,3-dihydro-5-hydroxymethyl-6-methyl-1,4-dithiin-1,1,4,4-tetraoxide

Metabolism

Animals

After oral administration of [^{14}C]dimethipin to rats, unchanged dimethipin, *N*-acetylcysteine conjugate, red-DMP, a cysteinylglycine conjugate and a polar fraction were identified in urine.

Two female goats (one lactating) were given [^{14}C]dimethipin orally at a dose of 20 mg/kg bw, equivalent to a nominal feeding rate of 500 ppm, for 3 consecutive days. The metabolites identified in urine were DMP-*prim*-OH, DMP-*tert*-OH, hydroxy-DMP and 2,3-dihydro-5-hydroxymethyl-1,4-dithiine-1,1,4,4-tetraoxide. Most of the residue in urine was not characterozed, but was thought to consist of polar conjugates. Bile extracts contained dimethipin and seven metabolites, including the ring-opened product 3-(2-hydroxyethylsulfonyl)butan-2-one and dimethipin L-cysteine and *N*-acetyl cysteine conjugates. The concentrations of radiolabelled residues in edible tissues were highest in liver and kidney and much lower in muscle and fat. Intact dimethipin accounted for 2% of the TRR in liver and kidney. The metabolites 3-(2-hydroxyethylsulfonyl)butan-2-one and DMP-*tert*-OH were identified in liver and kidney, while (-glucuronidase hydrolysis indicated the presence of a glucuronide conjugate. The high concentrations of polar and bound residues in liver and kidney indicated extensive conjugation.

Lactating goats were dosed orally with radiolabelled dimethipin once daily for 5 consecutive days, at doses of 0.15 and 50 mg/kg bw [^{14}C]dimethipin and 50 mg/kg bw [$^{13/14}$C]dimethipin, equivalent to feeding at 3, 1010 and 1290 ppm in the diet. Radiolabel in excreta collected up to 22 h after the last dose (slaughter) accounted for 95% of the administered dose, while 0.1–0.2% of the dose was eliminated in milk. The only metabolite detected in milk in significant quantities was DMP-S-cys. The association of most of the ^{14}C in liver with protein suggests that the metabolites in liver were protein conjugates. In kidney, 1,2-ethane disulfonic acid was the only metabolite found in the goat given the low dose, while 1,2-ethane disulfonic acid was the only free metabolite in the goat given the high dose, with conjugated products that were released on acid hydrolysis. The main metabolite in muscle was red-DMP, which was present at approximately 30% of the TRR; no other metabolite accounted for more than 8% of the TRR. The concentrations of radiolabel in fat were too low to permit characterization of metabolites.

The main route of transformation of dimethipin is a Michael addition of a sulfhydryl to the double bond. Addition of glutathione yields DMP-S-cys, via the mercapturic acid pathway, which is eliminated in urine and milk. This conjugate was not observed in edible tissues. If the addition is made to a protein sulfhydryl, the result is protein-bound reduced dimethipin, which was the only residue observed in liver and muscle and approximately half that observed in kidney. Hydrolysis of the bound residue and subsequent rearrangement gave three products: red-DMP, acetyl-dithiane and 1,2-ethane disulfonic acid. The latter was the only metabolite observed in kidney in the goat given the lower radiolabelled dose but represented about one-third of the radiolabelled residues in kidney in the goat given the higher dose.

White Leghorn pullets (1.3–2.4 kg bw) were given [^{14}C]dimethipin at nominal levels equivalent to 1 (0.06 mg/kg bw), 6 (0.34 mg/kg bw) and 30 (1.7 mg/kg bw) ppm in the feed. The concentration of radiolabelled residues in eggs plateaued 10 days after the start of dosing and reached maxima of 11, 41 and 198 (g/kg at the three doses, respectively. The TRR in eggs decreased to below the limit of detection of 6 (g/kg after 5 days' withdrawal from dosing at 1 ppm. After 11 days' withdrawal, the concentration of radiolabel in eggs was below the limit of detection for the group given 5 ppm and near the limit of detection for that given 30 ppm. Of the edible tissues, liver and kidney had the highest TRR and fat had the lowest. The concentration of dimethipin residues in liver was < 0.01 mg/kg at all doses.

The material balance after oral dosing of white Leghorn laying hens with [^{14}C]dimethipin for 5 days at 15.8 or 152 mg/bird (equivalent to feeding at 203 or 2770 ppm in the diet) was > 95%. Most of the radiolabel was eliminated in excreta (90–91%) within 24 h of the last treatment, and 5.1–5.6% of the amount given was recovered in edible tissues and eggs. The concentrations of radiolabelled residues were greatest in liver followed by kidney, muscle, eggs and fat. The main metabolite identified in hen liver was DMP-S-cys, and glu-cys-*S*-DMP was the main metabolite detected in other tissues. Other metabolites identified in liver included DMP-*prim*-OH, DMP-*tert*-OH, hydroxy-DMP, DMP-SH, DMP-*S*-methyl, DMP-SO-methyl and DMP-*S*-acetate.

It has been proposed that addition of glutathione to dimethipin (catalysed by glutathione *S*-transferase or spontaneous) gives DMP-GSH, which can be transported out of the cells in which it is

formed and the glutathione moiety degraded by endogenous peptidases to produce glu-cys-*S*-DMP and DMP-*S*-cys. Oxidative transamination and loss of pyruvic acid or decarboxylation can give DMP-SH and DMP-*S*-acetate. Methylation of DMP-SH in the presence of *S*-adenosine-methionine would produce DMP-*S*-methyl, which could be further oxidized to DMP-SO-methyl. Another product that could be formed is the *N*-acetylcysteinyl conjugate, which would be expected to be retained by the strong anion-exchange columns used. An unidentified metabolite found in several extracts had chromatographic behaviour similar to that of products obtained by reacting dimethipin with *N*-acetylcysteine. Reduction and hydroxylation reactions are also possible, as evidenced by the presence of red-DMP and the hydroxylated metabolites DMP-*tert*-OH and DMP-*prim*-OH.

The data on metabolism in rats, goats and hens show that dimethipin is extensively metabolized, almost no residual parent compound being retained in any of these species. The main residues in animals form as the result of glutathione, amino acid and protein conjugation and subsequent degradation. Minor metabolites are formed as a result of hydrolytic hydroxylation and/or oxidation.

Plants

Studies on metabolism in cotton, sunflower, potato, grape and rice were made available to the Meeting.

When mature indoor-grown cotton plants, each with one to four bolls open, were treated with a single application of [^{14}C]dimethipin at 1.12 kg ai/ha, the extractable residue in seeds with linters accounted for 94% of the TRR, of which 94% was identified as dimethipin. In acid-delinted seeds, 18% of the TRR was extractable with methanol, of which 38% was dimethipin.

Dimethipin was the major component (72%) of the residue in foliage of cotton plants treated with [^{13}C/^{14}C]dimethipin at 0.34 and 1.6 kg ai/ha 2 weeks before harvest. No other individual compound accounted for more than 5% of the TRR. Most of the radiolabelled residue (80–90%) in seeds was identified as dimethipin, no other component accounting for more than 5.2% of the extracted residue.

When the backs of the seed heads of mature sunflower plants were sprayed with [^{13}C/^{14}C]-dimethipin at 1.4 kg ai/ha and harvested 4 weeks later, dimethipin accounted for 61% of the extractable residue, with no other single component exceeding 5.7% of the TRR.

A field-grown potato plant (*cv.* Kennebec) was sprayed with a flowable formulation of [^{14}C]dimethipin at 2.24 g ai/ha and harvested 14 days later. Unchanged dimethipin accounted for 20–25% of the TRR (0.012–0.015 mg/kg) in unwashed potato tubers.

Indoor-grown rice plants were treated with [^{14}C]dimethipin at 2.24 g ai/ha, and the plants were harvested 17 days later. The TRRs in straw, hulls and seed were 162, 325 and 8 mg/kg, respectively, calculated as dimethipin. More than 78% of the radiolabelled residues in straw, hulls and grain were extractable in solvents, dimethipin representing 50–80% of the extractable TRR.

When Mueller-Thurgau grape vines were sprayed with [^{14}C]dimethipin at 115 mg/vine, the TRRs in leaves were 16, 7.8 and 3.6 mg/kg (calculated as dimethipin) 2 h and 6 and 24 days after application, respectively. The concentrations of dimethipin residues were 0.036 mg/kg in juice, 0.004 mg/kg in stems and seeds and 0.033 mg/kg in wine in combined 6- and 24-day samples. Numerous metabolites were detected, although none was identified. When samples of juice were processed into wine by alcoholic fermentation, no $^{14}CO_2$ evolved. In wine filtered after fermentation, 11% of the radiolabel was in yeast and solids and 89% in the clear wine.

Most of the radiolabel in the leaves of cotton seedlings grown hydroponically with [^{14}C]-dimethipin in the nutrient medium for 3 days were dimethipin (79%). Metabolites identified as minor constituents were cysteine and glutathione conjugates of dimethipin. Extracts of cotton callus cultures

treated with [^{14}C]dimethipin had metabolite profiles similar to that of hydroponically treated cotton plants, but with more dimethipin–L-cysteine reaction product. An additional polar metabolite with an identical HPLC retention time to an unidentified rat metabolite was observed in [^{14}C]dimethipin-treated potato callus cultures

As dimethipin is applied to plants close to harvesting, when the plants are close to natural senescence, the biochemical activity is very limited, resulting in minimal metabolism. As a result, the main plant residue is the parent compound. In a study of the fate of dimethipin in cotton seedlings and callus cell cultures of cotton and potato, most of the plant metabolites resulted from conjugation of dimethipin with glutathione and/or cysteine.

Environmental fate

Studies were reported on degradation, dissipation and mobility in soil, adsorption and desorption, photodegradation on soil, confined rotational crops and aquatic dissipation.

Soil

The aerobic metabolism of [^{14}C]dimethipin was studied on a silt loam, a sand, two loamy sands and a field loam at 25 °C. Under aerobic conditions, bound residues and $^{14}CO_2$ accounted for < 25 and 30% of the radiolabel, respectively. After 168 days of incubation, 50–66% of the radiolabel was recovered as dimethipin. The main metabolites identified were 2-methyl-3-methylene-1,4-dithiane-1,1,4,4-tetraoxide, 1,4-dithiane-1,1,4,4-tetraoxide and a carboxylic acid derivative of dimethipin. The mass balances for the radiolabel were 94–101%.

The anaerobic metabolism of [^{14}C]dimethipin was studied on a silt loam and a sand. Desorption of radiolabel from the soils to the water used to maintain anaerobic conditions was noted. On silt loam and sand, 60–80% of the radiolabel was present as dimethipin after incubation for 60 days at 25 °C. The mass balances for the radiolabel were 88–90% after 60 days' incubation.

Dimethipin is not susceptible to anaerobic photolytic degradation. In aerated solutions, the photolytic half-time was reduced to 14 days. The rate of photolysis was observed to be pH-dependent, with no significant degradation at pH 7 but half-times at pH 5 and 9 of 35 and 47 days, respectively.

Significant photolytic losses were seen after irradiation of [^{14}C]dimethipin on sandy loam soils when compared with degradation by hydrolysis and soil metabolism. After 30 days, dimethipin accounted for 47–65% and 81–99% of the radiolabel in irradiated and dark control samples, respectively. Volatile components accounted for < 1% of the applied radiolabel. The mass balances were 92 ± 7% for exposed samples and 94 ± 9% for dark samples.

The Meeting concluded that dimethipin is relatively persistent in soils.

Dimethipin was weakly absorbed onto each of the soils, and a strong relationship was observed between absorbed dimethipin and per cent organic matter. The desorption was essentially completely reversible. The adsorption K_a values (< 15) and ease of desorption indicate that the mobility of dimethipin was high in all soils studied.

Studies of leaching were reported for four soil types, sand, loamy sand, sandy loam and silt, treated with dimethipin at 1.7 kg ai/ha. Dimethipin was readily leached from 30-cm soil columns with 51 column cm of water. Between 77 and 102% of the applied radiolabel eluted, of which 71–96% was dimethipin. The rate of elution of the radiolabel was fastest in loamy sand, silt loam and aged sandy loam soil columns, with a more gradual rate in sand and sandy loam soils. Dimethipin is considered to be highly mobile and does not degrade significantly under conditions simulating leaching.

Field studies were conducted under natural conditions of rainfall and irrigation in several states of the USA at sites with loamy sand, clay loam and silt loam soils. The soils were treated according to GAP in the USA for cotton (two sprays, 0.35 and 0.25 kg ai/ha) and sunflowers (2.24 kg ai/ha). Dimethipin migrated below the top 30 cm of soil, and low concentrations of residue were detected at depths down to 91 cm (0.01 mg/kg). The half-time for degradation of dimethipin in the 0–122-cm depth was 168–196 days.

In a study of confined rotational crops, lettuce, barley and carrots were planted in soil treated with [^{14}C]dimethipin at 0.6 kg ai/ha after a fallow period of 30 days and grown to maturity. Dimethipin accounted for most of the radiolabel in soil at application and planting (85–100% of TRR). The percentage of bound, unextractable residue increased with time after application, reaching 60–93% of the TRR in soil samples at harvest. The concentrations of residues of dimethipin in immature and mature crops were 0.01–0.10 mg/kg. No residues of dimethipin were detected in wheat grain. Three crop metabolites were isolated, one of which was identified as hydroxy-DMP.

Lettuce, carrot and wheat or oats were planted in soil treated with two sprays of dimethipin at 0.35 and 0.26 kg ai/ha (GAP for cotton in the USA) after fallow periods of 1 and 6 months. The concentrations of residues of dimethipin in these rotational crops were significant (< 0.02–0.07 mg/kg) at a plant-back interval of 1 month and mostly negligible (< 0.02 mg/kg) in crops planted 6 months after application. The notable exception was carrot tops, which had concentrations ≤ 0.18 mg/kg at harvest in crops planted 6 months after the last application.

The Meeting concluded that the concentrations of inadvertent residues of dimethipin in rotational crops would not be significant after a 6-month plant-back period and that the carryover of dimethipin under field conditions should be < 0.02 mg/kg. Dimethipin is degraded only slowly under aerobic aquatic conditions or on soil under aerobic and anaerobic conditions. It is relatively persistent in the environment and considered to be highly mobile in all the soil types studied.

Water–sediment systems

The half-time of dimethipin in an anaerobic water–sediment system was 277 days. At the start of the experiment, 97% of the applied ^{14}C was present in the aqueous filtrate. By the end of the experiment (365 days), 56% of the applied radiolabel was associated with the water filtrate, dimethipin accounting for 65% of the radiolabel in water or 37% of that applied. Extractable residues from the soil accounted for 5% of the applied radiolabel, dimethipin comprising 89%. Bound residues and $^{14}CO_2$ accounted for 17 and 7% of the applied radiolabel, respectively.

Methods of analysis

Adequate methods have been developed for the analysis of residues of dimethipin on crops and of dimethipin and 1,2-ethane disulfonic acid in animal commodities. Dimethipin is extracted from the matrix with a polar solvent (methanol, aqueous methanol or acetonitrile). The extract is cleaned up with a hexane wash, GPC and a Florisil column. Dimethipin is quantified by GC with a sulfur-specific flame photometric detector, ECD or mass-selective detector. The LOQ and LOD depended on the detector used. The LOQs for most matrices were generally 0.01–0.05 mg/kg.

The Meeting concluded that adequate analytical methods are available for enforcement of MRLs and monitoring purposes.

Stability of residues in stored analytical samples

The stability of dimethipin during frozen storage of fortified samples of cotton seed, meal, hulls and crude oil, lettuce, carrot and wheat grain as well as bovine milk, muscle, kidney and liver was reported. The stability of the metabolite 1,2-ethane disulfonic acid in samples of bovine kidney with incurred residues was also reported.

The periods for which the concentrations of residues of dimethipin remained > 70% of the initial concentration were at least 12 months for lettuce, carrot root, wheat grain and cotton seed; 7 months for cotton seed meal, hulls and crude oil; and 2 months for bovine milk, muscle, kidney and liver. Residues of 1,2-ethane disulfonic acid in bovine kidney were stable for at least 6 months.

The Meeting concluded that dimethipin is stable in crop matrices stored frozen for periods of up to 12 months.

Definition of the residue

Dimethipin is not significantly metabolized by plants when applied close to harvest. The main component of the extractable residue in plants is dimethipin, comprising 38–72, 61, 20–25, 50 and 14–50% of the extractable residue in cotton, sunflower seeds, potatoes, rice grain and grape juice, respectively. In animals, dimethipin is extensively metabolized, the main pathways involving conjugation to glutathione, amino acids and peptides and subsequent degradation. Minor routes of metabolism include hydrolytic hydroxylation and oxidation. There is no reasonable expectation that feeding of dimethipin-treated commodities to animals would result in residues of dimethipin or metabolites in animal commodities that are above typical LOQs.

On the basis of the metabolism of dimethipin in plants, the conclusions of the 1999 JMPR on the toxicology of the compound and the available analytical methods, the Meeting concluded that the residue for compliance with MRLs and for estimation of dietary intake should continue to be defined as dimethipin.

Results of supervised trials

Dimethipin is registered as a plant growth regulator for use as a crop defoliant and harvest aid to accelerate desiccation of plant material. It is applied at the end of plant maturity and close to its natural senescence. At this time, the biochemical activity in plants is very limited, and the penetration, translocation and metabolism of dimethipin in plants are slow. As dimethipin is used as a growth regulator in crops, it is usually best to harvest crops at the appropriate stage of desiccation or defoliation rather than to set minimum pre-harvest intervals. Considerable latitude with respect to the PHI has been allowed in assessing compliance with GAP. Supervised trials were reported on potato, cotton, rape, linseed and sunflowers.

Data were available from supervised trials on potato in France, Germany, The Netherlands, Norway, Sweden and the United Kingdom, but with no corresponding GAP. The Meeting decided to evaluate the trials from France, Germany, The Netherlands and the United Kingdom according to the GAP of Ireland.

In Ireland, dimethipin is registered for application to potatoes at a rate of 0.63 kg ai/ha with a 21-day PHI. The concentrations of residues of dimethipin in four trials in France with application of 0.75 kg ai/ha and PHIs of 18–34 days were < 0.01 (3) and < 0.1 mg/kg. In six trials in Germany at 0.75 g ai/ha with PHIs of 13–14 days, the concentrations of residues of dimethipin were < 0.02 mg/kg (6). Six trials in The Netherlands conducted at 0.5–0.63 kg ai/ha with PHIs of 9–40 days showed concentrations < 0.05 (6)

mg/kg. The concentrations in three trials in the United Kingdom at 0.5 kg ai/ha and PHIs of 21–28 days were < 0.005 mg/kg (3).

The concentrations of residues of dimethipin in potatoes in 19 trials, in ranked order (median underlined), were < 0.005 (3), < 0.01 (3), < 0.02 (6), < 0.05 (6) and < 0.1 mg/kg. All the values in potato tubers were below the LOD. The Meeting considered that an appropriate LOQ for a regulatory analytical method is 0.05 mg/kg. The observation of detectable residues of dimethipin in a trial of metabolism in potatoes after application at an exaggerated rate led to the conclusion that the concentration could not be considered zero. The Meeting estimated a maximum residue level, an STMR value and a highest residue for dimethipin in potatoes of 0.05(*), 0.02 and 0.02 mg/kg respectively. The results of a number of trials conducted in countries without corresponding GAP but with PHIs and similar or excessive application rates in comparison with GAP in Ireland support the conclusion that the concentrations of residues are < 0.05 mg/kg. The estimated maximum residue level confirms the current recommendation (0.05(*) mg/kg) for potato.

Supervised field trials on cotton were reported from Spain and the USA.

The registered use pattern in Spain is 0.31 kg ai/ha with no specified PHI. The concentrations of residues in cotton seed in four trials at an application rate of 0.31 kg ai/ha were 0.02, 0.03 and 0.07 (2) mg/kg 5–14 days after application.

Fifteen trials in the USA followed GAP in that country, which is two sprays at 0.23–0.32 kg ai/ha with a minimum re-treatment interval of 5 days and a PHI of 7 days. The concentrations of residues of dimethipin were < 0.1 (4), 0.1 (3), 0.2 (6), 0.3 and 0.7 mg/kg.

The concentrations of dimethipin in cotton seed in the 19 trials, in ranked order, were 0.02, 0.03, 0.07 (2), < 0.1 (4), 0.1 (3), 0.2 (6), 0.3 and 0.7 mg/kg. The Meeting estimated a maximum residue level, an STMR value and a highest residue for dimethipin in cotton seed of 1, 0.1 and 0.7 mg/kg respectively. The estimated maximum residue level replaces the current recommendation (0.05(*) mg/kg) for cotton seed.

Supervised trials on linseed were provided from the Czech Republic. In two trials approximating GAP in that country (0.5 kg ai/ha; PHI, 10–15 days), the concentrations of residues of dimethipin were < 0.1 (2) mg/kg.

The number of trials with linseed is insufficient for setting a maximum residue level. The Meeting recommended withdrawal of the current maximum residue level of 0.2 mg/kg for linseed.

Supervised field trials on rape seed were reported from the Czech Republic, Germany, Hungary, Norway and the United Kingdom. Details of GAP in Norway were not provided. The trials in the United Kingdom did not approximate the relevant GAP and/or were not adequately described.

The registered use pattern in the Czech Republic is 0.38–0.5 kg ai/ha with a PHI of 10–14 days. The concentrations of residues in rape seed in three trials with application rates of 0.38–0.6 kg ai/ha were < 0.1 mg/kg 7–14 days after application.

Six trials in Germany approximated GAP in Hungary, which is application at 0.3–0.5 kg ai/ha with a PHI of 14 days. The concentrations of residues of dimethipin were < 0.1 (5) and 0.1 mg/kg.

In one trial in Hungary conducted according to GAP, the concentration in rape seed was < 0.05 mg/kg.

The concentrations of residues of dimethipin in rape seed in the 10 trials were < 0.05, < 0.1 (8) and 0.1 mg/kg. The Meeting estimated a maximum residue level, an STMR value and a highest residue for dimethipin in rape seed of 0.2, 0.1 and 0.1 mg/kg, respectively.

Data were available on a supervised trials on sunflowers conducted according to GAP in Hungary, which is application at 0.38–0.5 kg ai/ha with harvesting 14 days after the final spray. In 11 trials approximating GAP, the concentrations of residues of dimethipin were < 0.01 (4), < 0.1, 0.09, 0.26, 0.30, 0.38, 0.70 and 0.77 mg/kg.

The concentrations of residues of dimethipin in sunflower seed in the 11 trials in ranked order were < 0.01 (4), 0.09, < 0.1, 0.26, 0.30, 0.38, 0.70 and 0.77 mg/kg. The Meeting estimated a maximum residue level, an STMR value and a highest residue for dimethipin in sunflower seed of 1, 0.1 and 0.77 mg/kg respectively. The estimated maximum residue level replaces the current recommendation (0.1 mg/kg) for sunflower seed.

Fate of residues during processing

Information was provided to the Meeting on the fate of dimethipin residues during processing of cotton seed. Processing factors were calculated for dimethipin residues in processed commodities derived from this raw agricultural commodity only when dimethipin was the residue of concern for surveillance and estimation of dietary intake. When the concentrations of residues in a processed commodity did not exceed the LOQ, the processing factor was calculated from the LOQ and is prefixed with a 'less than' symbol (<).

The average factor for processing of cotton seed to meal was 0.2, that for cotton seed to hulls was 0.8, that for cotton seed to soapstock was < 0.2, that for cotton seed to crude oil was < 0.2 and that for cotton seed to refined oil was < 0.2. Application of a processing factor of 0.2 to the STMR of 0.1 mg/kg for cotton seed gives an STMR-P value for crude and refined oil of 0.02 mg/kg. The Meeting estimated maximum residue levels of 0.2 mg/kg (MRL x PF = 1 x 0.2) for crude cotton seed oil and edible cotton seed oil. The estimated maximum residue level for crude cotton seed oil confirms the current recommendation (0.1 mg/kg), while that for edible cotton seed oil replaces the current recommendation (0.02 * mg/kg).

Residues in animal commodities

The studies of animal transfer indicate that feeding dimethipin at concentrations up to 50 ppm in the diet will not result in residues in milk and tissues that exceed 0.01 mg/kg, the LOQ for dimethipin in milk and tissues with the analytical method provided.

The dietary burden of dimethipin residues in farm animals was estimated by the Meeting on the basis of the diets listed in Appendix IX of the *FAO Manual*. Potential feed items for which information on residues was available were cotton seed, cotton seed meal and hulls, rape seed and sunflower seed. The estimated intakes of dimethipin by beef and dairy cattle are shown in the table below.

Commodity	Group	Residue (mg/kg)	Basis	Dry matter (%)	Residue, dry weight (mg/kg)	Choose diets (%)			Residue contribution (mg/kg)		
						Beef cattle	Dairy cows	Poultry	Beef cattle	Dairy cows	Poultry
Cotton seed	SO	1	MRL	90	1.1	10	10		0.11	0.11	
Cotton seed meal	SO	0.02	STMR-P	88	0.02						
Cotton seed hulls	SO	0.08	STMR-P	90	0.09						
Potato culls		0.02	STMR	20	0.1						
Rape seed	SO	0.2	MRL	88	0.23						
Sunflower seed	SO	1	MRL	92	1.08	15	15	30	0.16	0.16	0.32
Total						25[a]	25[a]	30[b]	0.27	0.27	0.32

[a] Assuming that total oilseed products will not be fed at more than 25% of the diet to beef cattle and dairy cows
[b] Assuming that total oilseed products will not be fed at more than 30% of the diet to poultry

The dietary burden of dimethipin for beef and dairy cattle is 0.27 mg/kg. No residues of dimethipin were detected in milk or tissues of dairy cows fed at 50 ppm in the diet for 28 days, a level that is 185 times the estimated dietary burden for cattle. The Meeting estimated maximum residue levels, STMR values and highest residues for dimethipin in edible offal (mammalian) and meat (mammalian) of 0.01*, 0 and 0 mg/kg respectively. The Meeting also estimated a maximum residue level and STMR of *0.01 mg/kg and 0 mg/kg for milk. The estimated maximum residue levels replace the current recommendations (0.02* mg/kg) for edible offal (mammalian), meat (mammalian) and milk.

The dietary burden of dimethipin for poultry is 0.32 mg/kg. No residues of dimethipin were detected in eggs or tissues of hens dosed orally for 5 days at a rate equivalent to feeding at 2770 ppm, a level that is > 8000 times the estimated dietary burden for poultry. The concentrations of TRRs in tissues and eggs of hens dosed at up to 30 ppm in the diet for 30 days were < 1.4 mg/kg (calculated as dimethipin). The studies with radiolabelleed compound indicate that there is no reasonable expectation that detectable residues of dimethipin will be found in eggs or tissues of hens fed at the estimated dietary burden of 0.32 mg/kg. The Meeting estimated maximum residue levels, STMR values and highest reaisues for dimethipin in eggs, edible offal of poultry and poultry meat of 0.01*, 0 and 0 mg/kg, respectively. The estimated maximum residue levels replace the current recommendations (0.02* mg/kg) for eggs, poultry, edible offal and poultry meat.

Dietary risk assessment

Long-term intake

The periodic review of dimethipin resulted in recommendations for new and revised MRLs and new STMRs for raw and processed commodities. Data on consumption were available for 12 food commodities and were used in the dietary intake calculation. The results are shown in Annex 3.

The IEDIs for the five GEMS/Food regional diets, based on estimated STMRs, were 3-20% of the ADI of 0–0.02 mg/kg bw. The Meeting concluded that long-term intake of residues of dimethipin from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The IESTI for dimethipin was calculated for processed cotton seed products, potatoes, rape seed and sunflower seed as well as animal products for which maximum residue levels and STMRs were estimated and for which data on consumption were available. The results are shown in Annex 4. The IESTI represented 0–10% of the acute RfD (0.02 mg/kg bw) for the general population and 0–10% of the acute RfD for children.

The Meeting concluded that short-term intake of dimethipin residues is unlikely to present a public health concern.

4.9 DINOCAP (087)

Residue and analytical aspects

Dinocap was last evaluated for residues by the 1999 JMPR. In 2000, the Meeting conducted an assessment of short-term dietary risk from consumption of grapes, apples, curcubits, strawberry, peppers, peaches, and tomatoes. The IESTI of grapes exceeded the acute RfD for children (120% of the acute RfD) and for women of child-bearing age (140% of the acute RfD).

At the Thirty-third Session of the CCPR (2001), the representative of the manufacturer disagreed with the calculation of short-term intake as it was based on data on wine grapes grown in northern Europe, which have high residues levels, and considered that data on table grapes grown in southern Europe should have been used. The Committee, noting that the proposed draft MRL for grapes was based on European GAP, agreed to consider this compound at its next session (ALINORM 01/24A).

The IESTI estimated at the 2000 JMPR was based on supervised trials submitted to the 1998 JMPR, when dinocap was evaluated as a new compound. A highest residue value of 0.66 mg/kg for dinocap in a trial conducted in Germany in wine grapes according to French GAP was used to estimate short-term intake. At the present Meeting, a current French label was provided by the manufacturer, and the trials conducted in France and Germany provided to the 1998 JMPR were re-evaluated. The new label states a dose rate of 0.21 kg ai/ha. The concentrations of residues in the trials in northern France and Germany conducted on wine grapes were, in ranked order, 0.22, 0.27, 0.28 and 0.35 mg/kg. Those in trials conducted in southern France in table grapes were < 0.04 and 0.05 (2) mg/kg. In 21 trials with table grapes in Greece, Italy and Portugal, conducted according to GAP (0.021–0.073 kg ai/hl), the concentrations of residues were, in ranked order, < 0.02 (2), < 0.04 (8), < 0.05 (6), 0.06, 0.08, 0.09, 0.11 (2), 0.20 (2) and 0.30 (2) mg/kg. The Meeting agreed that the data from northern and southern Europe represent a single population and can be combined for the estimates, as follows (median underlined): < 0.02 (2), < 0.04 (9), < <u>0.05</u> (8), 0.06, 0.08, 0.09, 0.11 (2), 0.20 (2), 0.22, 0.27, 0.28, 0.30 (2) and 0.35 mg/kg.

The Meeting withdrew its previous recommendations and estimated a maximum residue level of 0.5 mg/kg, a STMR value of 0.05 mg/kg and highest residue of 0.35 mg/kg for dinocap in grapes. Although this highest residue is based on a supervised trial in wine grapes, the next two highest values (0.30 mg/kg) were found in a trial conducted on table grapes, indicating that wine and table grapes can contain similar concentrations of residues. The estimated short-term intake should reflect consumption of a single unit of a given commodity from any source, and no information was provided on the French label that wine variety grapes cannot be used for human consumption.

Dietary risk assessment

Long-term intake

Currently, the ADI for dinocap is 0–0.01 mg/kg bw. At the 1998 JMPR, the IEDI calculated for commodities for human consumption for which STMRs were estimated ranged from 0 to 2% of the ADI for the five GEMS/Food regional diets. At the present Meeting, the recommended STMR value for grapes of 0.105 mg/kg was replaced by 0.05 mg/kg. The Meeting confirmed its previous conclusion that the intake of residues of dinocap resulting from uses that have been considered by the JMPR is unlikely to present a public heath concern.

Short-term intake

An acute RfD of 0.03 mg/kg bw for dinocap was allocated for children and for the general population and a value of 0.008 mg/kg bw for women of child-bearing age by the 2000 JMPR. IESTIs were calculated for grapes and wine, and the results are shown in Annex 4. For grapes, the IESTI was 20% of the acute RfD for the general population, 60% of the acute RfD for children, and 80% of the acute RfD for women of child-bearing age. These values decreased to a maximum of 1% for wine. The Meeting concluded that the short-term intake of dinocap from its use on grapes is unlikely to present a public heath concern.

4.10 DIPHENYLAMINE (030)

Residue and analytical aspects

Diphenylamine was first evaluated in 1969. Its toxicology was reviewed by the 1998 JMPR, which allocated an ADI of 0–0.08 mg/kg bw and concluded that an acute RfD was unnecessary. Diphenylamine was reviewed by the present Meeting within the CCPR periodic review programme.

The Meeting received information on physical and chemical properties, metabolism and environmental fate, analytical methods, stability on storage, farm animal feeding, use pattern, residues in supervised trials on apples and pears and a study of processing.

Metabolism

Animals

When rats were dosed orally with [^{14}C-ring]diphenylamine at 5 or 750 mg/kg bw, the compound was extensively absorbed and was excreted mainly in urine. Only 0.14–0.28% of the dose remained in tissues and organs of animals at the low dose 168 h after dosing. The radiolabel in expired air accounted for < 0.01% of the administered dose. Twelve metabolites were identified, most of which were hydroxylated diphenylamines and their glucuronide and sulfate conjugates. The parent and these 12 metabolites accounted for 81–93% of the dose in excreta.

When two lactating goats were dosed orally with encapsulated [^{14}C]diphenylamine for 7 days at a level equivalent to 46 ppm in the feed, the total amount excreted in urine and faeces accounted for about 94% of the dose. TRRs in milk reached equilibrium rapidly. The concentrations of radiolabel in tissues were low, but more was found in kidney and liver than in fat or muscle. A significant proportion of the

residues in fat and kidney (30–36%) and some residues in liver and milk (4–12%) were unmetabolized parent compound.

Several polar metabolites were identified, including 4-hydroxydiphenylamine, 4,4'-dihydroxy-diphenylamine, indophenol and the sulfate and glucuronic acid conjugates of 4-hydroxydiphenylamine. Ring hydroxylation followed by conjugation with either a sulfate moiety or glucuronic acid was the main metabolic pathway.

Approximately 91% of the administered dose was recovered in the excreta of 15 laying hens dosed orally with encapsulated [^{14}C]diphenylamine for 7 successive days at a level equivalent to 50 ppm in feed. The concentrations of TRR (as diphenylamine) in liver, kidneys, breast muscle, thigh muscle and fat/skin samples were 0.15, 0.21, < 0.01 < 0.01, and 0.04 mg/kg, respectively, while those in egg yolk ranged from < 0.01 to 0.38 mg/kg and those in egg whites were < 0.01 mg/kg. A significant proprotion of the residues in fat and skin and egg yolk were unmetabolized parent compound (17–35%); however, most (58%) of the residues in egg yolk were identified as a sulfate conjugate of 4-hydroxydiphenylamine, which also appeared in the other tissues.

The study of metabolism in hens showed that diphenylamine can be hydroxylated on the ring at position 4 or 2 and hydroxylated on the second ring. All these metabolites may subsequently be conjugated with glucuronic acid, sulfate and other groups.

Plants

In a study of the metabolism of diphenylamine in stored Red Delicious apple, the fruit were treated with an emulsion of [U-^{14}C-ring]diphenylamine, resulting in a residue of approximately 50 mg/kg, and stored at 2 (C and 95% relative humidity for 40 weeks. Most of the pesticide was absorbed into the peel within 2 days. The residue then slowly migrated into the pulp, and, after 40 weeks, the pulp contained 32% of the residue. After 40 weeks' storage, the parent compound accounted for approximately 41% of the TRR in the apples, with 37% as conjugates and 8% as hydroxydiphenylamines. Diphenylamine was converted to 2-, 3- and 4-hydroxydiphenylamines and a dihydroxydiphenylamine, which was then conjugated with glucose and oligosaccharides. The unknown non-polar metabolites, accounting for 0.52% of the residue in the apples, were not related to 4-aminobiphenyl, 2-aminobiphenyl or *N*-nitrosodiphenylamine.

Environmental fate

Soil

When [^{14}C-ring]diphenylamine was incubated in a loam soil at a nominal rate of 10 mg/kg under aerobic conditions at 25 (C in the dark for 12 months, diphenylamine initially disappeared rapidly, but after about 7 days the disappearance was quite slow. After 12 months 15% of the dose remained as diphenylamine, 49% was unextractable, and 18% was mineralized. The metabolites were polymeric and not identified.

When [^{14}C-ring]diphenylamine was tested for adsorption and desorption on four soils and a sediment, its mobility ratings were slight, immobile, immobile, slight and low in a loam, a silty clay loam lake sediment, a clay, a loamy sand and a silt loam, respectively.

Residues of [^{14}C-ring]diphenylamine were aerobically aged on four soils for 1 day and then leached through columns of the soils with 0.01 mol/L $CaCl_2$. The mobility ratings for the aged residues were: loam, slight; loam sand, low; silt loam, low; clay, immobile. Metabolites were identified in extracts from the soil columns as *N*,*N*-diphenylformamide (2.0–4.7% of dose) and 4-nitro-*N*-phenylbenzenamine (1.3–5.3% of dose).

Water–sediment systems

In a photolysis study, carbazole was identified as a major product when diphenylamine in an aqueous solution was subjected to UV irradiation, with approximately 7% formed within 0.5 h and a maximum of 52% at 10.5 h. Hydroxydiphenylamine was also identified, reaching a maximum value of 16% by 36 h. A third product, an indenohydroxyindole, reached a value of 93% by the end of the 192-h irradiation period. Small amounts of trimeric products were also formed.

When [^{14}C-ring]diphenylamine was incubated with a lake water and sediment under anaerobic conditions in the dark at 25 (C, the half-life for disappearance was approximately 60 days. The products of decomposition were soil-bound or soil-incorporated residues, which mineralized slowly (2.7% of the dose in 1 year).

Methods of analysis

The Meeting received information on GLC methods for the analysis of diphenylamine residues in fruit, processed apples and animal commodities.

Plant matrices

Whole apples were homogenized in a food processor with liquid nitrogen to produce a white powder, and an analytical sample of homogenized whole apples or wet pomace, dry pomace or apple juice was blended with acetone and filtered. Diphenylamine residues were extracted from the aqueous acetone with hexane and then derivatized with trifluoroacetic anhydride in dichloromethane to produce trifluoroacetylated diphenylamine for GLC–MS analysis. The LOQ for diphenylamine residues in apples, juice and wet pomace was 0.08 mg/kg, and that for dry pomace was 1 mg/kg. The mean recovery from the four matrices was 85% (range, 51–150%, n = 85).

In the analytical method used in a supervised trial on pears, the sample was extracted with acetone and subjected to a number of solvent partitioning clean-up steps. The residue in the final solution was analysed, without derivatization, by GLC–NPD. The LOQ was 0.1 mg/kg. Recoveries were tested after addition of 0.1–24 mg/kg and were generally low, but satisfactory (mean, 77%; range, 58–93%; n = 20).

Animal matrices

In the method for analysis of diphenylamine residues in milk and animal tissues, the matrix was extracted with acetonitrile, which was partitioned with hexane to remove fats. The acetonitrile extract was then evaporated to dryness, redissolved in hexane, and analysed by GLC–mass-selective detection. The LOQ was 0.01 mg/kg. In validation testing for whole milk, skim milk, cream, muscle, kidney, liver and fat after spiking with 0.01–1 mg/kg, the mean recovery was 94% (range, 62–115%; n = 96).

Tissues and milk from goats in the study of metabolism were analysed for diphenylamine for comparison with the measurement of [^{14}C]diphenylamine. The results were reasonably close for liver and fat, but not for milk and kidney. However, the measurements were made approximately 3 years apart, and diphenylamine may have depleted during storage.

Stability of residues in stored analytical samples

Data on stability during freezer storage were provided for diphenylamine residues in whole apples, juice, wet pomace, dry pomace, whole milk, muscle and liver. The residues in whole apples, juice, wet pomace,

dry pomace were stable for 5–7 months, those in whole milk for 8 weeks and those in muscle and liver for 6 weeks.

Definition of the residue

The parent compound diphenylamine is the main component of the residue in apples. The gluconic and sulfate conjugates of 4-hydroxydiphenylamine and the parent compound are the main components in animal tissues, milk and eggs. The conjugates of 4-hydroxydiphenylamine can be regarded as intermediates in the process of detoxication and excretion and need not be included in the residue definition for dietary risk assessment. All the plant metabolites were also animal metabolites.

The Meeting concluded that the current definition (diphenylamine only) is suitable for assessing compliance with MRLs and for estimating dietary intake.

The measured log P_{ow} for diphenylamine is 3.6. The animal feeding study showed that the concentrations of diphenylamine residue in fat were higher than in muscle, and that in milk diphenylamine was associated with the cream, suggesting the compound should be designated fat-soluble. The Meeting recommended that diphenylamine be described as fat-soluble.

Results of supervised trials

Diphenylamine is registered for post-harvest use on apple in the USA as a dip, spray or drench at a concentration of 0.20 kg ai/hl for Red Delicious and 0.22 kg ai/hl for Granny Smith and a maximum contact time of 2 min. The concentrations of residues in apples in four trials meeting GAP in the USA were 3.4, 3.4, 5.5 and 6.3 mg/kg.

Although data were available on residues from only four trials, the Meeting agreed that the data were sufficient because post-harvest trials need not cover the range of variables that occur in a field situation. The trials did include dip and drench methods of application.

The Meeting estimated a maximum residue level and an STMR value for diphenylamine in apples of 10 and 4.45 mg/kg respectively. The estimated maximum residue level replaces the current recommendation (5 mg/kg) for apple.

Diphenylamine is registered for post-harvest use on pears in Australia as a dip at a concentration of 0.037–0.26 kg ai/hl and a minimum contact time of 10–30 s. The concentrations of residues in pears in eight trials in the USA that matched Australian GAP (The dip concentration of 0.20 kg ai/hl was 23% below specified GAP, but sufficiently close.), in rank order (median underlined), were: 1.8, 2.0, 2.1 (2), 2.3, 2.4, 2.5 and 2.9 mg/kg.

The Meeting agreed that Australian GAP could be applied to the trials in the USA for post-harvest use. The Meeting estimated a maximum residue level and an STMR value for diphenylamine in pears of 5 and 2.2 mg/kg, respectively.

Fate of residues during storage and processing

Treated apples from the supervised trials were held in commercial cold storage, and diphenylamine residues were measured at intervals. The concentrations declined with an average half-life of 7–8 months. There is some evidence that small amounts of diphenylamine may be transferred from treated to untreated fruit in the same store.

Fate of residues during processing

When diphenylamine-treated apples were processed into juice, wet pomace and dried pomace by procedures that simulated small-scale industrial practices, the residues tended to concentrate in the pomace and deplete in the juice. The first step in the process was washing, which would be expected to reduce surface residues.

The calculated processing factors for unwashed apples to processed commodity were: juice, mean 0.051, range 0.022–0.12; wet pomace, mean 4.7, range 2.3–8.4; dry pomace, mean 2.4, range 1.4–3.6. Diphenylamine is volatilized during drying, resulting in a lower processing factor for dry pomace than for wet pomace.

The Meeting applied these processing factors to the estimated maximum residue level (10 mg/kg) and STMR value (4.45 mg/kg) for apples to provide estimates for the processed commodities. The Meeting estimated a maximum residue level and an STMR-P value for diphenylamine in apple juice of 0.5 and 0.23 mg/kg respectively, an STMR-P value for diphenylamine in wet apple pomace of 21 mg/kg, and a maximum residue level and an STMR-P value for diphenylamine in dry apple pomace of 25 and 10.6 mg/kg, respectively.

Residues in animal commodities

Dietary burden in farm animals

The Meeting estimated the dietary burden of diphenylamine residues in farm animals on the basis of the diets listed in Appendix IX of the *FAO Manual*. As the only feed commodities listed are processed, the dietary burdens for the estimated MRL and STMR value are the same.

Commodity	Group	Residue (mg/kg)	Basis	Dry matter (%)	Residue, dry weight (mg/kg)	Choose diets (%)			Residue contribution (mg/kg)		
						Beef cattle	Dairy cows	Poultry	Beef cattle	Dairy cows	Poultry
Apple pomace, wet	AB	21	STMR-P	40	53	40	20		21	11.5	
Apple pomace, dry	AB	10.6	STMR-P	90	11.8						
					Total	40	20		21	11.5	

Feeding studies

Groups of three lactating Holstein dairy cows were dosed orally by capsule twice daily for 28 days (once after each milking) at a dose equivalent to 30, 90 and 300 ppm in the diet (dry weight). The animals were slaughtered on day 29 for tissue collection and analysis.

Diphenylamine residues were detected in milk on some occasions in the groups given 30 or 90 ppm, but at or about the LOQ (0.005 mg/kg). The concentrations of residues in milk from cows at 300 ppm were up to 0.014 mg/kg. When milk collected on day 14 was separated into cream and skim milk, the residues partitioned into the fat fraction.

The concentration of residues in muscle was < 0.005 mg/kg, even at the highest feeding level, and those in kidney were just measurable (0.006–0.01 mg/kg) at this level. Residues were measured in liver, fat and day-14 cream in cows at all three feeding levels, the mean values being 0.034, 0.053 and 0.153 mg/kg in liver; 0.006, 0.0177 and 0.053 mg/kg in fat; and 0.0098, 0.019 and 0.0492 mg/kg in cream at the three feeding levels. The transfer factor (residue in tissue (residue in feed) for fat was consistent across feeding levels: 0.00020, 0.00020 and 0.00018, but the factors for cream and liver were less consistent.

Maximum residue levels

The dietary burdens of diphenylamine for estimation of MRL and STMR values in animal commodities (residue concentrations in animal feeds expressed in dry weight) were 21 mg/kg for beef cattle and 11.5 mg/kg for dairy cows. As the dietary burden for beef cattle is higher than that for dairy cows, it should be used to estimate residues in tissues. The dietary burdens were lower than the lowest feeding level (30 ppm), so the resulting residues in tissues and milk were calculated by applying the transfer factors at the lowest feeding level to those dietary burdens.

The highest individual concentration of tissue residue in the relevant feeding group was used in conjunction with the dietary burden to calculate the probable highest residue in animal commodities. The mean value in tissues from animals in the relevant feeding group was used in conjunction with the dietary burden to estimate the STMR values for animal commodities. For milk (cream), the mean residue in milk (cream) at the plateau level in the relevant feeding group was used to estimate both the highest residue and the STMR value.

Feeding level (ppm) *Interpolated* / Actual	Diphenylamine residues (mg/kg)				
	Cream (mean)	Fat		Liver	
		High	Mean	High	Mean
MRL beef cattle *21* / 30		*0.0042* / 0.006		*0.048* / 0.068	
MRL dairy cows *11.5* / 30	*0.0038* / 0.0098				
STMR beef cattle *21* / 30			*0.0042* / 0.006		*0.024* / 0.034
STMR dairy cows *11.5* / 30	*0.0038* / 0.0098				

The concentrations of residues in muscle and kidney were < 0.005 mg/kg and 0.007 mg/kg, respectively, at the highest feeding level (300 ppm). The Meeting agreed that residues in muscle and kidney at a feeding level of 21 mg/kg were unlikely to exceed 0.0005 and 0.0007 mg/kg, respectively.

The Meeting estimated a maximum residue level and an STMR value for diphenylamine in cattle meat of 0.01* (fat) and 0.0005 mg/kg, respectively; a maximum residue level and an STMR value for diphenylamine in cattle liver of 0.05 and 0.024 mg/kg, respectively; a maximum residue level and an STMR value for diphenylamine in cream of 0.01* and 0.0038 mg/kg, respectively, which are equivalent to 0.0004* F and 0.00015 mg/kg for milk; and a maximum residue level and an STMR value for diphenylamine in cattle kidney of 0.01* and 0.0007 mg/kg, respectively.

Dietary risk assessment

Long-term intake

The periodic review of diphenylamine resulted in recommendations for new and revised MRLs and new STMR values for raw and processed commodities. Data on consumption were available for the food commodities and were used in calculating dietary intake. The results are shown in Annex 3.

The IEDIs for the five GEMS/Food regional diets, based on estimated STMRs, were 0–4% of the ADI. The Meeting concluded that long-term intake of residues of diphenylamine from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The 1998 JMPR concluded that an acute RfD for diphenylamine was unnecessary. The Meeting therefore concluded that the short-term dietary intake of diphenylamine residues is unlikely to present a risk to consumers.

4.11 FENPROPIMORPH (188)

Toxicology

Fenpropimorph was first evaluated by the 1994 Joint Meeting, which established an ADI of 0–0.003 mg/kg bw on the basis of a NOAEL of 10 ppm, equal to 0.3 mg/kg bw per day, in a 2-year study of toxicity and carcinogenicity in rats. At its Thirty-third Session, the Codex Committee on Pesticide Residues considered the evaluations of residues and dietary intake of fenpropimorph by the 1999 Joint Meeting and noted that the absence of an acute RfD had precluded completion of an assessment of acute dietary risk. The present Meeting was asked to consider the need to establish an acute RfD.

The 1994 JMPR noted that the LD_{50} of fenpropimorph after oral administration ranged from 1500 to 3500 mg/kg bw in rats, and that the values in rats after dermal application or inhalation were also low (dermal LD_{50}: 4300 mg/kg bw; inhalation LC_{50}: > 3.6 to > 8.5 mg/l). WHO has classified fenpropimorph as ‘unlikely to present acute hazard in normal use’.

Studies evaluated by the 1994 JMPR did not show any remarkable early signs of toxicity after repeated administration, even at high doses that eventually elicited signs of liver toxicity, anaemia, and growth retardation. In short-term studies in rats (but not dogs) treated in the diet, inhibition of plasma and erythrocyte cholinesterase activity was occasionally seen, but there were no consistent dose- or time-response relationships, nor were the sexes equally susceptible. In the 2-year study in rats treated in the diet, inhibition of brain acetylcholinesterase was seen, males being more severely affected than females. However, these effects were difficult to interpret because brain cholinesterase activity was also depressed in controls at terminal sacrifice and there were no effects on erythrocyte cholinesterase activity at any time. In rabbits treated by gavage on days 6–18 of gestation, embryotoxicity, fetotoxicity, and developmental anomalies were seen only at doses that were clearly toxic to the does (NOAEL, 12 mg/kg bw per day; LOAEL, 36 mg/kg bw per day). Similar findings were noted in studies of developmental toxicity in rats, in which the NOAEL was 10 mg/kg bw per day and the LOAEL was 40 mg/kg bw per day. The 1994 JMPR concluded that fenpropimorph is not genotoxic.

In a study submitted to the current Meeting, of behaviour and neuromorphology in male and female Wistar rats, a single dose of fenpropimorph administered by gavage at 0, 100, 500, or 1500 mg/kg bw

caused small, but significant, depression of body-weight gain only in males at the highest dose. The clinical and behavioural signs observed in animals of each sex at 500 and 1500 mg/kg bw included piloerection and decreased rearing activity. Decreased motor activity was observed in both males and females at the highest dose and in females at 500 mg/kg bw. The effects on rearing and motor activity did not persist beyond the day of dosing, while the piloerection persisted for a few days in animals at the highest dose. No substance-related effects on sensorimotor or reflex functions were seen. Statistically significant increases in hindlimb grip strength were seen in females at the highest dose on day 14 only and in landing foot-splay tests in males at the intermediate dose on day 7 only. However, these findings were probably incidental, in view of the weakness of the dose– and time–response relationships. No gross neuroanatomical or histopathological lesions of the central or peripheral nervous system were seen that could be attributed to treatment. The NOAEL was 100 mg/kg bw.

The Meeting considered that this was an appropriate study for assessing the acute hazard of fenpropimorph and used it as the basis for establishing an acute RfD of 1 mg/kg bw, which incorporates a safety factor of 100.

Some additional studies in mice and dogs treated with fenpropimorph in the diet for 4–6 weeks were submitted, but the Meeting considered that these were not relevant to establishing an acute RfD.

An addendum to the toxicological monograph that summarizes the new studies was prepared.

Dietary risk assessment

Short-term intake

The IESTI for fenpropimorph was calculated for the commodities for which MRLs have been recommended and STMR and highest residue values have been estimated and for which data on consumption of large portion sizes and unit weights were available. The results are shown in Annex 4.

The calculated short-term intakes were less than 100% of the acute RfD for children and for the general population. The Meeting concluded that the intake of residues of fenproprimorph resulting from uses that have been considered by JMPR is unlikely to present a public health concern.

4.12 FIPRONIL (202)

Residue and analytical aspects

Fipronil belongs to a new class of insecticides known as phenylpyrazoles and was first reviewed by the 1997 JMPR for toxicology only. The compound was identified by the 1998 CCPR as a candidate for the residue evaluation of a new compound by the 2000 JMPR. The evaluation was postponed to the Meeting in 2001.

The manufacturer sent the Meeting information on metabolism in animals and plants, environmental fate in soil and water, methods of residue analysis, stability of residues in stored analytical samples, uses, supervised trials and processing data as well as national MRLs. Information on national GAP was provided by the governments of Australia, The Netherlands and Poland.

Pure fipronil is a white powder with a melting-point of 203 °C and low volatility. It has limited solubility in water and medium–high solubility in certain organic solvents. The log P_{OW} for the parent and relevant metabolites of 3.5–4 suggests that bioaccumulation may occur.

The parent, metabolites and degradation products are identified by the code numbers shown below.

Code	Chemical name
MB 46030 (fipronil)	5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoro-methylsulphinyl-pyrazole
MB 45950 (fipronil-thioether)	5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoro-methylthio-pyrazole
MB 45897	5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-pyrazole
MB 46136 (fipronil-sulfone)	5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoro-methylsulphonyl-pyrazole
MB 46513 (fipronil-desulfinyl)	5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoro-methyl-pyrazole
RPA 104615	5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-pyrazole-4-sulfonic acid
RPA 105320	5-amino-3-carbamyl-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoro-methylsulphonyl-pyrazole
RPA 105048	1-(2,6-dichloro-4-trifluoromethylphenyl)-3-amido-5-amino-4-trifluoro-methyl-pyrazole
RPA 200761	5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoro-methylsulphinyl-pyrazole-3-carboxylic acid
RPA 200766	5-amino-3-carbamyl-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoro-methylsulphinyl-pyrazole

Metabolism

Animals

The absorption, distribution, metabolism and excretion of [phenyl ring ^{14}C]fipronil and its toxicologically relevant photodegradation product fipronil-desulfinyl were studied in rats, goats and hens.

Parent fipronil: Rats were given a single dose of 4 or 150 mg/kg bw or 4 mg/kg bw [^{14}C]fipronil after pretreatment with 14 daily non-radiolabelled doses. After absorption, metabolism was rapid, and no unmetabolized fipronil was detected in any tissues or urine. Most of the radiolabel was eliminated in faeces, which contained unchanged [^{14}C]fipronil and metabolites, suggesting both bilary elimination of absorbed fipronil (metabolized) and elimination of unabsorbed fipronil. This observation indicates that some metabolites are probably excreted in the bile. The tissue concentrations of total radioactive residues (TRR) were high 7 days after dosing, with the highest levels in fat. The main residue in fat and other tissues examined was fipronil-sulfone.

Goats were given seven daily oral doses of [^{14}C]fipronil by capsule, equivalent to 0.05, 2 or 10 ppm in the diet (dry matter basis). Animals given the lowest and highest concentrations excreted the radiolabel extensively, mainly in the faeces. In contrast, those at 2 ppm appeared to retain a greater proportion of the administered dose. After administration at 0.05 ppm in the diet, 83% of the total dose was recovered, most (64%) being found in faeces. Much of the remaining radiolabel was estimated to have been retained in tissues (18%). At this concentration, no radiolabel was detected in urine, and negligible amounts were recovered in milk (0.86%). At the concentration of 2 ppm, a total of 50% of the radiolabel was recovered, most of which was sequestered in tissues (25%), with 2.5%, 18% and 4.6% in urine, faeces and milk, respectively. At the nominal concentration of 10 ppm, 77% of the administered radiolabel was recovered, principally in faeces (61%), with the remainder in urine (6.6%), milk (1.3%) and tissues (7.4%).

Consistent with the lipophilic nature of the compound and its metabolites, most of the radiolabelled residues were found in fat, providing supporting evidence that the radiolabel that was not recovered was retained in the animal. The parent compound was the main residue in milk and fat in animals at the highest concentration, representing 0.099 and 1.4 mg/kg, respectively. The metabolites fipronil-thioether and fipronil-sulfone were also present in these samples. Although the individual components of the TRR in kidney and muscle represented < 0.05 mg/kg fipronil equivalents, the parent compound and fipronil-sulfone were also present. In the liver, the main metabolite was fipronil-sulfone (0.46 mg/kg fipronil equivalents), representing 53% of TRR; compounds identified in smaller amounts were RPA 200076 (0.098 mg/kg fipronil equivalents) and the parent compound (0.013 mg/kg).

Hens were given repeated oral doses of [^{14}C]fipronil by capsule at a concentration of 0.05, 2 or 10 ppm in the diet (dry matter basis). Approximately 52–58% of the administered radiolabel was eliminated, principally in the excreta. Plateau levels for both the excretion of radiolabel and residue concentrations in egg yolk and white were close to being attained. The high concentrations in egg yolk, skin and fat were consistent with the lipophilic nature of the compound. The metabolite fipronil-sulfone was identified as the principal component of the TRR in eggs and tissues at all concentrations.

The fate of fipronil has been shown to be similar in all species studied. It is relatively well absorbed and extensively distributed in the tissues, with a preference for tissues with a high lipid content. Faeces and then urine were the major routes of elimination of fipronil. Its biotransformation involved changes in the functional groups attached to the pyrazole ring. The compounds identified in faeces and urine were the parent and the fipronil-sulfone, the amide (RPA 200766) derived from the nitrile group, a reduction product (fipronil-thioether), a cleavage product (MB 45897) of the sulfone and its derivatives formed by further cleavage. The fipronil-sulfone was the main compound in eggs and tissues. Parent compound and fipronil-sulfone were identified as major compounds in milk and fat.

Fipronil-desulfinyl: Rats: The absorption, distribution, metabolism and excretion of [^{14}C]fipronil-desulfinyl were studied in rats that received either a single oral dose of 1 or 10 mg/kg bw or 14 daily oral doses of unlabelled fipronil-desulfinyl at 1 mg/kg bw per day followed by a single oral radiolabelled dose. Much more of the dose was eliminated in the faeces (46–70%) than in the urine with all dosing regimens. Appreciable quantities of residues were found in the tissues 1 week after treatment, the highest concentrations being present in fat and fatty tissues. Numerous metabolites or conjugates of fipronil-desulfinyl were present in urine and faeces. Biotransformation of the compound involved changes at the functional groups attached to the pyrazole ring. Only unchanged fipronil-desulfinyl was identified in the liver, fat, skin and residual carcass.

Goats were given repeated oral doses of [^{14}C]fipronil-desulfinyl by capsule at concentrations equivalent to 0.05, 2 and 10 ppm in the diet (dry matter basis) for 7 days. Excretion was mainly in the faeces, the percentage excreted declining with decreasing dose. Plateau levels appeared to have been attained after 104 h on the basis of measurements of radiolabel in milk. The high concentrations in fat were consistent with the lipophilic nature of the compound. Fipronil-desulfinyl was identified as the principal component of the TRR in milk and tissues at all concentrations.

Hens received 14 daily doses of [^{14}C]fipronil-desulfinyl by capsule at concentrations equiva-lent to 0.05, 2 and 10 ppm in the diet (dry matter basis). Approximately 53–71% of the administered radiolabel was eliminated in the excreta. Measurements of radiolabel in eggs indicated that plateau levels had been attained by the end of the dosing period. The high concentrations in egg yolk, omental fat, and skin with fat were consistent with the lipophilic nature of the compound. Fipronil-desulfinyl was identified as the principal component of the TRR in egg and tissues at all concentrations.

The metabolic pathway of the photodegradation product fipronil-desulfinyl in livestock is consistent with that in rats. Fipronil-desulfinyl is metabolized to more polar derivatives or forms polar conjugates, which are excreted. Unmetabolized fipronil-desulfinyl is distributed to eggs, milk, and/or tissues, the highest concentrations being found in fat, consistent with the lipophilic nature of the molecule. These results indicate that only unchanged fipronil-desulfinyl has the potential to transfer to animal substrates in measurable quantities.

Plants

The metabolism of [phenyl ring-^{14}C]fipronil was investigated after application to the soil or to the aerial part of the plant.

Studies of metabolism after soil incorporation were carried out on maize, sugar beet, cotton and sunflowers. Quantitative analysis of radiolabel showed that the uptake of soil-applied fipronil by plants is low (< 5% on the basis of the total radiolabel measured in whole plants at harvest). Analysis of extracts of maize forage samples revealed fipronil, fipronil-sulfone and amide RPA 200766 as the major metabolites; RPA 200761 was also found. In samples taken at harvest, sugar beet and sunflower leaves, maize fodder and cotton foliage contained two common metabolites, fipronil-sulfone and RPA 200766, in addition to various amounts of the parent compound. RPA 105320 and MB 45897 were identified only in beet leaves; RPA 200761 was identified in maize fodder and cotton foliage.

With regard to edible plant parts, fipronil-sulfone and RPA 200766 were present in sugar beet, but only amide RPA 200766 was found in field maize grain. Investigation of sunflower seed extract revealed a complex mixture of substances different from those found in the leaves; a number of components each representing < 0.01 mg/kg were separated. Cotton seed was not analysed as it was found to contain < 0.01 mg/kg of the TRR.

In summary, identification of residues in plant tissues after soil incorporation of fipronil showed that the metabolism proceeded mainly by oxidation to fipronil-sulfone and hydrolysis to amide RPA 200766. Further hydrolysis of metabolites RPA 200766 and fipronil-sulfone can also occur. Very small amounts of fipronil-thioether can be formed by reduction, but in no case was it found at > 5% of the TRR

Studies of metabolism after application by foliar spray were carried out on cabbage, rice, cotton and potato. Radiolabelled residues were quantified in all plant parts. In addition to the formation of previously known fipronil metabolites by oxidation (fipronil-sulfone), reduction (fipronil-thioether) and hydrolysis (RPA 200766, RPA 200761), the photodegradates fipronil-desulfinyl and RPA 104615 were shown to be possible terminal residues after foliar application of fipronil. The main residues found consistently after foliar application were the parent and fipronil-desulfinyl; lesser amounts of fipronil-thioether and fipronil-sulfone were also formed.

Environmental fate

Soil

The photolytic degradation of [^{14}C]fipronil was studied after surface application to a clay loam soil. Fipronil degraded rapidly in both the control (no irradiation) and irradiated phase of the study, with estimated half-times of 49 and 34 days, respectively. The enhanced degradation stimulated by photolysis yielded the photodegradates RPA 104615 and fipronil-desulfinyl, which were also observed after aqueous photolysis but not in the dark control experiments nor in studies of hydrolysis (dark).

Aerobic soil degradation of [^{14}C]fipronil in various soils (sandy loam, sandy clay loam, sand) resulted in DT_{50} values of 40–308 days, depending on the soil type and temperature. The main breakdown product of fipronil in all cases was RPA 200766 (30–47%). Fipronil-sulfone was also identified as a significant degradate (about 20%). Fipronil-thioether was found, but at levels < 10%; RPA 105320 and MB 45897 were present at very low levels. Polar metabolites not previously found appeared in the later stages of the study and were generated in significant amounts (5.9–29.2%, collectively). These metabolites occurred at higher concentrations in the sandy clay loams than in the other soils. The polar metabolites were identified as acid homologues of fipronil and its metabolites, the result of hydrolysis of nitrile to amide and to carboxylic acid.

In a study of adsorption and desorption in soil, fipronil, fipronil-thioether and fipronil-desulfinyl showed medium–low mobility, and fipronil-sulfone was classified as having low mobility to immobility.

Studies of rotational crops were carried out with [^{14}C]fipronil at recommended use rates for soil incorporation or surface treatment. The results were consistent with the established pathways of environmental degradation and plant metabolism.

[^{14}C]Fipronil incorporated into soil at 157 g ai/ha was taken up at a low rate by carrot, radish, lettuce, mustard, sorghum and wheat. Only cereal forage and fodder contained concentrations of residues > 0.01 mg/kg.

After application of [^{14}C]fipronil to soil surface at 369 g ai/ha, neither fipronil nor its relevant metabolites were found in cereal grains 30–365 days later. Further, residues were not found in root crops or leafy vegetables 5 months after treatment.

A field study on radish, soya bean, pea, mustard, lettuce, sorghum and wheat confirmed that soil-surface application at 340 g ai/ha would result in low residues of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone in the vegetative portions of crops, and none in grains. At plant-back intervals of 119–367 days after treatment, concentrations of residues of the parent and its relevant metabolites ranging from < 0.005 to 0.026 mg/kg were found. Only at a short plant-back interval of 31 days were residues found in leafy and root crops (< 0.002–0.016 mg/kg).

Water–sediment systems

A study of the fate and behaviour of [^{14}C]fipronil in two water–sediment systems showed that the major degradate under aerobic conditions was the fipronil-thioether (80–88% of applied radiolabel). The DT_{50} values were 6–14 days in water, 48–75 days in sediment and 22–32 days in the total systems. Under anaerobic conditions, decomposition resulted mainly in the formation of fipronil-thioether and the amide RPA 200766, accounting for 32 to 47% of applied radiolabel, respectively. The DT_{50} value for fipronil under anaerobic conditions was 123 days.

In an investigation of the fate and behaviour of the photodegradation product [^{14}C]fipronil-desulfinyl in two water–sediment test systems (Manningtree, UK, and Ongar, UK), it was found that any fipronil-desulfinyl reaching or formed in the water after an application of fipronil moved to the sediment at an initially rapid rate. The degradation (principally hydrolysis) of the compound then proceeded steadily in both water and sediment phases. The movement of the compound from water to sediment and the degradation resulted in DT_{50} values of 4.2 days and 9.9 days and DT_{90} values of 174 days and 146 days in the two test systems.

Methods of analysis

Plant material is extracted with acetonitrile or water:acetone, and the crude extract is purified by liquid–liquid partition and column chromatography (e.g. silica gel, alumina, Florisil or C18 cartridge). Determination is conducted by GLC with an ECD, MSD or electrochemical detector. The methods have been validated for fipronil, fipronil-thioether, fipronil-sulfone, fipronil-desulfinyl and RPA 200766 in numerous matrices. The LOQs of all compounds ranged from 0.002 mg/kg in e.g. cereal grains, banana and potato to 0.01 mg/kg in cereal straw and forage.

The analytical methods for animal products follow the same steps described above. Numerous validation studies resulted in LOQs for fipronil, fipronil-desulfinyl, fipronil-thioether and MB 56136 of 0.002– 0.01 mg/kg in bovine muscle, milk, liver, kidney, fat and eggs.

The multi-residue analytical method DFG S19, suitable for enforcement, was modified and successfully validated for the determination of residues of fipronil and its metabolites (fipronil-thioether, fipronil-sulfone, fipronil-desulfinyl) in plants and animal products at 0.002 mg/kg per analyte (LOQ) and 0.02 mg/kg per analyte (10 x LOQ).

Methods were developed for the analysis of fipronil, fipronil-sulfone, fipronil-thioether, fipronil-desulfinyl, and RPA 200766 in soil. The residues are extracted from soil with acetonitrile:acetone (70:30). The sample is centrifuged, the extract is dried with Na_2SO_4, and the analytes are adsorbed onto activated charcoal and eluted with acetonitrile. The residues are quantified by GC with ECD. The LOQ is 0.005 mg/kg for all compounds.

Stability of residues in stored analytical samples

Studies of the stability of fipronil, fipronil-thioether and fipronil-sulfone on animal products (milk, liver, kidney, muscle, fat, eggs) under storage conditions indicated that they are stable at –10 °C for at least 3 months. Studies of stability in storage were also reported for residues of fipronil, fipronil-thioether, fipronil-sulfone and fipronil-desulfinyl in lettuce, potato, broccoli, cabbage, cauliflower, maize (grain, forage, fodder, oil, starch) and cotton (seed, hulls, meal, oil, gin trash). The residues were shown to be stable at –20 °C for 12–24 months.

Definition of the residue

Toxicological background

Fipronil was evaluated for toxicology by the 1997 and the 2000 JMPR. The 1997 Meeting concluded that the toxicity of the mammalian metabolites is comparable to or substantially less than that of fipronil. Because the photodegradation product fipronil-desulfinyl is of toxicological concern but not a mammalian metabolite of fipronil, it was reviewed separately.

After considering additional data, the 2000 JMPR established a group ADI of 0–0.0002 mg/kg bw for fipronil and fipronil-desulfinyl, alone or in combination. The acute RfD established by the 1997 JMPR of 0.003 mg/kg bw for fipronil and fipronil-desulfinyl, alone or in combination, was confirmed. Other toxicologically significant compounds are fipronil-sulfone and fipronil-thioether. The 2000 JMPR concluded that the metabolite RPA 200766 is significantly less toxic than fipronil, the acknowledged relevant metabolites fipronil-thioether and fipronil-sulfone and the degradation product fipronil-desulfinyl. Therefore, RPA 200766 should not be relevant for dietary risk assessment.

Plant material

Studies of plant metabolism have shown that, after soil incorporation, residues of the parent and fipronil-sulfone represent most of the total residues, the concentrations of fipronil-thioether usually being low.

In studies of foliar metabolism, most of the residues in edible plant parts (cabbage, potato tubers) consisted of the parent compound and fipronil-desulfinyl, whereas in animal feed items (rice straw, husk, bran), the parent compound, fipronil-sulfone, fipronil-desulfinyl and fipronil-thioether were the residues most relevant for consideration.

The results of supervised residue trials indicated that the parent compound is the main component of the residue. The Meeting concluded that fipronil is a good indicator compound for enforcement purposes for plant commodities. The Meeting considered that, for the purposes of long-term and short-term dietary risk assessment, the residue should be defined as the sum of fipronil, fipronil-sulfone, fipronil-desulfinyl and fipronil-thioether, calculated as fipronil.

Animal products

In a study of metabolism in goats, fipronil, fipronil-sulfone and fipronil-thioether were the principal compounds. In a study of metabolism in laying hens, fipronil-sulfone was identified as the major component of the TRR in eggs and tissues. The results of studies in which fipronil was fed to cows and hens showed that most of the residues in milk, eggs and tissues consisted of fipronil-sulfone.

The Meeting concluded that the definition of residue for enforcement purposes should be the sum of fipronil and fipronil-sulfone, expressed as fipronil. For the purposes of long-term and short-term dietary risk assessment, the residue should be defined as the sum of fipronil, fipronil-sulfone, fipronil-desulfinyl and fipronil-thioether, calculated as fipronil.

The residue definitions are thus:

- for compliance with MRLs for plant commodities: fipronil
- for compliance with MRLs for animal commodities: sum of fipronil and fipronil-sulfone, expressed as fipronil.
- for estimation of long-term and short-term dietary intake from plant and animal commodities: sum of fipronil, fipronil-desulfinyl, fipronil-sulfone and fipronil-thioether, expressed as fipronil.

The Meeting concluded that the residue is fat-soluble.

Results of supervised trials

The residues reported in supervised trials consisted of three (after soil treatment) or four (after foliar spray) components. The studies of metabolism and the supervised trials showed that after soil incorporation, residues of parent and fipronil-sulfone represented most of the total residues. After foliar uses (including soil surface treatment; broadcast treatment of flooded paddy rice), most of the residues in edible plant parts consisted of fipronil and fipronil-desulfinyl, whereas those in animal feed items were fipronil, fipronil-sulfone and fipronil-desulfinyl. If the concentrations of all components are below the LOQ (or MLD), a reasonable assumption is that the concentrations of combined residues are:

- after soil incorporation and seed treatment, for food and feed commodities *(banana, potato, sugar beet, barley, wheat, maize, rice, sweet corn, sorghum, sugar cane, sunflower seed, sugar beet leaves or tops, maize forage and fodder, cereal straw)*: lower than the combined LOQs for fipronil and fipronil-sulfone;

- after foliar and soil surface use and treatment of flooded paddy rice, for food commodities *(banana, flowerhead brassicas, head cabbage, potato, rice, sorghum, cotton seed)*: lower than the combined LOQs for fipronil and fipronil-desulfinyl;

- after foliar and soil surface use and treatment of flooded paddy rice, for feed items *(pasture grass, cereal straw, sorghum forage and fodder, cotton gin trash)* and sugar cane: lower than the combined LOQs for fipronil, fipronil-sulfone and fipronil-desulfinyl.

When the concentration of one component is above and the other below the LOQ, that of the combined residue is assumed to be close to the measurable component plus the LOQ of the other. To indicate that one of the results was a real measurement, the Meeting agreed to express the sum of the values as a real figure (e.g. < 0.002 + 0.004 mg/kg = 0.006 mg/kg). The method for calculating the total residue in various situations is illustrated below.

Fipronil	Fipronil-sulfone or fipronil-desulfinyl	Total
< 0.002	< 0.002	< 0.004
< 0.002	0.004	0.006
0.003	0.005	0.008

The concentrations of residues of fipronil (437.2 g/mol) and the metabolites fipronil-thioether (421.1 g/mol, factor 1.04), fipronil-sulfone (453.1 g/mol, factor 0.965) and fipronil-desulfinyl (389.02 g/mol, factor 1.1) are given in the evaluation tables for the individual compounds but were calculated in the appraisal according to the respective residue definition. The LOQs of the individual compounds are not corrected by these factors.

Banana: Common practice worldwide is to apply 300–400 g ai/ha fipronil around the base of the banana stem or plant with or without incorporation into the soil. The number of treatments and the PHI are not specified in most countries.

Two studies, each of 300 and 600 g ai/ha, and one study with 800 g ai/ha were available from Australia. As separate plots were treated on different dates and the bananas were harvested at different times (PHI, 0–166 days), these were considered to be individual trials. In all 10 trials conducted according to Australian GAP (stem and soil surface treatment, 300 g ai/ha), the concentrations of fipronil, fipronil-thioether, fipronil-sulfone and fipronil-desulfinyl residues were no higher than the LOQ of 0.002 mg/kg.

Five studies of soil treatment in Guadeloupe (10 trials, 1 x 400 kg ai/ha; three trials, 2 x 400 g ai/ha) with PHIs of 0–149 days were carried out according to French GAP. A further soil treatment trial was carried out according to GAP (400 g ai/ha, soil broadcast at base of plant) in Cameroon. The ranked orders of concentrations of residues after stem and soil surface spray were < 0.002 (10) mg/kg for fipronil and < 0.004 (10) mg/kg for the sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone (calculated as fipronil). The ranked orders of concentrations of residues after soil incorporation were < 0.002 (12) and 0.003 mg/kg for fipronil and < 0.004 (12) and 0.005 mg/kg for the sum of fipronil, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

The combined results of 23 trials with foliar spray and soil incorporation were, in ranked order (median underlined), < 0.002 (22) and 0.003 mg/kg for fipronil and <u>< 0.004</u> (22) and 0.005 mg/kg for the sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

The Meeting estimated the following residue levels in bananas: maximum residue level (fipronil), 0.005 mg/kg; STMR (sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone), 0.004 mg/kg; highest residue (sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone), 0.005 mg/kg.

Foliar spray use of fipronil on broccoli and cauliflower is registered in Australia with a maximum GAP of 4 x 48 g ai/ha and a PHI of 7 days. Numerous trials were carried out in Australia, but only one trial on broccoli and two on cauliflower were conducted in accordance with the maximum GAP (4 or 5 x 48 g ai/ha; PHI, 7 days). The results of further trials with two to ten applications at an interval of 7 days showed that the number of applications is of secondary relevance to the residue concentration. Therefore, further trials with 48 g ai/ha and a PHI of 7 days were used for evaluation, two on broccoli (six or ten treatments) and four on cauliflower (two, eight or nine treatments). The ranked orders of concentrations of residues after foliar spray were < 0.002 (2), 0.002, 0.003 (3), 0.005, 0.006 and 0.008 mg/kg for fipronil and < 0.004 (2), 0.004, <u>0.005</u> (3), 0.007, 0.008 and 0.01 mg/kg for the sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

Foliar spray use of fipronil in head cabbage is registered in Australia (4 x 24–48 g ai/ha; PHI, 7 days), in New Zealand (4 x 24 g ai/ha; PHI, 7 days), the Philippines (6–8 x 25–50 g ai/ha; PHI, 7 days) and other countries in Asia and Latin America. Supervised trials with various numbers of applications were available from Australia and New Zealand. The Meeting noted that the number of applications is of secondary importance for the concentration of residue, and therefore the results from trials with two, four and eight applications were combined.

In four of the trials in Australia and one in New Zealand that conformed to New Zealand GAP (24 g ai/ha), the concentrations of residues were lower than the LOQ of 0.002 mg/kg.

In five trials in Australia and one in New Zealand that complied with the Australian maximum GAP (48 g ai/ha) and in which there were detectable residues, the ranked orders of concentrations of residues were < 0.002 (3), 0.002, 0.004 and 0.014 mg/kg for fipronil and < 0.004, 0.004, 0.0042, 0.0053, 0.0062 and 0.0215 mg/kg for the sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

The Meeting noted that the data on flowerhead brassica and head cabbage were similar and could be combined for mutual support. The combined residues were, in ranked order, for fipronil: < 0.002 (6), 0.002 (2), 0.003 (3), 0.004, 0.005, 0.006, 0.008 and 0.14 mg/kg, and for the sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone (calculated as fipronil) (median underlined): < 0.004 (3), 0.004 (2), 0.0042, 0.005 (3), 0.0053, 0.0062, 0.007, 0.008, 0.01 and 0.0215 mg/kg.

The Meeting estimated the following residue levels for flowerhead brassicas and cabbages, head: maximum residue level (fipronil), 0.02 mg/kg; STMR (sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone), 0.005 mg/kg; and HR (sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone), 0.0215 mg/kg.

The use of fipronil on Brussels sprouts is registered in Australia (4 x 24–48 g ai/ha; PHI, 7 days), but the results of only one trial were received. The Meeting could not recommend extrapolation of the results for cabbages, head or flowerhead brassicas to Brussels sprouts and concluded that there were insufficient data to estimate a maximum residue level.

The results of four trials on brassica leafy vegetables in Malaysia with 2 x 25 or 50 g ai/ha (GAP, 4–6 x 36 g ai/ha) were received. The Meeting could not recommend extrapolation from the results for cabbages, head or flowerhead brassicas to brassica leafy vegetables and concluded that there were insufficient data to estimate a maximum residue level.

Fipronil may be used on potato as a foliar spray e.g. in Hungary (1–2 x 20 g ai/ha; PHI, 14 days), in Spain (3 x 20–24 kg ai/ha; PHI, 14 days), the Czech Republic, Poland and Slovakia (20 g ai/ha; PHI, 14 days; number of treatments not specified) and Romania (3 x 20 g ai/ha; PHI, 30 days). Another use is soil incorporation at planting, e.g. in Italy (1 x 150 g ai/ha).

For foliar spray, the results of 29 European trials conducted according to the above GAPs were submitted. Most of the samples were analysed for fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone at an LOQ of 0.002 mg/kg for each. Two trials in Hungary were analysed with a less sensitive method (LOQ, 0.01 mg/kg), resulting in unquantifiable concentrations of residues of each compound. These trials were considered to belong to another population and were excluded from the evaluation. The concentrations of residues, in ranked order, were < 0.002 (26) and 0.003 mg/kg for fipronil and < 0.004 (23) mg/kg for the sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

For soil incorporation, six trials were carried out according to Italian GAP. The samples were analysed for fipronil, fipronil-thioether and fipronil-sulfone. One study showed high concentrations of

0.017 mg/kg fipronil and 0.009 mg/kg fipronil-sulfone. No residue was determined in the corresponding untreated sample. The Meeting considered that there was no reason to exclude this value from the evaluation. The concentrations of residues, in ranked order, were < 0.002 (4), 0.005 and 0.017 mg/kg for fipronil and < 0.004 (4), 0.007 and 0.028 mg/kg for the sum of fipronil, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

The combined results of the 27 trials with foliar spray and the six trials with soil incorporation were, in ranked order: < 0.002 (30), 0.003, 0.005 and 0.017 mg/kg for fipronil and ≤ 0.004 (27), 0.007 and 0.028 mg/kg for the sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

The Meeting estimated the following residue levels for potato: maximum residue level (fipronil), 0.02 mg/kg; STMR (sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone), 0.004 mg/kg; highest residue (sum of fipronil, fipronil-desulfinyl, fipronil-thioetherand fipronil-sulfone), 0.028 mg/kg.

Fipronil can be used on sugar beet by soil application, e.g. in France and Italy (1 x 150–160 g ai/ha). In France, another GAP is broadcast soil incorporation before sowing at 200 g ai/ha. A further use is by foliar spray at 20–24 g ai/ha (PHI, 30 days) in Hungary and Romania.

For foliar spray, only one trial conducted in Hungary according to the GAP was reported. The concentrations of the residues of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone were lower than the LOQ of 0.01 mg/kg. The Meeting considered that one trial was inadequate to allow assessment the residue of fipronil in sugar beet after foliar spray.

Numerous trials (34) by soil treatment were carried out in France at 150–200 g ai/ha according to French or Italian GAP. Ten were analysed with a method with a LOQ of 0.01 mg/kg, but concentrations greater than the LOQ were determined in three of the trials. Hence, these trials were included in the assessment. One study showed high values of 0.16 mg/kg for fipronil and 0.015 mg/kg for fipronil-sulfone. No residue was determined in the corresponding untreated sample. The Meeting noted that there was no reason to exclude this value from the evaluation. The concentrations of residues, in ranked order, were: < 0.002 (7), 0.002, 0.003 (6), 0.005 (2), 0.007, 0.009, < 0.01 (9), 0.011, 0.013, 0.014, 0.018 (2), 0.072 and 0.16 mg/kg for fipronil and < 0.004 (7), 0.005 (2), 0.007 (3), 0.008 (2), 0.008, 0.009, 0.01, 0.011, 0.014, 0.018, < 0.02 (9), 0.021, 0.024, 0.028 (2), 0.082 and 0.17 mg/kg for the sum of fipronil, fipronil-thioether, fipronil-sulfone (calculated as fipronil).

The Meeting estimated the following residue levels for sugar beet on the basis of use by soil incorporation: maximum residue level (fipronil), 0.2 mg/kg; STMR (sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone), 0.0125 mg/kg; highest residue (sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone), 0.17 mg/kg.

Fipronil is registered for use as a foliar spray on cereal grains (barley, oats, rye, triticale, wheat) in many countries, but adequate data on residues have not been submitted. In France, fipronil may be used as a seed treatment at 50 g ai/100 kg in cereals. There is specific GAP for wheat in Belgium (50 g ai/100 kg seed) and in Chile (50–100 g ai/100 kg seed).

Six seed treatment trials with two- to threefold excess doses on barley were reported from France (treatment with 100 or 150 g ai/100 kg of seed). The grains were analysed for fipronil, fipronil-thioether and fipronil-sulfone. At harvest, 249–271 days after sowing, the concentrations of residues of all analytes were below the LOQ of 0.002 mg/kg of grain.

Five trials on wheat seed treatment that complied with GAP (50 g ai/100 kg seed) were carried out in France. The grains were analysed for fipronil, fipronil-thioether and fipronil-sulfone. At harvest, 128–145 days after sowing, the concentrations of residues of all analytes were below the LOQ of 0.002

mg/kg of grain. In 17 trials conducted in France and Greece trials at higher application rates (75–150 g ai/100 kg seed), the concentrations of residues in the analytes were < 0.002–0.003 mg/kg. The concentrations of residues in barley and wheat after seed treatment were < 0.002 (11) mg/kg for fipronil and ≤ 0.004 (11) mg/kg for the sum of fipronil, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

The Meeting agreed to extrapolate the data on residues in barley and wheat to oats, rye and triticale for seed treatment use, and estimated the following residue levels: maximum residue level (fipronil), 0.002* mg/kg; STMR (sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone), 0.004 mg/kg; and highest residue (sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone), 0.004 mg/kg.

The use of fipronil as seed treatment of maize is registered in many countries: e.g. France and Italy 250 g ai/100 kg seed; Mozambique and Zimbabwe, 400 g ai/100 kg seed. Eleven trials were reported from France and Spain at 250–375 g ai/100 kg seed. The samples were analysed for fipronil, fipronil-thioether and fipronil-sulfone. Residues of all analytes were undetectable (< 0.002 mg/kg). The ranked orders were thus: < 0.002 (11) mg/kg for fipronil and < 0.004 (11) mg/kg for the sum of fipronil, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

Another use is by soil treatment before or at sowing (e.g. France 200, Italy 100–150, USA 112–146 g ai/ha). Fifteen southern European trials complied with French and Italian GAP and 46 North American trials with GAP in the USA. The ranked orders of residues were < 0.002 (39), 0.002, < 0.004 (16), 0.004 and < 0.01 (4) mg/kg for fipronil and < 0.004 (13), 0.004, < 0.005 (24), < 0.007 (16), 0.007, < 0.012 (2), <0.013 (3) and < 0.02 mg/kg for the sum of fipronil, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

Hungarian GAP allows one foliar spray at 20 g ai/ha and a 30-day PHI. The concentration of residues in maize grain in a trial that complied with GAP was < 0.01 mg/kg for fipronil and its metabolites. The Meeting considered that one trial was inadequate to allow assessment of residues of fipronil in maize after foliar spray.

The combined results of trials with seed treatment and soil incorporation for maize were, in ranked order, < 0.002 (50), 0.002, < 0.004 (16), 0.004 and < 0.01 mg/kg for fipronil and < 0.004 (24), 0.004, ≤ 0.005 (24), < 0.007 (16), 0.007, < 0.012 (2), <0.013 (3) and < 0.02 mg/kg for the sum of fipronil, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

The Meeting estimated the following levels for maize: maximum residue level (fipronil), 0.01 mg/kg; STMR (sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone), 0.005 mg/kg; and highest residue (sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone), 0.02 mg/kg.

Sweet corn (corn-on-the-cob) was analysed in four French trials after soil treatment with fipronil before or at sowing at 200 g ai/ha. The concentrations of residues, in ranked order, were: < 0.002 (3) and 0.003 mg/kg for fipronil and < 0.004, < 0.004, 0.007 and 0.01 mg/kg for the sum of fipronil, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

The Meeting decided that four trials were insufficient to allow estimation of a maximum residue level for sweet corn.

Fipronil may be used on rice worldwide as a seed treatment, as soil or flooded paddy application or as a foliar spray. Numerous supervised trials with various application scenarios were reported. The following trials were conducted in accordance with GAP:

- seed treatment at 10–13 g ai/100 kg seed: one trial in Australia, five trials in France
- seed treatment at 120 g ai/100 kg seed, equal to 56 g ai/ha: 17 trials in the USA
- seed-box treatment at 0.5 g ai/nursery box: five trials in Japan
- soil incorporation before planting at 56 g ai/ha: 17 trials in the USA
- broadcast treatment on flooded paddy at 1 x 50 g ai/ha: three trials in the Philippines, one trial in Taiwan, three trials in Thailand (with no analysis for fipronil-thioether or fipronil-sulfone)
- foliar treatment: six trials in the Philippines at 1 x 50 g ai/ha and four trials in Thailand at 1 x 50 g ai/ha, with no analysis for fipronil-thioether or fipronil-sulfone; one trial in Indonesia at 1 x 25 g ai/ha, with analysis for fipronil, fipronil-thioether, fipronil-sulfone and fipronil-desulfinyl.

The concentrations of residues after seed treatment, including seed boxes and soil incorporation, in ranked order, were: < 0.001 (5), < 0.002 (6), < 0.003 (31) and < 0.01 (3) mg/kg for fipronil and < 0.002 (5), < 0.004 (6), ≤ 0.006 (31) and < 0.013 (3) mg/kg for the sum of fipronil, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

The concentrations after broadcast treatment on flooded paddy, were < 0.001 (7) mg/kg for fipronil and ≤ 0.001 (7) mg/kg for fipronil-desulfinyl. The sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone could not be calculated, as fipronil-thioether and fipronil-sulfone were not analysed.

The concentrations after foliar spray were < 0.001 (9), 0.002 and 0.008 mg/kg for fipronil; < 0.001 (8), 0.001 (3) and 0.005 mg/kg for fipronil-desulfinyl; and 0.016 mg/kg for the sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone (calculated as fipronil; only one sample was analysed for fipronil-thioether and fipronil-sulfone).

The Meeting decided that the data on use as a foliar spray and by broadcast onto flooded paddy were insufficient because most of the samples were not analysed according to the residue definition. It decided to derive the maximum residue levels from the data for seed or seed-box treatment and soil incorporation. The Meeting estimated the following residue levels for rice: maximum residue level (fipronil), 0.01 mg/kg; STMR (sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone), 0.006 mg/kg; highest residue (sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone), 0.013 mg/kg.

Use of fipronil on sorghum is registered in Australia for seed treatment (75 g ai/100 kg seed) and as a foliar spray (1.5 g ai/ha; PHI, 14 days). The results of supervised trials were available only from Australia. Three trials by foliar spray and two by seed treatment were conducted according to GAP. The samples were analysed for fipronil, fipronil-thioether, fipronil-sulfone and fipronil-desulfinyl. The concentrations of residues after seed treatment, in ranked order, were: < 0.002 (2) mg/kg for fipronil and < 0.004 (2) mg/kg for the sum of fipronil, fipronil-thioether and fipronil-sulfone (calculated as fipronil). The concentrations of residues after foliar treatment, in ranked order, were: < 0.002 and 0.002 (2) mg/kg for fipronil and < 0.004 and 0.004 (2) mg/kg for the sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

The Meeting concluded that two trials of seed treatment and three of foliar treatment were inadequate for estimating a maximum residue level or STMR for a major crop such as sorghum.

The registered Australian use pattern on sugar cane allows application of 75 g ai/ha as one spray directed at the soil at the time of planting and/or spray to the bottom 40 cm of the stalk (PHI, 84 days). In Brazil, 200 g ai/ha are used as a soil spray in furrows at the time of planting.

Five trials of soil treatment were received from Australia, but only two complied approxi-mately with GAP. The samples were analysed for fipronil, fipronil-thioether and fipronil-sulfone. The concentrations of residues for all analytes were lower or at the LOQ of 0.002 mg/kg at PHIs of 245 and 340 days.

Five trials in which the last treatment was spray to the bottom of the stalk were carried out in Australia. Two were approximately in accordance with Australian GAP. The concentrations of residues were lower than or at the LOQ of 0.002 mg/kg, with PHIs of 95 and 101 days for all analytes (fipronil, fipronil-thioether, fipronil-sulfone and fipronil-desulfinyl).

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

Fipronil may be used worldwide for seed treatment of cotton (e.g. in Australia at 50 g ai/100 kg seed) or as foliar spray (e.g. in Mexico at 2 x 50 g ai/ha; PHI, 45 days; Brazil at 4–7 x 12–80 g ai/ha; PHI, 15 days). In the USA, GAP for foliar treatment at 28–56 g ai/ha (maximum, 224 g ai/ha per season) and a PHI of 60 days is pending approval. Numerous supervised trials of seed or soil treatment followed by foliar spray or foliar spray only were reported from Australia, Brazil, Mexico and the USA. Three from Australia and one from Brazil complied with GAP.

The concentrations of residues after foliar treatment were < 0.002, 0.003, 0.004 and < 0.01 mg/kg for fipronil and < 0.004, 0.01 (2) and < 0.02 mg/kg for the sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

Forty trials in the USA complied with the pending GAP. These trials were not evaluated as pending GAP is not considered by the Meeting.

The Meeting concluded that four trials were inadequate to allow estimation of a maximum residue level or an STMR for cotton seed, as it is a major crop.

Australian GAP permits treatment of sunflower seed at 75 g of fipronil per 100 kg. Data were available from four supervised trials conducted according to GAP and four trials with a twofold overdose. The samples were analysed for fipronil, fipronil-thioether and fipronil-sulfone. The concentrations of residues of all analytes were < 0.002 mg/kg.

French GAP permits seed treatment with 500 g of fipronil per 100 kg of sunflower seed. Data were available from six supervised trials conducted approximately according to GAP (375 g ai/100 kg seed) and three trials in Spain with a twofold overdose (1 kg ai/100 kg seed). The samples were analysed for fipronil, fipronil-thioether and fipronil-sulfone. The concentrations of residues were < 0.002 mg/kg (6) for fipronil and from < 0.002 to 0.004 for the other analytes.

GAP in France also allows application of 200 g ai/ha as a spray directed at the soil. Data were available from eight supervised trials in France conducted approximately according to GAP, and one trial in France and one in Italy at overdoses. The samples were analysed for fipronil, fipronil-thioether and fipronil-sulfone The concentration of residues was < 0.002 mg/kg (9) for each analyte. Eight further trials in France that complied with GAP resulted in concentrations below the LOQ of 0.01 mg/kg. As no concentration > 0.01 mg/kg was detected, the Meeting did not consider the data from France based on an LOQ of 0.01 mg/kg.

The concentrations of residues after soil and seed treatment, in ranked order, were: < 0.002 (19) mg/kg for fipronil and ≤ 0.004 (17), 0.007 and 0.008 mg/kg for the sum of fipronil, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

The Meeting estimated the following levels from trials with an LOQ of 0.002 mg/kg for sunflower seed: maximum residue level (fipronil), 0.002* mg/kg; STMR (sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone), 0.004 mg/kg; and highest residue (sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone), 0.008 mg/kg.

A total of 27 trials were carried out in France on soil treatment of sugar beet leaves or tops at 150–200 g ai/ha according to French (160 g ai/ha) or Italian GAP (150 g ai/ha). The concentrations of residues on a fresh weight basis were < 0.002 (5), < 0.01(14), 0.011, 0.012, 0.014, 0.015, 0.017, 0.018, 0.021 and 0.029 mg/kg for fipronil and < 0.004 (2), 0.004, 0.005, 0.008, ≤ 0.02 (13), 0.021, 0.023, 0.024, 0.025, 0.027, 0.028, 0.029, 0.033 and 0.041 mg/kg for the sum of fipronil, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

Allowing for the standard 23% dry matter (*FAO Manual*), the Meeting estimated the following residue levels (dry weight) in sugar beet leaves or tops for soil incorporation use: maximum residue level (fipronil), 0.2 mg/kg; STMR (sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone), 0.087 mg/kg (0.02/0.23).

Numerous supervised trials were available on maize forage (n = 72) and fodder (n = 55) after seed or soil treatment. To prepare silage for feed, the whole aerial portion of the immature plant must be cut at the late dough or early dent stage. Hence, the data on residues in fodder 77–120 days after treatment were used for evaluation.

The ranked orders of concentrations of residues in forage or silage on a fresh weight basis after seed treatment and soil incorporation were: < 0.002, < 0.005 (19), < 0.007 (18), < 0.01, < 0.02 (29), 0.022 (2), 0.023 and 0.038 mg/kg for fipronil and < 0.004, < 0.01 (17), < 0.012 (11), 0.012, 0.016, < 0.02, < 0.025 (2), ≤ 0.027 (5), < 0.04 (24), 0.041, 0.042, 0.044, 0.046, 0.048, 0.05, 0.053, 0.055 and 0.079 mg/kg for the sum of fipronil, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

Allowing for the standard 40% dry matter (*FAO Manual*), the Meeting estimated the following residue levels (dry weight) in maize forage: maximum residue level (fipronil), 0.1 mg/kg; and STMR (sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone), 0.0675 mg/kg (0.027/0.4).

The ranked orders of residues in the corresponding dry maize fodder samples taken at harvest, on a fresh weight basis (seed treatment and soil incorporation) were: < 0.002, < 0.003 (5), < 0.005 (3), < 0.02 (41), 0.02, 0.022, 0.025 and 0.04 (2) mg/kg for fipronil and < 0.004, < 0.005, < 0.008 (2), < 0.01 (2), < 0.023 (2), < 0.025, ≤ 0.04 (23), 0.041, 0.043, 0.044 (4), 0.046, 0.05, 0.052, 0.053, 0.055, 0.057 (2), 0.061, 0.062, 0.064, 0.066 (2), 0.069, 0.072, 0.09, 0.093 and 0.14 mg/kg for the sum of fipronil, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

Allowing for the standard 83% dry matter in maize stover (*FAO Manual*), the Meeting estimated the following residue levels (dry weight) in maize fodder: maximum residue level (fipronil), 0.1 mg/kg, and STMR (sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone), 0.048 mg/kg (0.04/0.83).

Use of fipronil as a foliar spray on pasture grass is registered in Australia (1 x 1.3 g ai/ha; PHI, 14 days) and South Africa (1 x 7.5 g ai/ha; PHI, 21 days). Numerous supervised trials on pasture grass were carried out in Australia with one application of 1.25, 2.5, 5, 7.5, 10, 20 or 30 g ai/ha; one trial was conducted in Mauritania with 11 g ai/ha; one trial was conducted in the Russian Federation with 4 g ai/ha and three trials in South Africa, each with 7.5 g ai/ha and 15 g ai/ha, were submitted. Of the trials submitted, two from Australia and the three from South Africa were in accordance with the respective GAP. The ranked orders of concentrations of residues on a fresh weight basis were < 0.002, 0.004, < 0.05, 0.21 and 0.44 mg/kg for fipronil, and < 0.006, 0.009, 0.079, 0.51 and 0.66 mg/kg for the sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

The Meeting decided that five trials were insufficient to estimate a maximum residue level or an STMR for pasture grass.

Straw and fodder (dry) of cereal grains (barley, oats, rye, triticale, wheat): The two- to threefold overdoses used in the French trials of seed treatment for barley showed residues of fipronil-sulfone (maximum 0.038 mg/kg) in the straw. These results could not be used for evaluation because the trials were not conducted according to GAP and the results do not indicate a 'nil residue situation' as in the corresponding grain samples.

Five trials of treatment of wheat seed that complied with GAP (50 g ai/100 kg seed) were carried out in France. Samples were taken at harvest, 128–286 days after sowing. The ranked orders of concentrations of residues in wheat straw, on a fresh weight basis, were < 0.01 (3) and 0.011 (2) mg/kg for fipronil and < 0.02 (3), 0.021 and 0.025 mg/kg for the sum of fipronil, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

For foliar spray use, only one trial in Poland was received, which complied with Czech and Slovak GAP. The concentrations of residues (fresh weight) were 0.017 mg/kg for fipronil and 0.063 mg/kg for the sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

The Meeting concluded that five trials with soil treatment and one with foliar treatment were insufficient to estimate a maximum residue level and an STMR for cereal straw and fodder, dry.

Numerous supervised trials with different applications to rice straw and fodder, dry were reported. The trials conducted in accordance with GAP were:

- seed treatment at 10–13 g ai/100 kg seed: one trial in Australia, five trials in France
- seed treatment at 120 g ai/100 kg seed: 17 trials in the USA
- seed-box treatment at 0.5 g ai/box: five trials in Japan
- soil incorporation before planting (56 g ai/ha): 17 trials in the USA
- broadcast treatment on flooded paddy (1 x 50 g ai/ha): one trial in the Philippines, one in Taiwan and three in Thailand
- foliar treatment (1 x 50 g ai/ha): four trials in Thailand, one in the Philippines (at Thai GAP) and one in Taiwan (at Thai GAP)
- broadcast treatment after transplanting, followed by foliar treatment (2 x 50 g ai/ha): one trial in the Philippines.

Rice straw was the only feed item used in the calculation of the dietary burden of cattle with detectable residues of the photodegradation product fipronil-desulfinyl. As separate studies of cattle feeding were carried out with fipronil and fipronil-desulfinyl, the dietary burden must be calculated differently than for other feed items, and different STMR values are needed.

The ranked orders of concentrations of residues, on a fresh weight basis, after seed treatment, including seed box and soil incorporation, were: < 0.002 (2), < 0.003 (4), < 0.005 (4), < 0.01 (29), 0.01 (2), 0.012, 0.016 and 0.04 (2) mg/kg for fipronil and < 0.004 (2), < 0.006 (4), < 0.01 (4), < 0.013 (3), < 0.02 (15), 0.02, 0.021, 0.022, 0.023 (2), 0.024 (2), 0.026 (2), 0.03 (2), 0.031, 0.033, 0.06, 0.069, 0.11 and 0.26 mg/kg for the sum of fipronil, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

The ranked orders of concentrations of residues, on a fresh weight basis, after foliar and broadcast onto flooded paddy were: < 0.005 (5), 0.006, 0.017, 0.02, 0.027, 0.061, 0.09 and 0.13 mg/kg for fipronil; < 0.005 (2), 0.006, 0.012, 0.021, 0.025, 0.028, 0.049, 0.075, 0.084, 0.095 and 0.2 mg/kg for fipronil-desulfinyl; < 0.01 (2), 0.011, 0.014, 0.019, 0.024, 0.038, 0.058, 0.077, 0.12, 0.19 and 0.33 mg/kg for the sum of fipronil, fipronil-thioether and fipronil-sulfone (calculated as fipronil); and < 0.015 (2), 0.018, 0.032, 0.039, 0.047, 0.069, 0.11, 0.17, 0.2, 0.3 and 0.55 mg/kg for the sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

The Meeting noted that the data resulting from different uses (seed treatment including seed box and soil incorporation on the one hand and foliar and broadcast onto flooded paddy on the other hand)constituted one population. The combined results of the two data sets were: < 0.002 (2), < 0.003 (4), < 0.005 (9), 0.006, < 0.01 (29), 0.01 (2), 0.012, 0.016, 0.017, 0.02, 0.027, 0.04 (2), 0.061, 0.09 and 0.13 mg/kg for fipronil; < 0.005 (2), 0.006, 0.012 (2), 0.025, 0.028, 0.049, 0.075, 0.084, 0.095 and 0.2 mg/kg for fipronil-desulfinyl; < 0.004 (2), < 0.006 (4), < 0.01 (6), 0.011, < 0.013 (3), 0.014, 0.019, ≤ 0.02 (15), 0.02, 0.021, 0.022, 0.023 (2), 0.024 (3), 0.026 (2), 0.03 (2), 0.031, 0.033, 0.038, 0.058, 0.06, 0.069, 0.077, 0.11, 0.12, 0.19, 0.26 and 0.33 mg/kg for the sum of fipronil, fipronil-thioether and fipronil-sulfone (calculated as fipronil); and < 0.004 (2), < 0.006 (4), < 0.01 (4), < 0.013 (3), < 0.015 (2), 0.018, ≤ 0.02 (15), 0.02, 0.021, 0.022, 0.023 (2), 0.024 (2), 0.027 (2), 0.03, 0.031, 0.032 (2), 0.034, 0.039, 0.047, 0.06, 0.07 (2), 0.11 (2), 0.17, 0.2, 0.26, 0.3 and 0.55 mg/kg for the sum of fipronil, fipronil-desulfinyl, fipronil-thioether and fipronil-sulfone (calculated as fipronil).

Allowing for the standard 90% dry matter (*FAO Manual*), the Meeting estimated the following residue levels (dry weight) for rice straw: maximum residue level (fipronil), 0.2 mg/kg; STMR (fipronil-desulfinyl), 0.029 mg/kg (0.0265/0.9); STMR (sum of fipronil, fipronil-thioether, fipronil-sulfone), 0.022 mg/kg (0.02/0.9).

Sorghum forage and fodder: Fipronil is registered for use as a foliar spray on sorghum at 1.5 g ai/ha (PHI, 14 days). Registration as a seed treatment at 75 g ai/100 kg seed is pending. The results of supervised trials were available only from Australia. Forage samples from trials conducted in accordance with registered or pending GAP were available from three trials with foliar spraying and two with seed treatment, but straw samples were available only from the two seed treatment trials. The samples were analysed for fipronil, fipronil-thioether, fipronil-sulfone and fipronil-desulfinyl. The concentration of residues in each analyte was < 0.002 mg/kg.

The concentrations of residues, in ranked order, in forage on a fresh weight basis after foliar spray were: < 0.002 (2) and 0.002 mg/kg for fipronil and < 0.006 (2) and 0.006 mg/kg for the sum of fipronil, fipronil-desulfinyl, fipronil-thioether, fipronil-sulfone (calculated as fipronil).

The Meeting did not consider trials conducted according to a pending GAP and concluded that three trials of foliar treatment were inadequate for estimating a maximum residue level or STMR for sorghum forage or fodder.

Cotton gin trash used as animal feed includes plant parts resulting from ginning cotton, which consist of burrs, leaves, stems, lint and seeds. Data on residues after foliar spray use were reported from one trial in Australia and 30 in the USA conducted according to the pending GAP in the USA. The Meeting does not consider trials according to a pending GAP and concluded that the data were inadequate for estimating a maximum residue level or an STMR for cottonseed.

Sunflower forage and fodder samples were taken from each of four seed treatment trials conducted in Australia at 75 or 150 g ai/100 kg seed and analysed for fipronil, fipronil-thioether, fipronil-sulfone and fipronil-desulfinyl. The concentration of residues was < 0.002 mg/kg in each analyte in all samples.

The Meeting noted that sunflower forage and fodder is not a feed item and did not recommend an MRL or STMR.

The results of analyses for residues in sugar cane leaves for forage and fodder in numerous trials conducted in Australia were submitted, but only two had been conducted according to GAP. The concentrations of all the residues (parent, fipronil-thioether, fipronil-sulfone, fipronil-desulfinyl) were < 0.002 mg/kg (fresh weight).

The Meeting considered that two trials were insufficient to allow estimation of a maximum residue level or an STMR.

Fate of residues during processing

The effect of processing on the concentrations of residues of fipronil has been studied in potatoes, maize, cotton seed, sunflower seed and sugar cane. No study on the effects of processing on the nature of the residue was received. As cauliflower, broccoli, cabbages and potatoes are usually eaten cooked, studies of the effects of processing would be desirable, as the proportions of parent compound and the relevant metabolites might be changed by cooking.

In one trial on potato treated by foliar spray in the USA, 0.0035 mg/kg of fipronil and 0.003 mg/kg of fipronil-desulfinyl were detected in the tubers. The concentrations of residues of fipronil-thioether and fipronil-sulfone were lower than the LOQ/MLD of 0.003/0.001 mg/kg. When the tubers were processed to chips, flakes and wet peel, the following processing factors were calculated:

Commodity	Fipronil + fipronil-desulfinyl (mg/kg), calculated as fipronil	Processing factor
Tuber	0.0068	
Chips	< 0.004	< 0.59
Flakes	< 0.004	< 0.59
Wet peel	0.056	8.2

In a second processing study in the USA, potatoes were treated in the furrow and then by spraying of foliage. Residues of fipronil, fipronil-thioether, fipronil-sulfone and fipronil-desulfinyl were detected in the tubers, which were processed to chips, flakes and wet peel. The following processing factors were calculated:

Commodity	Fipronil + fipronil-thioether + fipronil-sulfone + fipronil-desulfinyl (mg/kg), calculated as fipronil	Processing factor
Tuber	0.057	
Chips	< 0.0126	< 0.221
Flakes	0.0156	0.274
Wet peel	0.394	6.91

As the concentrations of residues in raw agricultural commodities in the first study were near the LOQ, the Meeting applied only the processing factors from the second study to the STMR value of 0.004 mg/kg for whole potatoes in order to calculate the following STMR-P values: chips, 0.0009 mg/kg; flakes, 0.0011 mg/kg; wet peel, 0.0276 mg/kg.

A study of maize processing was carried out in the USA after a single in-furrow application at planting at an exaggerated application rate. No detectable residues were reported in raw or processed commodities. No STMR-P value could be estimated.

The results of two processing studies carried out in the USA on cotton seed were submitted. The processed fractions were meal, hulls, crude and refined (edible) oil. Two further, limited studies carried out in Mexico show no fipronil or its metabolites in oil. The processing factors were based on the studies in the USA and the second Mexican study and are shown below:

Commodity	Fipronil + fipronil-thioether + fipronil-sulfone + fipronil-desulfinyl (mg/kg), calculated as fipronil	Processing factor
Seed	0.337	
Meal	< 0.008	< 0.025
Hulls	0.042	0.12
Crude oil	0.111	0.33
Refined oil	0.074	0.22
Seed	0.289	
Meal	< 0.0126	< 0.044
Hulls	0.062	0.21
Crude oil	0.109	0.38
Refined oil	0.097	0.34
Seed	< 0.031	
Crude oil	<0.024	< 0.77
Seed	0.148	
Crude oil	< 0.031	0.21

The mean processing factors were 0.035 for cotton meal, 0.165 for cotton hulls, 0.307 for cotton crude oil and 0.28 for cotton refined oil. As no STMR value was derived for cotton seed, no STMR-P values were estimated.

In numerous supervised trials conducted on sunflower seed in southern Europe, residues in sunflower oil extracted from the seeds and the cake solid were also measured. As neither fipronil nor its metabolites were detected in raw agricultural commodities, no STMR-P value could be estimated.

Nine studies on processing of sugar cane were submitted, but only two (each with two independent trials) showed residues in raw agricultural commodities and could be used to estimate processing factors:

Commodity	Fipronil + fipronil-thioether + fipronil-sulfone + fipronil-desulfinyl (mg/kg), calculated as fipronil	Processing factor
	1 x 100 g ai/ha soil treatment + 2 x 50 g ai/ha foliar treatment	
Cane	0.0198	
Bagasse	0.0123	0.621
Juice	< 0.007	< 0.35
Cane	0.0198	
Bagasse	0.0154	0.778
Juice	0.007	0.35
	2 x 100 g ai/ha foliar treatment	
Cane	0.0363	
Bagasse	0.0213	0.587
Juice	< 0.008	< 0.22
Cane	0.0303	
Bagasse	0.0283	0.934
Juice	< 0.009	< 0.297

A mean processing factor of 0.73 was calculated for bagasse, the material left over after pressing out the juice; the juice is made into molasses and sugar. The mean processing factor was < 0.3 for sugar juice. As no STMR value was derived for sugar cane, no STMR-P values were estimated.

Residues in animal commodities

Dietary burden in animals

The Meeting estimated the dietary burden of fipronil residues and its toxicologically significant metabolites in farm animals on the basis of the diets listed in Appendix IX of the *FAO Manual*.

Separate feeding studies were carried out in cattle to determine the residues of fipronil and of its photodegradation product fipronil-desulfinyl. Detectable amounts of fipronil-desulfinyl were found only in rice straw among all the feed items considered for cows. The dietary burden was therefore calculated separately for comparison with the results of:

- the feeding study of fipronil by summing the concentrations of residues of fipronil, fipronil-thioether and fipronil-sulfone, calculated as fipronil (all animal feed)
- the feeding study of fipronil-desulfinyl by summing the concentrations of residues of fipronil-desulfinyl (rice straw only).
-

As the plateau concentration of fipronil in milk in the feeding study in dairy cows was reached slowly (> 2 weeks), the STMR and STMR-P values of the feed item were used to calculate the dietary burden for estimation of MRLs, STMR values and HR values for animal commodities, as follows:

Dietary burden of sum of fipronil, fipronil-thioether and fipronil-sulfone, calculated as fipronil

Commodity	Group	STMR or STMR-P (mg/kg)	Dry matter (%)	Residue, dry weight (mg/kg)	Choose diets (%)			Residue contribution (mg/kg)		
					Beef cattle	Dairy cows	Poultry	Beef cattle	Dairy cows	Poultry
Barley grain	GC	0.004	88	0.0045						
Maize	GC	0.005	88	0.0057			80			0.00456
Maize forage	AF	0.0675	100	0.0675	5	50		0.0034	0.0338	
Maize fodder	AS	0.048	100	0.048						
Oats	GC	0.004	89	0.0045						
Potato, wet peel		0.0276	15	0.184	75	40		0.138	0.0736	
Rice	GC	0.006	88	0.0068			20			0.00136
Rice straw and fodder	AS	0.022	100	0.022						
Rye	GC	0.004	88	0.0045						
Sugar beet leaves or tops		0.087	100	0.087	20	10	–	0.0174	0.0087	
Wheat	GC	0.004	89	0.0045						
		Total			100	100	100	0.159	0.116	0.006

Dietary burden of fipronil-desulfinyl

Commodity	Group	STMR (mg/kg)	Dry matter (%)	Residue, dry weight (mg/kg)	Choose diets (%)			Residue contribution (mg/kg)		
					Beef cattle	Dairy cows	Poultry	Beef cattle	Dairy cows	Poultry
Rice straw and fodder	AS	0.029	100	0.029	10	10	–	0.0029	0.0029	–

Feeding studies

Cows, fipronil: Groups of three lactating cows were given fipronil in bolus doses equivalent to 0.04, 0.13 or 0.43 ppm in the diet, daily for 35 days. Milk was analysed for fipronil and for fipronil-thioether and fipronil-sulfone. A plateau concentration of fipronil-derived residues was observed in milk after 25 days at the high dose. The residue in milk consisted almost entirely of fipronil-sulfone. Fipronil-thioether was detected in a single sample of milk; trace amounts of fipronil (< 0.01 mg/kg) were detected at the high dose. After 35 days of dosing, the cows were killed, and liver, kidney, fat and muscle were collected for analysis from each animal. Of the four tissues examined, fat contained the highest concentration of fipronil residues. Most of the residues consisted of fipronil-sulfone; fipronil was detected in fat of cows at the high dose at a concentration slightly above the LOQ.

The residue for compliance with the MRL is defined as the sum of fipronil and fipronil-sulfone, and that for the STMR as the sum of fipronil, fipronil-sulfone, fipronil-thioether and fipronil-desulfinyl. Fipronil-desulfinyl was not determined. As no concentrations of fipronil-thioether or fipronil above the LOQ were determined in milk, muscle, kidney or liver at the highest dose, the Meeting decided to calculate both the maximum residue levels and the STMR values on the basis of the fipronil-sulfone residues. Both fipronil and fipronil-sulfone were found in fat samples from cows at the highest dose. If all concentrations are below the LOQ, it is reasonable to assume that the concentration of combined residues is lower than the LOQ for fipronil-sulfone in milk, muscle, kidney and liver and lower than the combined LOQs for fipronil and fipronil-sulfone in fat. When one component is above and the other below the LOQ, the concentration of combined residue is assumed to be below or close to that of the measurable component plus the LOQ of the other.

The dietary burden was calculated as follows: 0.159 mg/kg (typical residue value in beef cattle) and 0.116 mg/kg (typical residue value in dairy cows). The table below shows the actual and interpolated concentrations of residues used to estimate dietary intake as the sum of fipronil and fipronil-sulfone (calculated as fipronil), on the basis of actual concentrations in cows given the intermediate dose (0.13 ppm):

Feed level (ppm) *Interpolated* / actual	Fipronil and fipronil-sulfone residues (mg/kg), calculated as fipronil								
	Milk (mean)	Muscle		Liver		Kidney		Fat	
		Highest	Mean	Highest	Mean	Highest	Mean	Highest	Mean
MRL beef cattle *0.159* / 0.13		*0.0183* / 0.015		*0.0746* / 0.061		*0.0171* / 0.014		*0.279* / 0.228	
MRL dairy cows *0.116* / 0.13	*0.0107* / 0.012								
STMR beef cattle *0.159* / 0.13			*0.0143* / 0.0117		*0.0596* / 0.0487		*0.0134* / 0.011		*0.215* / 0.176
STMR dairy cows *0.116* / 0.13	*0.0107* / 0.012								

Cows, fipronil-desulfinyl: The concentrations of fipronil-desulfinyl residues were determined in animal commodities after repeated dosing of groups of three lactating given bolus doses of fipronil-desulfinyl equivalent to 0.025, 0.075, 0.3 or 1 ppm in the diet, daily for 35 consecutive days. At the plateau (after 15–20 days), the concentration of the analyte in milk paralleled the administered dose in all but the high-dose group. Fipronil-desulfinyl residues were associated more with milk fat rather than skim milk; the milk fat concentration factor was determined to be approximately 16.

The dietary burden was calculated as 0.0029 mg/kg (STMR for beef and dairy cattle). The following table shows the highest and the mean actual and interpolated concentrations of residues of fipronil-desulfinyl, on the basis of the actual concentrations in the group given the lowest dose (0.025 ppm):

Feeding level (ppm) *Interpolated* / actual	Fipronil-desulfinyl residues (mg/kg), calculated as fipronil									
	Milk (mean)	Muscle		Liver		Kidney		Fat		
		Highest	Mean	Highest	Mean	Highest	Mean	Highest	Mean	
MRL, beef and dairy cattle *0.0029* / 0.025	*0.0004* / 0.0033	*0.0004* / 0.0033		*0.0048* / 0.0418		*0.0008* / 0.0066		*0.0055* / 0.0473		
STMR, beef and dairy cattle *0.0029* / 0.025	*0.0004* / 0.0033		*0.0003* / < 0.0022		*0.0046* / 0.0396		*0.0006* / 0.0055		*0.0051* / 0.044	

The following tables show the combined data from the two feeding studies and the values selected for estimation of MRLs, STMR values and HR values for animal commodities. The residue concentrations are calculated as fipronil.

MRLs for animal commodities:

Commodity	Sum of fipronil and fipronil-sulfone (mg/kg)	Proposed MRL (mg/kg)
Milk	0.0107	0.02
Liver	0.0746	0.1
Kidney	0.0171	0.02
Meat (fat)	0.279	0.5 (fat)

Highest residues for animal commodities:

Commodity	Sum of fipronil and fipronil-sulfone (mg/kg)	Fipronil-desulfinyl (mg/kg)	Sum of fipronil, fipronil-sulfone and fipronil-desulfinyl (mg/kg)	Proposed HR (mg/kg)
Liver	0.0746	0.0048	0.0794	0.079
Kidney	0.0171	0.0008	0.0179	0.018
Meat (muscle)	0.0183	0.0004	0.0187	0.019

STMR values for animal commodities:

Commodity	Sum of fipronil and fipronil-sulfone (mg/kg)	Fipronil-desulfinyl (mg/kg)	Sum of fipronil, fipronil-sulfone and fipronil-desulfinyl (mg/kg)	Proposed STMR (mg/kg)
Milk	0.0107	0.0004	0.0111	0.011

Liver	0.0596	0.0046	0.0642	0.064
Kidney	0.0134	0.0006	0.014	0.014
Meat (muscle)	0.0143	0.0003	0.0146	0.015

The Meeting estimated maximum residue levels of 0.02 mg/kg for cattle milk, 0.1 mg/kg for cattle liver, 0.02 mg/kg for cattle kidney and 0.5 mg/kg (fat) for cattle meat. It recommended that the HR values be 0.079 mg/kg for cattle liver, 0.018 mg/kg for cattle kidney and 0.019 mg/kg for cattle meat. The estimated STMR values are 0.011 mg/kg for cattle milk, 0.064 mg/kg for cattle liver, 0.014 mg/kg for cattle kidney and 0.015 mg/kg for cattle meat.

Hens, fipronil: The concentrations of fipronil-derived residues in poultry commodities were determined after repeated dosing of groups of 10 laying hens given bolus doses equivalent to 0.01, 0.031 or 0.103 ppm, daily for 42 consecutive days. Eggs were collected and analysed during this period. A plateau concentration of fipronil-derived residues was observed in eggs after about 15 days of dosing. The hens were killed 42 days after dosing was initiated, and liver, skin with adhering fat and muscle were collected for analysis; eggs and tissues were analysed for fipronil, fipronil-sulfone and fipronil-thioether.

The average concentration of fipronil-sulfone equivalents in eggs from hens at the lowest dose reached a plateau by day 12 of treatment, when there were only trace amounts (< 0.01 mg/kg) of fipronil-sulfone equivalents. In hens given the intermediate and highest doses, plateau concentrations were reached after about 28 days. No fipronil-thioether was observed in eggs at any dose, and only trace amounts of fipronil (< 0.01 mg/kg) were observed at the high dose.

The concentrations of residues were < 0.01 mg/kg in muscle and liver in hens on the low-dose regime and 0.013 mg/kg in skin with adhering fat. At all doses, fipronil-sulfone was found at much higher concentrations in skin with adhering fat than in all other tissues. The total residue in fat comprised almost entirely fipronil-sulfone, fipronil constituting < 10% in the high-dose group.

The dietary burden was calculated as 0.006 mg/kg (STMR). The following table shows the highest and the mean actual and interpolated concentrations of the sum of fipronil and fipronil-sulfone, based on the actual concentrations found in the group given the low dose (0.01 ppm):

Feed level (ppm) *Interpolated* / actual	Fipronil and fipronil-sulfone residues (mg/kg), calculated as fipronil							
	Eggs		Muscle		Liver		Skin with fat	
	Highest	Mean	Highest	Mean	Highest	Mean	Highest	Mean
MRL *0.006* / 0.01	*0.0078* / 0.013		*< 0.006* / < 0.01		*< 0.006* / < 0.01		*0.0084* / 0.014	
STMR *0.006* / 0.01		*0.006* / 0.01		*< 0.006* / < 0.01		*0.006* / < 0.01		*0.008* / 0.0133

Hens, fipronil-desulfinyl: A separate feeding study was not provided, but in a study of metabolism in hens given [^{14}C]fipronil-desulfinyl 50–70% of the dose was recovered in the excreta. The edible tissues and eggs contained < 6% of the total applied dose, with 1–2% in egg white, 3–5% in yolk and 4–6% in tissues. The only poultry feed item that contained detectable residues of fipronil-desulfinyl was rice grain. The concentrations of residues in 29 samples of rice treated by foliar spray or in flooded paddies were < 0.001 (27), 0.002 and 0.005 mg/kg. The Meeting concluded that quantifiable residues of fipronil-desulfinyl are unlikely to occur in eggs or edible poultry tissues.

On the basis of the results of the feeding study with 0.01 ppm fipronil, the Meeting estimated maximum residue levels of 0.02 mg/kg for eggs, 0.02 mg/kg for poultry, edible offal and 0.0* for poultry meat. It recommended HR values of 0.0078 mg/kg for eggs, 0.0084 mg/kg for poultry, edible offal and 0.006 mg/kg for meat. The estimated STMRs were 0.006 mg/kg for eggs, 0.008 mg/kg for poultry, edible offal and 0.006 mg/kg for meat.

Further work or information

Desirable

- Study of hydrolysis to determine the nature of residues after processing
- Studies of processing of cabbages (cooking, sauerkraut preparation)
- Studies of processing of potatoes (cooking, oven baking, microwaving)

Dietary risk assessment

Long-term intake

The Meeting estimated 22 STMR values for fipronil, which were used to calculate dietary intake. The results are shown in Annex 3.

The IEDIs for the five GEMS/Food regional diets, based on estimated STMR values, were 20–60% of the ADI. The Meeting concluded that dietary intake of fipronil residues is unlikely to present a public health concern.

Short-term intake

The IESTI of fipronil was calculated for the food commodities (and their processing fractions) for which MRLs, STMR values and/or HR values were established and for which data on consumption were available. The results are shown in Annex 4.

The calculated short-term intakes were less than 100% of the acute RfDs for children and for the general population. The Meeting concluded that short-term intake of residues of fipronil, when used in ways that have been considered by the JMPR, is unlikely to present a public health concern.

4.13 HALOXYFOP (194)

Residue and analytical aspects

Haloxyfop was evaluated for the first time in 1995 and again in 1996. The 1995 JMPR provisionally estimated maximum residue levels for a number of commodities, including fodder crops and commodities of animal origin, noting the lack of critical supporting data on the uptake of the soil degradation products by crops. The 1996 JMPR received reports of studies on the uptake of the parent compound or its degradation products from soil treated with haloxyfop but agreed to withdraw the provisional maximum residue levels for fodder crops and cattle tissues and milk, as no information was available on the moisture content of fodder crops, and the expected intake of residues by cattle would exceed the maximum dose used in the feeding studies. It therefore requested the results of further feeding studies in which ruminants were fed a concentration comparable to the maximum residue level found in fodder crops. Information on the moisture content of fodder crops was noted as desirable.

The Meeting received information on methods of analysis for milk and cattle tissues and feeding studies in dairy and beef cattle.

Results of supervised trials

Estimation of STMR values for fodder crops for which provisional maximum residue levels were estimated by the 1995 JMPR

The 1995 JMPR estimated provisional MRLs of 5.0 mg/kg for alfalfa forage (green), 0.3 mg/kg for beet leaves or tops, and 0.3 mg/kg for sugar beet leaves or tops. The 1996 JMPR agreed to withdraw these provisional MRLs because: the concentrations of residues found in supervised trials on these fodder crops were expressed on a wet weight basis, whereas the Codex Classification of Food and Feeds indicates that MRLs for fodder and forage crops should, if relevant, preferably be set and expressed on a ‘dry weight’ basis; furthermore, no information was available on the moisture content of these commodities. The current Meeting agreed to reinstate the MRLs for these commodities, with a footnote to indicate that the MRLs are set on a fresh weight basis.

The concentrations of residues on alfalfa from two trials conducted in Australia in compliance with the maximum GAP for haloxyfop (0.16 kg ai/ha; PIH, 21 days) and two trials conducted in Australia in compliance with the maximum GAP of Australia for haloxyfop-R (0.078 kg ai/ha; PHI, 21 days), in ranked order, were (median underlined): 1.8, 2.2, 2.4 and 3.1 mg/kg.

The Meeting agreed to reinstate the MRL of 5 mg/kg (on a fresh weight basis) and estimated an STMR value of 2.3 mg/kg and a high residue of 3.1 mg/kg.

Both the 1995 and the 1996 JMPR agreed to consider the data for beet and sugar beet fodder together, as these crops and the use pattern of haloxyfop on them are similar.

In 13 trials on sugar beet carried out in the United Kingdom with racemic haloxyfop according to the maximum French GAP (0.21 kg ai/ha, up to early weed tillering), the concentrations of residues in the leaves and tops were < 0.02 (3), 0.02, < 0.03 (3), 0.03, 0.04 (2), 0.09, 0.11 and 0.28 mg/kg. In eight trials on sugar beet carried out in Germany with racemic haloxyfop according to the maximum German GAP (0.21 kg ai/ha; PHI, 90 days), the concentrations in the leaves and tops were < 0.01, < 0.02 (2), 0.03, 0.04, 0.08, 0.28 and 0.3 mg/kg. In four trials on sugar beet with haloxyfop-R in Germany and Italy conducted according to maximum French GAP (0.1 kg ai/ha, up to early weed tillering), the concentrations of residues in the leaves and tops were < 0.02, 0.09 (2) and 0.14 mg/kg.

In five trials on fodder beet with racemic haloxyfop conducted in Germany according to maximum German GAP (0.21 kg ai/ha; PHI, 90 days), the concentrations in the leaves or tops were < 0.02 (3), 0.03 and 0.05 mg/kg.

The concentrations of residues in the leaves or tops in a total of 30 trials, in ranked order, were: < 0.01, < 0.02 (9), 0.02, < 0.03 (3), 0.03 (3), 0.04 (3), 0.05, 0.08, 0.09 (3), 0.11, 0.14, 0.28 (2) and 0.3 mg/kg. The Meeting agreed to reinstate the MRL of 0.3 mg/kg (on a fresh weight basis) and estimated an STMR value of 0.03 mg/kg and a highest residue of 0.3 mg/kg.

In four supervised trials on pasture with racemic haloxyfop and two with haloxyfop-R in Australia conducted in accordance with maximum Australian GAP (0.1 kg ai/ha with racemic haloxyfop, 0.052 kg ai/ha with haloxyfop-R; PHI, 7 days in both cases), the concentrations of residues, in ranked order, were 0.49, 0.99, 1.5, 1.7, 2.0 and 3.4 mg/kg.

The Meeting estimated an STMR value of 1.6 mg/kg and a HR value of 3.4 mg/kg. As pasture is not traded internationally in bulk, no maximum residue level was recommended.

Residues in animal commodities

Feeding studies

Haloxyfop-R (as its methyl ester) was determined in milk and cattle tissues by GC–ECD after solvent extraction and derivatization, with 98–117% recovery.

Dairy cows were dosed with haloxyfop-R at rates equivalent to 0, 10, 20 or 30 ppm of diet for 28 days. Residues were detected rapidly in milk (1 day after treatment), and the concentration appeared to reach a plateau by day 10 and a peak at day 26. The maximum concentrations in milk were 0.65 mg/kg at 10 ppm of diet, 0.97 mg/kg at 20 ppm and 2.2 mg/kg at 30 ppm. The concentrations varied widely between cows, and one cow each at 20 and 30 ppm had consistently low values. In the study considered by the 1995 Meeting, in which cows were dosed with haloxyfop for 28 days at 2.5 ppm of diet, the concentration in milk reached a maximum of 0.04 mg/kg at day 20.

Beef cattle were dosed with haloxyfop-R at a rate equivalent to 0, 10, 20 or 30 ppm of diet for 28 days. Low concentrations of residue were detected in kidney and renal fat in the control group. The concentrations in animals at the highest dietary rate on day 28 were highest in the kidney (1.8 mg/kg at 30 ppm) and liver (0.46 mg/kg at 30 ppm). The mean concentrations in muscle did not exceed 0.06 mg/kg in any group, and the highest levels in abdominal, renal and subcutaneous fat were similar in all groups: 0.05, 0.04 and 0.03 mg/kg, respectively. Residues were detectable 28 days after cessation of dosing in all tissues except muscle. The concentrations did not appear to be strongly correlated to dietary rate, those in animals at 20 and 30 ppm being similar.

The 1995 Meeting noted that haloxyfop-S undergoes rapid and nearly complete inversion to haloxyfop-R. In rats dosed with haloxyfop, nearly all of the residue recovered from urine and faeces was in the form of haloxyfop-R. The current Meeting therefore considered that the new studies in cattle dosed

with haloxyfop-R could be used in estimating maximum residue levels, STMR values and highest residues in cattle tissues and milk.

Dietary burden of farm animals

The 1996 Meeting calculated that the intake by cattle was 17 ppm in the diet, on the basis of the highest residue in pasture of 3.35 mg/kg and 80% moisture content. This was higher than the maximum concentration of 10 ppm used in the studies available to the Meeting. However, the 1997 and 1998 Meetings elaborated principles for estimating maximum residue levels and STMR values for commodities of animal origin, and the 1997 JMPR distinguished situations in which the plateau was reached rapidly and those in which it was reached slowly. It recommended that the MRLs of feed items should be used to calculate the dietary burden of animals for estimating maximum residue levels if the plateau was reached rapidly, while STMR values should be used if the plateau was reached slowly. For estimating STMR values, it recommended that, in both cases, the STMR values of feed items should be used to calculate the dietary burden of animals.

The concentrations of residues of haloxyfop in milk reached a plateau on day 10 in the study provided to the current Meeting; they reached a maximum on day 20 in a study reviewed by the 1995 JMPR. The current Meeting agreed that the plateau concentration of haloxyfop residues in milk was reached slowly and re-estimated the dietary burden of cattle on the basis of the diets in Appendix IX of the *FAO Manual*. Calculation from STMRs provided feed concentrations suitable for estimating both maximum residue levels and STMRs for cattle commodities.

The 1995 JMPR estimated MRLs of 0.01 mg/kg for chicken meat, 0.1 mg/kg for edible offal of chicken and 0.01 mg/kg (*) for chicken eggs. The 1996 JMPR re-calculated an intake of 0.035 ppm (dry weight basis) by poultry on the basis that feed could contain up to 50% pulses, 7% rape seed meal and 30% soya bean meal and using the STMR values of 0.03, 0.15 and 0.03 mg/kg for these three feed items, respectively. The current Meeting re-estimated the dietary burden of haloxyfop residues for poultry on the basis of the diets in Appendix IX of the *FAO Manual*. As no information was available on the time at which the concentrations reached a plateau in chicken, the maximum and STMR dietary burdens were calculated on the basis of the highest residue level or STMR-P value and STMR or STMR-P value, respectively.

Estimated dietary burden of cattle

Commodity	Group	STMR or STMR-P (mg/kg)	Dry matter (%)	Residue, dry weight (mg/kg)	Per cent of diet		Residue contribution (mg/kg)	
					Beef cattle	Dairy cows	Beef cattle	Dairy cows
Pasture	AF	1.59	25	6.36	30	40	1.9	2.5
Alfalfa forage (green)	AL	2.33	35	6.66	70	60	4.7	4.0
Fodder beet, leaves or tops	AV	0.04	23	0.17				
Sugar beet, leaves or tops	AV	0.04	23	0.17				
Pulses (field pea, dry)	VP	0.03	90	0.04				
Rape seed meal	SO	0.15	88	0.17				
Rice bran	CM	0.02	90	0.02				
Soya bean meal	VP	0.03	92	0.03				
				Total	100	100	6.6	6.5

Maximum dietary burden of poultry

Commodity	Group	MRL or STMR-P (mg/kg)	Dry matter (%)	Residue on dry basis (mg/kg)	Per cent of diet	Residue contribution (mg/kg)
Pulses (field pea, dry)	VD	0.2	90	0.22	20	0.044
Rape seed meal	SO	0.15	88	0.17	15	0.026
Rice bran	CM	0.02	90	0.02	25	0.006
Soya bean meal	VD	0.03	92	0.03	20	0.007
				Total	80	0.082

Dietary burden of poultry at STMR

Commodity	Group	STMR or STMR-P (mg/kg)	Dry matter (%)	Residue on dry basis (mg/kg)	Per cent of diet	Residue contribution (mg/kg)
Pulses (field pea, dry)	VD	0.03	90	0.04	20	0.008
Rape seed meal	SO	0.15	88	0.17	15	0.026
Rice bran	CM	0.02	90	0.02	25	0.006
Soya bean meal	VD	0.03	92	0.03	20	0.007
				Total	80	0.044

The dietary burden of haloxyfop for estimating the MRL and STMR value for cattle commodities (residue concentrations in animal feeds expressed as dry weight) was calculated to be 6.6 mg/kg for beef cattle and 6.5 mg/kg for dairy cows. The dietary burden for poultry commodities was calculated to be 0.082 mg/kg for estimating the MRL and 0.044 mg/kg for the STMR value.

A study in which cattle were fed a diet containing 10 ppm haloxyfop for 28 days was considered by the 1995 JMPR, and the current Meeting agreed to use the data from this study in estimating MRLs and STMR and highest residues for various tissues of cattle. The highest individual values in the group at 5 and 10 ppm were used in conjunction with the dietary burden at the STMR to calculate the probable highest concentration of residues in animal commodities. The mean concentrations in animal tissues at 5 and 10 ppm were used in conjunction with the dietary burden at the STMR to estimate the STMR values for animal commodities. For milk, the mean plateau concentration of residues in the group fed a diet containing 10 ppm haloxyfop-R was used to estimate both the STMR and the highest residue.

Feeding level (ppm) *Interpolated* / actual	Residues of haloxyfop (mg/kg)							
	Milk (mean)	Liver		Kidney		Muscle		Fat	
		High	Mean	High	Mean	High	Mean	High	Mean
MRL beef									
6.6 /		*0.33* /		*0.95* /		*0.03* /		0.23 /	
5		0.15		0.51		0.01		0.09	
10		0.72		1.90		0.06		0.53	
MRL dairy									
6.5 /	*0.22* /								
10	0.34								
STMR beef									
6.6 /			*0.28* /		*0.73* /		0.02 /		0.18 /
5			0.15		0.43		0.01		0.08
10			0.56		1.37		0.04		0.39
STMR dairy									
6.5 /	*0.22* /								
10	0.34								

The Meeting estimated a maximum residue level and STMR value in milk of 0.3 and 0.22 mg/kg; a maximum residue level, STMR value and highest residue in cattle liver of 0.5, 0.28 and 0.33 mg/kg; a maximum residue level, STMR value and highest residue in cattle kidney of 1, 0.73 and 0.95 mg/kg; and a maximum residue level, STMR value and highest residue in cattle meat of 0.05, 0.02 and 0.03 mg/kg, respectively.

The 1995 and 1996 JMPR considered a study in which laying hens were fed a diet containing 0.25–2.5 ppm haloxyfop for 28 days.

Feeding level (ppm) *Interpolated* / actual	Residues of haloxyfop (mg/kg)							
	Muscle and skin		Liver		Fat		Eggs	
	High	Mean	High	Mean	High	Mean	High	Mean
MRL	*< 0.003* /		*0.030* /		*0.010* /		*< 0.003* /	
0.082 / 0.25	< 0.01		0.09		0.03		< 0.01	
STMR		*< 0.002* /		*0.009* /		*0.004* /		*< 0.002* /

0.044 / 0.25	< 0.01	0.05	0.02	< 0.01

The Meeting estimated a maximum residue level, STMR value and highest residue in chicken meat (with adhering skin) of 0.01(*), 0.002 and 0.003 mg/kg; a maximum residue level, STMR value and HR value in chicken, edible offal of 0.05, 0.009 and 0.030 mg/kg; and a maximum residue level, STMR value and highest residue in chicken eggs of 0.01(*), 0.002 and 0.003 mg/kg, respectively.

Dietary risk assessment

Long-term intake

The Meeting estimated 10 STMR values for four commodities of cattle origin, three commodities of chicken origin and three fodder crops. These STMR values were used in combination with the STMR and STMR-P values estimated by the 1996 Meeting to calculate the long-term dietary intake of haloxyfop. The result is shown in Annex 3.

The IEDIs for the five GEMS/Food regional diets, on the basis of the estimated STMRs, were in the range of 50–440% of the ADI. The Meeting concluded that long-term dietary intake of haloxyfop residues from uses that have been considered by the JMPR might exceed the ADI in three GEMS/Food regional diets.

Short-term intake

The IESTI of haloxyfop by children and adults was calculated for commodities derived from cattle and chicken. The results are shown in Annex 4. The Meeting concluded that it might be necessary to establish an acute reference dose for haloxyfop. As one has yet been established, the acute risk assessment for haloxyfop was not finalized

4.14 IMAZALIL (110)

Toxicology

Imazalil is used as a human and veterinary pharmaceutical, under the name enilconazole. Imazalil was evaluated by the 1977 JMPR, when a temporary ADI of 0–0.01 mg/kg bw was allocated. An ADI of 0–0.01 mg/kg bw was allocated in 1986 on the basis of the NOAEL in a 2-year study in dogs. The compound was re-evaluated in 1991, when an ADI of 0–0.03 mg/kg bw was established on the basis of the NOAEL in a new study in dogs and a safety factor of 100. The 2000 JMPR determined that an acute RfD was unnecessary and affirmed the ADI of 0–0.03 mg/kg bw; however, the Meeting was made aware of the existence of a new long-term study in rats. The report of this study was supplied, together with those of studies on the mechanism by which imazalil affects the thyroid and liver, to the present Meeting.

All the mechanistic studies were carried out in rats and were conducted at dietary concentrations which produced daily intakes of up to approximately 350 mg/kg bw per day. These studies consisted of a 3-month dose range-finding and toxicity study and a 3-month study of the toxicity of imazalil given orally, which included a 1-month interim sacrifice. A 1-month study was also undertaken with repeated oral doses of imazalil, with interim sacrifices at 1 and 2 weeks and recovery periods of 4 and 9 weeks. Hepatocellular hypertrophy and vacuolation were observed, and there was evidence of liver enzyme induction. Some effects were observed on thyroid weight and pituitary and thyroid hormones (increased thyroid-stimulating hormone and decreased thyroxine levels), but the effects were weak and inconsistent, and clear dose-effect relationships were not always found. The Meeting concluded that imazalil is a relatively non-specific enzyme inducer in vivo and its enzyme-inducing effects are reversible. Thus, imazalil may alter thyroid status by affecting hepatic and thyroid enzymes involved in the synthesis, metabolism, and excretion of thyroxine.

In a long-term study, rats received diets containing imazalil at dietary concentrations of 0, 50, 200, 1200, or 2400 ppm, providing intakes of 0, 2.4, 9.7, 58, and 120 mg/kg bw per day for males and 0, 3.3, 14, 79, and 160 mg/kg bw per day for females. Consistent decreases in body weights, weight gain, and food consumption were seen in males and females at the two higher doses. Changes in hematological parameters were seen at 200 ppm and above in both sexes. Increased blood glucose concentrations were observed at the two higher dietary concentrations in animals of each sex. Increased blood glucose concentrations were seen in females at 200 ppm at all times. The changes in thyroid hormone concentrations in serum were inconsistent: in males, concentrations of thyroid-stimulating hormone tended to be higher and those of thyroxine definitely lower at the two higher dietary concentrations; in females, the level of triiodothyronine was decreased at the two higher dietary concentrations, that of thyroxine was decreased only at 1200 ppm. Males, at the highest dietary concentration, had an increased prevalence of hepatocellular adenoma and an increased incidence of follicular-cell neoplasia of the thyroid was observed in males at 1200 and 2400 ppm. An increased frequency of pigment-laden hepatocytes was seen in females at the three highest dietary concentrations.

Effects on body weight, weight gain, and food consumption, seen at some times, in males and females at 50 ppm were considered not to be dose-related because they were mild, and no effect on body weight or body-weight gain was noted at 200 ppm. The overall NOAEL was 50 ppm, equal to 2.4 mg/kg bw per day, on the basis of minor haematological changes in animals of each sex and increased blood glucose concentrations and hepatic changes (increased relative liver weight and an increase in the frequency of pigment-laden hepatocytes) in females at 200 ppm. The NOAEL for tumours in males was 200 ppm, equal to 9.7 mg/kg bw per day, whereas that in females was 2400 ppm, the highest dose tested, equal to 160 mg/kg bw per day.

The Meeting concluded that the ADI of 0–0.03 mg/kg bw established by the 1991 Joint Meeting and reaffirmed by the 2000 Joint Meeting was supported by the new data.

An addendum to the toxicological monograph was prepared.

Dietary risk assessment

The theoretical maximum daily intakes from the five GEMS/Food regional diets, on the basis of existing MRLs, represented 10–100% of the ADI (Annex 4). The Meeting concluded that the intake of residues of imazalil resulting from its uses that have been considered by the JMPR is unlikely to present a public health concern.

4.15 IMIDACLOPRID

Toxicology

Imidacloprid (1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine), which acts as an agonist at postsynaptic nicotinic acetylcholine receptors of insects, is a new insecticide and has not previously been evaluated by the JMPR.

Imidacloprid is rapidly and almost completely absorbed (> 92%) from the gastrointestinal tract of rats, and is eliminated from the organism rapidly and completely, with no indication of bioaccumulation of the parent compound or its metabolites. On average, 75% of an administered dose is excreted in the urine and the remainder in the faeces. Most of that in the faeces originates from biliary excretion. Peak plasma concentrations of radiolabel were reached within approximately 2.5 h. The radiolabel was rapidly distributed from the intravascular space to the peripheral tissues and organs; the concentrations in tissues after 48 h were very low. Imidacloprid penetrated the blood-brain barrier to only a very limited extent.

The metabolism of imidacloprid in rats was rapid, and the amount of unchanged parent compound represented 10–16 % of a given dose. The main urinary metabolites were 6-chloronicotinic acid and its glycine conjugate and the two corresponding imidazolidine ring-containing biotransformation products. The two monohydroxylated metabolites (5-OH-imidacloprid) and (4-OH-imidacloprid) and an unsaturated compound were also detected in urine.

Imidacloprid given orally as a single dose was moderately toxic to rats (LD_{50}, 380–650 mg/kg bw) and mice (LD_{50}, 130–170 mg/kg bw). Behavioural and respiratory signs, disturbances of motility, narrowed palpebral fissures, transient trembling, and spasms were seen in rats and mice treated orally at doses (200 mg/kg bw and (71 mg/kg bw, respectively. The clinical signs were reversed within 6 days. Imidacloprid given intraperitoneally showed moderate to low acute toxicity in rats, the signs being similar to those after oral administration. Very little toxicity was seen after acute dermal application. The LC_{50} for acute exposure to an aerosol could not be determined exactly, as rats tolerated inhalation for 4 h of the maximum concentration of dust that could be produced technically (0.069 mg/l of air) without signs or deaths. Imidacloprid did not irritate the skin or eyes of rabbits and did not sensitize the skin of guinea-pigs in a maximization test.

Reduced body-weight gain was the most sensitive toxicological end-point in mice at doses (86 mg/kg bw per day, in rats at doses (30 mg/kg bw per day, in rabbits at doses (24 mg/kg bw per day, and in dogs at doses (22 mg/kg bw per day. Furthermore, decreased body-weight gain was the main effect

observed in rat pups during lactation from dams given doses (6.6 mg/kg bw per day. In some studies, the lower body weights were accompanied by a simultaneous increase in feed intake.

The liver was the other main target organ after repeated administration of imidacloprid to mice, rats, and dogs at doses (410 mg/kg bw per day, (17 mg/kg bw per day, and (31 mg/kg bw per day, respectively. The spectrum of changes observed ranged from induction of hepatic microsomal enzymes through disturbances of hepatic function to histologically apparent damage to the organ. The initial sign of an effect on the liver was increased activity of cytochrome P450 enzymes, accompanied by slight hepatocellular hypertrophy and necrosis, swollen cell nuclei, round-cell infiltration, and increased liver weight. Changes in blood cholesterol, triglyceride, protein, and albumin concentrations as well as increased activities of alanine aminotransferase, alkaline phosphatase, and galactodehydrogenase in plasma were also observed.

Slight follicular atrophy of the thyroid gland and slightly depressed triiodothyronine in plasma were found at the highest dietary concentration, providing an average intake of 49 mg/kg bw per day, in a short-term study in dogs. However, these effects were not found in the 1-year study in dogs given a dietary concentration providing an average intake of 72 mg/kg bw per day. An increased incidence of mineralization was seen in the colloid of thyroid gland follicles in a long-term study in rats given a dietary concentration equal to 17 mg/kg bw per day, although the plasma concentrations of thyroid hormones remained unchanged. The NOAEL in this study was 5.7 mg/kg bw per day.

No evidence of a carcinogenic effect of imidacloprid was found in either mice or rats in the long-term studies of dietary administration.

Imidacloprid gave negative results in an adequate range of assays for genotoxicity in vitro and in vivo. Weak induction of sister chromatid exchange was found in one test with Chinese hamster ovary cells in vitro, but not in vivo.

The Meeting concluded that imidacloprid is unlikely to be genotoxic or to pose a carcinogenic risk to humans.

Imidacloprid was investigated for reproductive toxicity in a two-generation study in rats and in studies of developmental toxicity in rats and rabbits. Reproductive behaviour and outcome were not affected. An increased incidence of wavy ribs was observed at a maternally toxic dose of 30 mg/kg bw per day. Reduced body weights and retarded ossification were found in rabbit fetuses at a maternally toxic dose of 24 mg/kg bw per day. The Meeting concluded that imidacloprid has no teratogenic potential.

The animal metabolites 1-(6-chloro-3-pyridylmethyl)-2-imidazolidinone and 1-(6-chloro-3-pyridylmethyl)-*N*-nitroso(4-imidazolin 2-ylidene)amine as well as the plant nitroso-metabolite 1-(6-chloro-3-pyridylmethyl)-*N*-nitroso(imidazolidin-2-ylidene)amine were tested for acute toxicity by oral administration to rats and for their ability to induce point mutations in *Salmonella typhimurium*. They were found to be less acutely toxic than the parent compound, and no indications of genotoxic potential were found. In a 12-week study in rats in which the plant nitroso- metabolite was administered in drinking-water, the NOAEL was 100 ppm, equal to 13 mg/kg bw per day, on the basis of increased lymphocyte counts and reduced polymorphonuclear cell counts.

In a study of acute neurotoxicity in rats, clinical signs and effects on motor and locomotor activity and in the “functional observational battery” were observed at doses (150 mg/kg bw 1 day after application. Complete recovery was observed within 7 days. The NOAEL was 42 mg/kg bw. In a 13-week study of neurotoxicity in rats, the NOAEL of 140 ppm, equal to 9.3 mg/kg bw per day, was based on reduced body-weight gain and food consumption at doses (960 ppm, equal to 63 mg/kg bw per day. Behavioural effects were observed only in the “functional observational battery” in males at 3000 ppm, equal to 200 mg/kg bw per day.

The results of periodic examinations of employees exposed to imidacloprid showed no adverse health effects. No epidemiological studies of the effects of imidacloprid and no information on symptoms of poisoning or clinical signs were available. A 4-year-old child who ingested about 10 mg/kg bw of a veterinary preparation of imidacloprid showed no signs of poisoning or adverse health effects.

The Meeting concluded that the existing database was adequate to characterize the potential hazards of imidacloprid to fetuses, infants, and children.

The Meeting established an ADI of 0–0.06 mg/kg bw on the basis of the NOAEL for effects on the thyroid gland of 100 ppm, equal to 5.7 mg/kg bw per day, in the long-term study of toxicity and carcinogenicity in rats and a safety factor of 100. This ADI is supported by the NOAEL for effects on the liver in parental animals in the multigeneration study of reproductive toxicity.

The Meeting established an acute RfD of 0.4 mg/kg bw on the basis of the NOAEL of 42 mg/kg bw in the study of acute neurotoxicity in rats.

A toxicological monograph was prepared.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Mouse	2-year studies of toxicity and carcinogenicity[a]	Toxicity	330 ppm, equal to 66 mg/kg bw per day	1000 ppm, equal to 210 mg/kg bw per day
		Carcinogenicity	1000 ppm, equal to 210 mg/kg bw per day[b]	
Rat	2-year studies of toxicity and carcinogenicity[a]	Toxicity	100 ppm, equal to 5.7 mg/kg bw per day	300 ppm, equal to 17 mg/kg bw per day
		Carcinogenicity	300 ppm, equal to 100 mg/kg bw per day[b]	–
	Two-generation reproductive toxicity[a]	Parental toxicity	100 ppm, equivalent to 6.6 mg/kg bw per day	250 ppm, equivalent to 17 mg/kg bw per day
		Offspring toxicity	250 ppm, equivalent to 17 mg/kg bw per day	700 ppm, equivalent to 47 mg/kg bw per day
	Developmental toxicity[c]	Maternal toxicity	10 mg/kg bw per day	30 mg/kg bw per day
		Embryo- and fetotoxicity	30 mg/kg bw per day	100 mg/kg bw per day
	Acute neurotoxicity[b,c]		42 mg/kg bw per day	150 mg/kg bw per day
Rabbit	Developmental toxicity[c]	Maternal toxicity	8 mg/kg bw per day	24 mg/kg bw per day
		Embryo- and fetotoxicity	24 mg/kg bw per day	72 mg/kg bw per day
Dog	13- and 52-week studies of toxicity[a,d]		500 ppm , equal to 15 mg/kg bw per day (52-week study)	600 ppm, equivalent to 22 mg/kg bw per day (13-week study)

[a]Diet
[b]Highest dose tested
[c]Gavage
[d]Two or more studies combined

Estimate of acceptable daily intake for humans
0–0.06 mg/kg bw

Estimate of acute reference dose
0.4 mg/kg bw

Studies that would provide information useful for continued evaluation of the compound
Further observations in humans

List of end-points relevant for setting guidance values for dietary and non-dietary exposure

Absorption, distribution, excretion and metabolism in mammals	
Rate and extent of oral absorption:	Extensively absorbed (95%) on basis of urinary and biliary excretion
Distribution:	Uniformly and rapidly distributed, highest residues (after 48 h) in liver, kidney, lung, and skin
Potential for accumulation:	No evidence of accumulation
Rate and extent of excretion:	Rapidly and completely (~25% in faeces, 75% in urine within 48 h)
Metabolism in animals	Extensively metabolized by oxidative cleavage, hydroxylation, conjugation
Toxicologically significant compounds (animals, plants, and environment)	Parent compound and metabolites, including plant nitroso- metabolite, 1-(6-chloro-3-pyridylmethyl)-*N*-nitroso(imidazolidin-2-ylidene)amine
Acute toxicity	
Rat, LD_{50}, oral	380-650 mg/kg bw
Rabbit, LD_{50}, dermal	> 5000 mg/kg bw
Rat, LC_{50}, inhalation	> 0.69 mg/l of air (4 h, nose only)
Skin irritation	Not irritating
Eye irritation	Not irritating
Skin sensitization	Not sensitizing (Magnussen and Kligman)
Short-term toxicity	
Target / critical effect	Decreased body-weight gain, liver; thyroid
Lowest relevant oral NOAEL / NOEL	52 weeks, dog: 500 ppm (15 mg/kg bw per day)
Genotoxicity	No potential for genotoxicity
Long-term toxicity and carcinogenicity	
Target/critical effect	Decreased body-weight gain, liver; thyroid
Lowest relevant NOAEL / NOEL	2 years, rat: 100 ppm (5.7 mg/kg bw per day)
Carcinogenicity	No potential for carcinogenicity
Reproductive toxicity	
Reproduction target / critical effect	Decreased body-weight gain in pups during lactation at parentally toxic doses
Lowest relevant reproductive NOAEL	250 ppm (17 mg/kg bw per day)
Developmental target / critical effect	Reduced body weight, increased incidence of retarded ossification at maternally toxic doses
Lowest relevant developmental NOAEL	Rabbit: 24 mg/kg bw per day
Neurotoxicity	
	Clinical signs and neurobehavioural effects ascribed to acute cholinergic toxicity; short-term effects related to general toxicity
NOAEL (acute neurotoxicity)	42 mg/kg bw
NOAEL (short-term study of neurotoxicity)	140 ppm (9.3 mg/kg bw per day)

Other toxicological studies	Studies of kinetics and metabolism, acute toxicity, short-term effects, and mutagenicity of the plant nitroso-metabolite revealed no evidence of particular risk
Human data	No evidence of adverse effects

Summary	**Value**	**Study**	**Safety factor**
ADI	0–0.06 mg/kg bw	Rat, 2 years	100
Acute reference dose	0.4 mg/kg bw	Rat, acute neurotoxicity	100

4.16 IPRODIONE (111)

4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)
4.16 IPRODIONE (111)

Residue and analytical aspects

Iprodione was first evaluated in 1977 and was subsequently reviewed for residues in 1980 and 1994. In the periodic review of iprodione in 1994, the Meeting recommended withdrawal of the CXL for tomato of 5 mg/kg, as there were insufficient supervised trials with corresponding GAP. The CCPR at its Twenty-eighth Session maintained the existing CXL, pending provision of new data. At its Thirtieth Session, the CCPR retained the CXL, as the manufacturer confirmed the availability of new data from indoor trials. The evaluation was scheduled for 2001 by the CCPR at its Thirty-first Session.

The Meeting received information on analytical methods and GAP as well as supplementary data on residues, stability in storage and processing of tomatoes.

Methods of analysis

The Meeting received information on a HPLC and a GC method for the analysis of iprodione in crops and processed commodities. In the HPLC method, iprodione, its isomer N-(3,5-dichloro phenyl)-3-isopropyl-2,4-dioxoimidazolidine-1-carboxamide (RP-30228) and its metabolite 3-(3,5-dichlorophenyl)-2,4-dioxoimidazolidine-1-carboxamide (RP-34290) were measured, while the GC method can be used to determine residues of iprodione. The LOQs were 2.5 and 0.02 mg/kg for the HPLC and GC method, respectively. Both methods were validated for at least 25 crops, including tomatoes.

Stability of residues in stored analytical samples

Iprodione was stable in tomato extracts for at least 13 months when stored at (20 (C. In another study, the stability of iprodione, its isomer RP-30228 and its metabolite RP-32490 in 43 commodities and processed fractions was investigated. Residues in tomatoes were stable for at least 24 months when stored at (10 (C.

Results of supervised trials

Labels from products registered in Belgium, Brazil, Canada, China, Denmark, France, Italy, Japan, The Netherlands and the United Kingdom were provided to the Meeting. Many of the labels indicated use indoors (glasshouse or under cover) and in the field. In the United Kingdom, two PHIs are indicated, one for indoor use and another for field use. The manufacturer indicated that re-registration of the compound in the European Union is pending; therefore, use in some of the more recent European trials did not correspond to existing labels.

Several of the trials provided to the Meeting had been reviewed by the 1994 JMPR. Data from field and indoor trials on tomato were provided.

Field trials

In China, iprodione is registered for use (in the field or under cover) at rates ranging 0.37 to 0.75 kg ai/ha, with a PHI of 7 days. One to three sprays are recommended. Concentrations of 1.6, 0.53, 0.15 and 0.09 mg/kg were found in trials corresponding to GAP, with samples taken 7 days after treatment at 0.75 kg ai/ha.

Iprodione is registered in Italy for field use only, with application at concentrations of 0.05–0.075 kg ai/hl and a PHI of 21 days. In one trial in Italy that did not correspond to GAP, iprodione was applied three times at 0.075 kg ai/hl, and samples were taken 15 and 28 days after treatment. A single value of 0.03 mg/kg was obtained 28 days after treatment.

Registered labels in France allow use of iprodione on tomatoes in the field at rates of 0.75–1 kg ai/ha and a re-treatment interval of 15–20 days; the PHI is 3 days. The field trials did not correspond to GAP, as the PHI was 19 days in one trial and the application rate was 2.2 kg ai/ha in the other.

The Meeting considered that there were inadequate data from field trials, which could not be pooled or directly compared with data from trials conducted under cover. Therefore, these data were not used in estimating a maximum residue level.

Indoor trials

Trials in glasshouses were conducted in Canada, Denmark, France, Japan, The Netherlands and the United Kingdom.

In four trials in Canada which approximated national GAP (0.05 kg ai/hl; PHI, 2 days), the concentrations of residues were 0.2, 0.3, 0.4 and 0.4 mg/kg 2–3 days after spraying at 0.05 kg ai/hl.

In one trial in Denmark, iprodione was applied once at 0.05 kg ai/hl, and samples were collected 0, 4 and 7 days after treatment. The trial approximated GAP in Denmark (0.022–0.052 kg ai/hl; PHI, 3 days). A concentration of 0.74 mg/kg was found on day 4. In a second trial, the spray volumes used were not reported, and low concentrations of iprodione were present in control samples taken on days 1 and 3. These data were not considered in estimating an MRL.

Registered labels in France allow use of iprodione on tomatoes under cover at rates of 0.75–1 kg ai/ha and a re-treatment interval of 10–15 days; the PHI is 3 days. Five trials conducted under cover in northern and southern France did not approximate national GAP. The data were evaluated by comparison with GAP in the United Kingdom (0.05 kg ai/hl; PHI, 1 day). A concentration of 1.7 mg/kg (2) was found in crops treated five times at 0.05 kg ai/hl and sampled 3 days after treatment.

The results of numerous trials conducted in Japan were provided to the Meeting. Iprodione is registered for use on tomatoes (in the field and under cover) at spray concentrations of 0.026–0.05 kg ai/hl and a PHI of 1 day; a maximum number of three sprays is recommended. Four trials which approximated national GAP showed concentrations of residues of 0.61, 1.1, 1.2 and 1.6 mg/kg 1–3 days after spraying at 0.05 kg ai/hl.

In three trials conducted in glasshouses in The Netherlands, a spray concentration of 0.075 kg ai/hl was applied five times to tomatoes. However, the trial did not correspond to registered uses in The Netherlands, which allow application at a spray concentration of 0.025 kg ai/hl and a PHI of 3 days.

In the United Kingdom, iprodione may be applied to tomatoes under cover at a spray concentration of 0.05 kg ai/hl. A maximum of six sprays may be applied, with a PHI of 1 day. In the 1981 trials, finite levels of iprodione were present in untreated samples at levels that were 20–30% of the treated samples in two trials and 3% in a third. Only data from the trial with low contamination in the control sample were considered in estimating an MRL. Four trials conducted in 1977 approximated GAP in the United Kingdom, with application at 0.05 kg ai/hl and sampling 2 days after the last spray. Iprodione residues from trials approximating GAP were 0.23, 0.28, 1.4, 1.4, 2.8 and 4.2 mg/kg, from samples taken at 1–2 days after treatment at 0.05 kg ai/hl.

The results of all indoor trials conducted at GAP showed concentrations, in ranked order (median underlined), of: 0.2, 0.23, 0.28, 0.3, 0.4 (2), 0.61, 0.74, <u>1.1</u>, 1.2, 1.4 (2), 1.6, 1.7 (2), 2.8 and 4.2 mg/kg. The Meeting estimated a maximum residue level of 5 mg/kg, an STMR value of 1.1 mg/kg and a highest residue value for iprodione in tomatoes of 4.2 mg/kg. The estimated maximum residue level confirms the current recommendation (5 mg/kg) for tomato.

Fate of residues during processing

A study of processing conducted in the USA which was reviewed by the 1994 JMPR was re-submitted by the manufacturer. Iprodione was applied five times at 7–14-day intervals, at a rate equivalent to 1.1 or 2.2 kg ai/ha. Samples of treated fruit were taken on the day of the final application. Residues of iprodione, its isomer and its metabolite were determined in all samples. The concentrations were 0.22–1.6 mg/kg after application at 1.1 kg ai/ha and 0.46–1.9 mg/kg after application at 2.2 kg ai/ha.

Tomatoes collected after both treatments were processed into wet and dry pomace, juice, purée and ketchup. The calculated processing factors for the concentration of iprodione were 4.2 in wet pomace and 21 in dry pomace. In the 1994 evaluation, factors of 5 and 21, respectively, were reported; however, the data had not been corrected for recovery. Processing factors of 0.5, 0.5 and 0.9 were calculated for juice, purée and ketchup, resulting in corresponding STMR-P values of 0.55, 0.55 and 0.99.

Dietary risk assessment

Long-term intake

The IEDIs for the five GEMS/Food regional diets, on the basis of the estimated STMR values, were 3–50% of the ADI. The Meeting concluded that long-term intake of residues of iprodione from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The present Meeting considered that the toxicological profile of iprodione includes effects of concern that might indicate a need for an acute RfD. The IESTI for iprodione was calculated as described in Section 3 for commodities for which maximum residue levels and STMR values were estimated and for which data on consumption were available. The results are shown in Annex 4. The IESTI for tomatoes was 0.060 mg/kg bw for the general population and 0.244 mg/kg bw for children. As no acute RfD has been established yet, the risk assessment for iprodione was not finalized.

4.17 KRESOXIM-METHYL (199)

Residue and analytical aspects

Kresoxim-methyl was first evaluated for toxicology and residues by the Meeting in 1998. The 1998 Meeting allocated an ADI of 0–0.4 mg/kg bw and concluded that an acute RfD was unnecessary. The Meeting recommended that the definition of the residue both for compliance with MRLs and estimation of dietary intake be: commodities of plant origin, kresoxim-methyl; and commodities of animal origin, α-(*para*-hydroxy-*ortho*-tolyloxy)-*ortho*-tolyl(methoxyimino)acetic acid, expressed as kresoxim-methyl. It estimated MRLs for pome fruits, barley, cucumber, grapes, dried grapes, rye, straw and fodder (dry) of cereal grains, wheat, edible offal (mammalian), mammalian fats (except milk fats), meat (from mammals other than marine mammals), milks and poultry meat. The IEDIs were 0% of the ADI for all of five GEMS/Food regional diets. The 1998 JMPR agreed that information was desirable on whether (E)-methoxyimino[α-*ortho*-tolyloy)-*ortho*-tolyl]acetic acid was esterified to kresoxim-methyl when methanol was used for extraction in studies of metabolism and the analysis of samples from supervised trials.

New information on registered uses, the results of supervised residue trials and processing studies on citrus fruits, olive and sunflower and from a study of metabolism in sugar beet was made available by the manufacturer to the Meeting. Information on current GAP was received from Germany and Japan.

Metabolism

Plants

Sugar beet was sprayed with [phenyl-^{14}C]kresoxim-methyl at 0.15 kg ai/ha twice, the first time 91 days after sowing and the second 3 weeks later or 28 days before harvest. Most of the TRR was found in leaves at both 0 day (1.8 mg/kg determined by direct combustion and 1.4 mg/kg calculated as the sum of the methanol and water extracts and the residual residues) and 28 days after the second treatment (1.7 mg/kg by direct combustion and 1.2 mg/kg calculated). Only minor TRR were found in roots 0 day (0.053 mg/kg by combustion and 0.024 mg/kg calculated) and 28 days after the second application (0.008 mg/kg by combustion and 0.009 mg/kg calculated). These results indicate that only a small amount of the applied kresoxim-methyl was translocated from leaves to roots. Extraction with methanol and subsequently with water (twice) extracted most of radiolabelled residues (91.1–98.9% of TRR in leaves and 63.3–93.3% in roots). The predominant component of the extracted residues was identified as the parent compound by HPLC. A small amount of a free acid metabolite, BF 490-1, was detected in water extracts and some water phases after solvent partition, and an additional small peak corresponding to the sugar conjugate of BF 490-2 was found in some cases. The result of a study of stability in storage showed that the radiolabelled residues in the methanol extract of sugar beet leaves were stable at –18 ºC for approximately 7.5 months. These results confirm the definition of the residue in commodities of plant origin recommended by the 1998 JMPR and agree with the results of the studies of metabolism in apple and wheat, which also demonstrated that the parent compound kresoxim-methyl was the dominant radiolabelled residue, with minor amounts of BF 490-1 and the sugar conjugate of BF 490-2 in various matrices of these crops. The question of whether BF 490-1 is esterified to kresoxim-methyl during methanol extraction remained unanswered.

Results of supervised trials

GAP for citrus fruits was reported for Japan and South Africa. Fifteen trials on Valencia orange and five trials on Marsh grapefruit were conducted in South Africa. The label in South Africa states that the water-dispersible granule formulation should be applied only with 0.5 l of narrow-range mineral oil per hl of spray solution. Trials conducted with and without mineral oil (0.02 kg ai/hl) showed a similar percentage

decline in residue concentration. Therefore, the Meeting concluded that seven trials on Valencia orange and three trials on Marsh grapefruit conducted in accordance with South African GAP (maximum of two applications at 0.01 kg ai/hl; PHI, 56 days) but without mineral oil could be considered for estimating the MRL.

Kresoxim-methyl persisted in whole fruit after the PHI of 56 days. As in most cases the concentration of residues 56–84 days after the last application was < 30%, the concentration of 0.21 mg/kg (in Malelane, 0.01 kg ai/hl, 8000 l, 84 days after last application) was taken into consideration for estimating the MRL and STMR value. The concentrations in whole fruit were < 0.01, 0.07, 0.09, 0.13, 0.19, 0.21 (2) and 0.22 mg/kg for orange and 0.06, 0.11 and 0.18 mg/kg for grapefruit. These values are within the same range. The combined values, in ranked order (median underlined), were: < 0.01, 0.06, 0.07, 0.09, 0.11, 0.13, 0.18, 0.19, 0.21 (2) and 0.22 mg/kg. The Meeting estimated a maximum residue level of 0.5 mg/kg for oranges and grapefruits. The concentrations of residues in the edible portion (flesh) resulting from use at the maximum GAP and comparable conditions were: ≤ 0.01 (7) and 0.04 mg/kg. The Meeting estimated an STMR value of 0.01 mg/kg for the edible portion (flesh or pulp) of oranges and grapefruit.

GAP for olives was reported for Spain. Eight trials were conducted, four of which were on oil olives. These trials could be considered to comply with the Spanish GAP for oil olives (maximum of one application after flowering; 0.005–0.01 kg ai/ha; 1000 l/ha; PHI, 30 days). The concentrations of residues in fruit, in ranked order, were: ≤ 0.05 (7) and 0.09 mg/kg. The Meeting estimated a maximum residue level of 0.2 mg/kg and an STMR value of 0.05 mg/kg for olives.

The results of eight trials on sunflower conducted in France, which were considered to comply with proposed French GAP (maximum of one application; 0.1 kg ai/ha; PHI, 60 days), and of a processing study became available to the Meeting. However, as the Committee was informed that there was no GAP for sunflower at the time of the review, the Meeting did not take action.

Fate of residues during processing

No information was available on the processing of citrus fruits to juice, pomace and citrus pulp, dry. As the concentration of residues of kresoxim-methyl in the flesh of oranges and grapefruits is usually < 0.01 mg/kg, the Meeting considered it unlikely that the concentrations in orange or grapefruit juice would significantly increase the dietary intake of kresoxim-methyl.

Olives were processed into oil and pomace in Spain according to the "Laboratories and Pilot Installations of the Experimental Oil Mill (Laboratorios e Instalaciones Piloto de la Almazara Experimental)", reflecting commercial practice. The concentrations of residues of kresoxim-methyl in crude oil and pomace were determined and reported in each trial. The concentrations in pomace were similar to those in fruit, while those in crude oil were about four times those in fruit (< 0.05–0.11 mg/kg in fruit, 0.12–0.49 mg/kg in crude oil).

The concentrations of residues in olive pomace and in crude oil in trials conducted according to GAP were ≤ 0.05 (4), 0.05, 0.06, 0.07, 0.12 and 0.22 mg/kg and 0.12, 0.13, 0.17, 0.20, 0.23, 0.24, 0.28 and 0.49 mg/kg, respectively. The Meeting estimated a maximum residue level of 0.7 mg/kg and an STMR value of 0.22 mg/kg for olive oil, virgin. Since olive pomace is not generally regarded as a feedstuff, no maximum residue level was estimated.

Further work or information

Desirable

- Experimental determination of whether (E)-methoxyimino[α-(*ortho*-tolyloxy)-*ortho*-tolyl]acetic acid is methylated to kresoxim-methyl when methanol is used as an extractant in studies of metabolism or analysis of samples from supervised trials (1998 JMPR)

Dietary risk assessment

Long-term intake

STMR values have been estimated for three commodities, and concentrations of residues in the edible portion of oranges and grapefruit have been estimated. IEDIs were calculated for the five GEMS/Food regional diets from the STMR values for 16 commodities estimated by the current Meeting and by the 1998 JMPR (Annex 3). The calculated IEDIs were 0% of the ADI for all regional diets. The Meeting concluded that intake of residues of kresoxim-methyl resulting from uses considered by the 1998 and current JMPR was unlikely to present a public health concern.

Short-term intake

The 1998 JMPR concluded that an acute RfD for kresoxim-methyl was unnecessary. The Meeting therefore concluded that the short-term dietary intake of kresoxim-methyl residues is unlikely to present a risk to consumers.

4.18 METHOMYL (094)

Toxicology

Methomyl (*S*-methyl-*N*-((methylcaramoyl)oxy(thioacetamidate) was evaluated toxicologically by the JMPR in 1978, 1986, and 1989. In 1989, an ADI of 0-0.03 mg/kg bw was established on the basis of a NOAEL of 3 mg/kg bw per day in a 2-year study of toxicity in dogs and a 100-fold safety factor. This ADI was maintained by a 1994 WHO Core Assessment Group that prepared Environmental Health Criteria 178. JMPR was asked to establish an acute RfD for methomyl by the Codex Committee on Pesticide Residues. The present Meeting therefore evaluated data submitted in support of an acute RfD and additional data on the toxicity of repeated doses and of dermal application and on genotoxicity.

The acute oral LD_{50} of methomyl is approximately 20 mg/kg bw in rats, and the compound is classified by WHO as ‘highly hazardous’.

Methomyl was tested for genotoxicity in a range of studies in vitro and showed cytogenetic potential in one study in human lymphocytes; it was not cytogenetic in rats in vivo. In studies evaluated by the present Meeting, methomyl did not induce gene mutation in vitro or micronuclei in mice treated in vivo. The Meeting concluded that methomyl is unlikely to be genotoxic.

Methomyl was not a reproductive or a developmental toxicant.

Rats given methomyl by gavage at a dose of 3 mg/kg bw showed peak effects (clinical signs and inhibition of erythrocyte cholinesterase activity) at 30 min and almost complete recovery by 2 h. In a study of acute neurotoxicity, male rats preconditioned to eat within 2 h received methomyl at a single dose of 0, 1.0, 1.9, 3.7, and 10 mg/kg bw. Significant reductions (> 20%) in erythrocyte and brain cholinesterase activities were seen at doses (3.7 mg/kg bw. The NOAEL was 1 mg/kg bw on the basis of a dose-related diminution in response to tail pinch at doses (1.9 mg/kg bw. In a study of acute neurotoxicity, rats received methomyl at a dose of 0, 0.25, 0.5, 0.75, or 2 mg/kg bw by gavage in an aqueous vehicle. The NOAEL was 0.25 mg/kg bw on the basis of rapidly reversible inhibition of erythrocyte and brain cholinesterase activity.

In a 13-week study of neurotoxicity, groups of rats received diets containing methomyl at a concentration of 0, 20, 50, 150, or 1500 ppm. At 1500 ppm (equal to 95 mg/kg bw per day), several treatment-related effects were seen in animals of each sex, including decreased brain cholinesterase activity, tremors, and abnormal pupil responses. The NOAEL was 150 ppm, equal to 9.4 mg/kg bw per day. The Meeting noted that this NOAEL, observed with repeated dietary administration, was higher than the NOAELs observed in the studies of acute exposure described above.

Male volunteers received single capsules containing methomyl at a dose of 0, 0.1, 0.2, or 0.3 mg/kg bw soon after breakfast. On the basis of dose-related, statistically significant inhibition of erythrocyte cholinesterase activity, by > 20%, and a statistically significantly increase in saliva secretion at doses (0.2 mg/kg bw, the NOAEL was 0.1 mg/kg bw.

The Meeting allocated an acute RfD of 0.02 mg/kg bw on the basis of the NOAEL of 0.1 mg/kg bw in the study with volunteers. A safety factor of 5 was used because the effects were rapidly reversible and driven by the maximal concentration in plasma (see Annex 5 of JMPR 2000 report). This value was supported by the results of the study of acute neurotoxicity in rats treated in the diet, with a NOAEL of 1 mg/kg bw, the study of acute neurotoxicity in rats treated by gavage, with a NOAEL at 0.25 mg/kg bw, and the absence of any significant sex difference in studies in rats.

The Meeting noted that this acute RfD was lower than the current ADI. This is plausible in view of the toxicological profile of methomyl, which shows very rapid recovery from cholinesterase inhibition, such that the NOAELs for dietary intake over 2 h or over 13 weeks were higher than the NOAEL for a single bolus dose. For this reason, setting an acute RfD on the basis of a single meal rather than daily consumption might be justified. Practical implications associated with this situation were noted, as intake data do not allow subdivision of daily intake into individual meals (see section 2.1). The Meeting concluded that the ADI and acute RfD for methomyl should be based on the same NOAEL and revised the ADI to 0–0.02 mg/kg bw on the basis of the NOAEL of 0.1 mg/kg bw in the study with volunteers and a safety factor of 5.

An addendum to the toxicological monograph was prepared.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Rat	Acute neurotoxicity after administration by gavage	Inhibition of erythrocyte and brain cholinesterase	0.25 mg/kg bw	0.5 mg/kg bw
	Acute neurotoxicity after administration in the diet	Reduced response to tail pinch	1.0 mg/kg bw	1.9 mg/kg bw
	13-week study of neurotoxicity after administration in the diet	Clinical signs and brain cholinesterase inhibition	150 ppm (equal to 9.4 mg/kg bw per day)	1500 ppm (equal to 95 mg/kg bw per day)
Human	Single capsule given to male volunteers	Erythrocyte cholinesterase inhibition and salivation	0.1 mg/kg bw	0.2 mg/kg bw

Estimate of acceptable daily intake for humans

0–0.02 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

Residue and analytical aspects

Methomyl is a carbamate insecticide. It is registered throughout the world for foliar application to numerous agricultural crops.

Metabolism

Animals

The metabolism of [^{14}C]methomyl has been studied in the rats, monkeys, goats, cows and hens. The radiolabel is located on C with a double-bond to N. The main metabolite identified in rat urine was a mercapturic acid derivative; acetonitrile, acetate, methomyl oxime sulfate and acetamide were tentatively identified in urine, but methomyl (both *syn* and *anti* isomers) and methomyl oxime (*S*-methyl *N*-hydroxythioacetimidate) were absent. About 75% of orally administered radiolabelled methomyl was eliminated within 3 days of the final treatment, with 50% in expired air and 25% in urine.

The findings in monkeys were similar to those in rats: 36% of the orally administered dose was found in expired air and 25% in urine. Urine also contained acetonitrile, acetate, acetamide, methomyl oxime sulfate and a trace of the mercapturic acid derivative of methomyl. Methomyl and methomyl oxime were absent. About 5% of the administered dose was found in tissues, the liver containing the largest portion (0.9 mg/kg as equivalents).

A definitive study of metabolism in goats confirmed the results of earlier studies on metabolism in goats and cows. A lactating goat was dosed orally for 3 consecutive days with radiolabelled methomyl at a concentration of about 160 ppm determined on the basis of actual feed consumption. About 30% was collected as expired volatile compounds (18% $^{14}CO_2$ and 13% [^{14}C]acetonitrile). The concentrations of radiolabel in milk and tissues were adequate to permit isolation and identification of metabolites (12 mg/kg of liver, 5 mg/kg of kidney, 1.5 mg/kg of muscle, 0.32 mg/kg of fat, 9 mg/kg of milk). Methomyl, methomyl *S*-oxide, methomyl *S*,*S*-dioxide, methomyl oxime and hydroxymethyl methomyl were not detected in any tissue or in milk, with an LOD of 0.007–0.018 mg/kg. Radiolabelled acetamide and thiocyanate were found in all tissues and milk, the latter constituting 7–50% of the total radiolabelled residue in the matrices.

Further characterization of the residues in tissues and milk indicated extensive incorporation of the radiolabel into natural components. About 30% of the TRR in milk was shown to be associated with fatty acids, and about 10% was [^{14}C]lactose. About 13% of the TRR in muscle, liver, kidney and fat was shown to be in amino acids.

The metabolism of [^{14}C]- or [^{13}C]methomyl was studied in white Leghorn laying hens dosed orally for 3 consecutive days at a rate equivalent to 45 ppm in the diet. Respired acetonitrile and CO_2 accounted for > 50% of the administered dose. The concentrations of equivalents of radiolabelled material in eggs and tissues were: 3 mg/kg in liver, 0.5 mg/kg in muscle, 0.8 mg/kg in fat, 1.5 mg/kg in egg white and 2 mg/kg. in egg yolk Methomyl and methomyl oxime were not detected in any tissue or in egg (LOD, 0.007–0.015 mg/kg.) Acetamide was found in egg white, and acetonitrile was found in all matrices, constituting 89% of the TRR in egg white.

Further characterization of the radiolabelled residue revealed that 60% of the TRR in egg yolk was associated with lipids, 87% with fat and 32% with liver. Small amounts (3% TRR) in the eggs and tissues were characterized as radiolabelled amino acids.

The Meeting concluded that the metabolism of methomyl is adequately understood in animals, and that similar mechanisms exist in rats, monkeys, ruminants and hens. Methomyl is degraded to acetonitrile, acetamide and CO_2, and these metabolites are incorporated into natural products. The Meeting further concluded that methomyl oxime is a probable intermediate, but neither it nor methomyl showed any propensity to bioaccumulate over the duration of the studies.

Plants

The metabolism of [^{14}C]methomyl was studied in tobacco, corn, cabbage and cotton. When tobacco plant roots were exposed to a solution of radiolabelled compound for 28 days, they absorbed 25% of the available radiolabel over 4 weeks. About 25% of that absorbed was retained, and the other 75% was released as CO_2 and acetonitrile, in equal proportions.

About 45% of a dose of [^{14}C]methomyl applied to the leaves of maize plants was volatilized within 10 days. About 26% of the radiolabel was extractable with methanol.

About 20% of a dose of [^{14}C]methomyl applied to the leaves of cabbage plants volatilized within 10 days, and 54% of the radiolabel was extractable with methanol. Methomyl comprised about 4% of the radiolabelled residue; no other related metabolite, such as methomyl oxime, was detected. Saponification of a non-polar fraction yielded radiolabelled fatty acids.

The translocation of methomyl was studied in tobacco plants by applying radiolabelled compound to the fifth leaf from the ground No translocation was found after 3 days; after 7 days, < 1% of the residual radiolabel was found in plant parts other than the fifth leaves.

The metabolism of [^{14}C]methomyl was studied in maize, cabbage, and cotton under field conditions. Plants received repeated foliar treatments, and crops of maize and cabbage were harvested 8 days after the final treatment, while cotton leaves were harvested 0–192 hours after a single treatment. The outer leaves of cabbage heads contained methomyl at 0.9 mg/kg or 4% of the TRR, and the head contained 0.09 mg/kg. Methomyl oxime was not detected in head or leaves. Maize grain contained no methomyl or methomyl oxime, and most of the extractable radiolabel was associated with polar materials Fodder contained about 2 mg/kg methomyl, and about 50% of the radiolabel could not be extracted.

In cotton, methomyl was the only component identified on the leaf surface. Radiolabel was initially found in leaves (extract) but disappeared within 48 h of treatment. Methomyl oxime was not found at any interval.

A study of confined rotational crops was conducted in sandy loam soil with cabbage, red beet and sunflower. Seeds were planted 30 and 120 days after treatment of the soil with [^{14}C]methomyl at a rate of 4.5 kg ai/ha, and the crops were harvested at normal maturity. At the 30-day plant-back interval, beets and cabbage contained 0.1–0.2 mg/kg methomyl equivalents, and sunflower seeds contained 2 mg/kg. At 120 days, the concentrations had declined to 0.05 mg/kg and 1.5 mg/kg, respectively. The concentrations of methomyl and its immediate metabolites, as determined by methanol extraction, were ≤ 0.01 mg/kg at both plant-back intervals.

The Meeting concluded that the nature of the residues in and on plants is adequately understood. Methomyl is degraded to CO_2 and acetonitrile, and these metabolites may then be incorporated into natural products. The Meeting further concluded that methomyl has little tendency to translocate and does

not translocate (as methomyl) into rotational crops (< 0.01 mg/kg) at 30-day or longer plant-back intervals. The Meeting also noted that methomyl oxime, if present, occurs as a minor metabolite.

Environmental fate

Soil

Under anaerobic conditions, [^{14}C]methomyl degraded rapidly, with a first-order half-time of 11 days. Over a 3-month study period, the main degradate was $^{14}CO_2$, representing 75% of the applied material; methomyl oxime represented 3% of the applied material. In experiments with various soil types, 30–45% of the applied material was isolated as $^{14}CO_2$ after 42 days. The main component in soil extracts was [^{14}C]methomyl, representing < 10% of the applied radiolabel. In sterile soil, [^{14}C]methomyl represented 89% of the applied radiolabel after 45 days.

[^{14}C]Methomyl had a first-order half-time of < 1 day to 14 days in various experiments under anaerobic conditions. Ferrous ion accelerated degradation to methanethiol and dimethyl disulfide.

The photolysis of [^{14}C]methomyl under natural sunlight for 30 days was studied after application at a rate of 1.1 kg ai/ha to silt loam, maintained at 25 °C. The radiolabelled compound decomposed with a half-time of 34 days, and the only decomposition product detected was acetonitrile. Controls showed no decomposition.

The mobility of [^{14}C]methomyl was studied on various types of loam soil. Methomyl was highly mobile in loams with a high sand content and less mobile in loams with more organic matter. Likewise, a higher clay content decreased the mobility of methomyl. In column leaching experiments performed with Speyer 2.1, 2.1 and 2.3 soils, the percentage of radiolabel in the leachate increased from 8% to 52% as the sand content of the soil increased from 65% to 91%. The leachate contained a maximum of 2% methomyl oxime.

The Meeting concluded that methomyl degrades at a moderate rate under both aerobic and anaerobic conditions and that microbes are essential to the degradation under aerobic conditions. CO_2 is the main degradate under aerobic conditions. Methomyl on soil is also subject to photodegradation. The Meeting further concluded that methomyl has low to moderate mobility in soil, greater mobility in sandy soils and less mobility in clay and in soils with a high content of organic matter.

Water–sediment systems

The fate of [^{14}C]methomyl added at a nominal concentration of 0.45 µg/ml to two natural water–sediment systems was studied. After an equilibrium had been established in the systems, the mixtures were spiked with the [^{14}C]methomyl, and sediment and water phases were taken and analysed at intervals up to 102 days. Acetonitrile accounted for about 25% of the applied radiolabel and CO_2 for about 40% after 102 days. Sediment contained about 15% of the radiolabel and water contained about 1%. By day 29, methomyl had virtually disappeared from both water and sediment. Analysis of extracts confirmed the absence of methomyl oxime, anti-methomyl, methomyl sulfoxide, acetaldehye and acetic acid. The first-order half-time of methomyl was about 5 days.

The Meeting concluded that methomyl degrades rapidly in water–sediment systems, with the formation of acetonitrile and CO_2.

Methods of analysis

Methods were described for the determination of methomyl in plant commodities, animal commodities and environmental samples. The original methods for plant commodities consist of extraction with an

organic solvent, liquid–iquid partition and hydrolysis with sodium hydroxide. The latter converts methomyl and thiodicarb to methomyl oxime. The final extract is analysed by GC, usually with a flame photometric detector in the sulfur mode.

The more recent method is based on HPLC. The plant matrix is extracted with solvent, cleaned-up on a Florisil column and analysed by HPLC with post-column reaction to convert separated thiodicarb and methomyl to methyl amine. Methyl amine is derivatized (on-line) and detected by fluorescence.

The GC method has been validated for numerous plant commodities at a LOD of 0.02 mg/kg. The HPLC method and its modifications have been validated at a LOD of 0.02 mg/kg for methomyl.

Similar GC and HPLC methods exist for the determination of methomyl in meat, milk, poultry and eggs. The LOQs for the GC method are 0.080 mg/kg for liver, 0.080 mg/kg for kidney, 0.020 mg/kg for muscle and 0.040 mg/kg for fat. Difficulties were experienced in obtaining acceptable recoveries from milk. The HPLC method has a LOQ of 0.02 mg/kg or 0.01 mg/kg, depending on the extent of sample preparation.

The Meeting concluded that adequate methods exist for the determination of methomyl in plant and animal commodities.

Stability of residues in stored analytical samples

Information on stability in storage was provided for methomyl in soya bean hay, maize (kernels), bean seed, potato, peanut (nutmeat), grain sorghum forage, grain sorghum hay, grain sorghum stover, head lettuce, broccoli, orange (chopped), orange (half), apple, grape and onion (whole) stored frozen (nominal temperature, –20 °C). Adequate stability (> 80% remaining) was demonstrated after 24 months' storage for all commodities except chopped orange and onions. The residues on onions were incurred in the field, and the variability in the recovery at different times was attributed to differences in the portion of onion bulb exposed (above ground) at the time of methomyl application. The stability on an orange half was satisfactory.

Methomyl was unstable in or on liver stored at –4 to –20 °C, declining by at least 50% on day 1. The compound was stable in milk for 24 months at –20 °C but unstable in fat, muscle and kidney. Methomyl was stable in all ruminant commodities for 6 months when stored under cryogenic conditions (–70 °C).

These studies included use of the HPLC analytical method, in which methomyl is determined as methomyl. Any hydrolysis to methomyl oxime during storage would have been reflected as loss of methomyl. This was not observed.

The Meeting concluded that methomyl is stable under frozen conditions on most plant commodities for up to 24 months, the interval studied, but that it is not stable in ruminant fat, kidney, muscle or liver under ordinary freezer conditions. Special conditions must be used to store ruminant commodities for analysis.

Definition of the residue

Studies of the nature of the residue in animals and plants showed that methomyl is substantially metabolized to CO_2 and acetonitrile. Methomyl oxime was generally absent, although its sulfate was found in some studies in animals.

The older GC methods for analysis rely on conversion of methomyl to methomyl oxime, and thus, methomyl and methomyl oxime are determined. In the newer HPLC methods, only methomyl is determined, although thiodicarb may also be determined (separately) by the same method.

The Meeting noted that thiodicarb is readily metabolized to methomyl and that it is appropriate to combine the considerations for thiodicarb and methomyl. The Meeting agreed that the residue in both plant and animal commodities should be defined as methomyl for use of methomyl and as the sum of thiodicarb and methomyl, expressed as methomyl, for the use of thiodicarb. The Meeting further noted that expression of thiodicarb residue can be expressed as methomyl or thiodciarb, as the conversion factor from thiodicarb to methomyl is 0.92 and that from methomyl to thiodicarb is 1.1.

Results of supervised trials

Supervised trials were conducted with foliar application of methomyl to numerous agricultural commodities, primarily in Europe and the USA.

Citrus

Supervised field trials were conducted on oranges and mandarin in Greece (GAP: soluble concentrate, 0.09 kg ai/hl, 1.4 kg ai/ha; one to three applications; PHI, 20 days), Italy (GAP: soluble concentrate, wettable powder; 0.04 kg ai/hl; PHI, 10 days) and Spain (GAP: wettable powder, soluble concentrate, 0.05 kg ai/hl; 0.6, 0.5 kg ai/ha; five applications; PHI, 7 days). Seven trials o oranges were conducted in Spain, three in Greece and four in Italy. Five trials on mandarin were conducted in Spain, three in Greece and two in Italy. When Spanish GAP is applied to the trials on orange, the ranked order of concentrations of residues was: < 0.02 (2), 0.02, 0.03, 0.06 (2), 0.07, 0.09, 0.14, 0.25, 0.30, 0.35, 0.43 and 0.59 mg/kg. There were five trials on mandarin in Spain, three in Greece and two in Italy. When Spanish GAP is applied to the trials on orange, the ranked order of concentrations of residues was: 0.05, 0.06, 0.17 (2), 0.19, 0.32, 0.38 (2), 0.43 and 0.89 mg/kg.

The Meeting considered the combined data sufficient for citrus. The ranked order of concentrations was therefore (median underlined): < 0.02 (2), 0.02, 0.03, 0.05, 0.06 (3), 0.07, 0.09, 0.14, 0.17 (2), 0.19, 0.25, 0.30, 0.32, 0.35, 0.38 (2), 0.43 (2), 0.59 and 0.89 mg/kg. The Meeting estimated a maximum residue level of 1 mg/kg for citrus. The Meeting agreed to maintain the current recommendation of 1 mg/kg. A study of consumer-type peeling showed that the concentration of residue on flesh is reduced by a factor of 0.2 when the peel is removed from unwashed oranges. Using this factor, the Meeting estimated an STMR value of 0.034 mg/kg and a highest residue of 0.18 mg/kg for citrus flesh.

Stone fruit

Supervised field trials were conducted on peach, apricot and nectarine. Trials on peach were conducted in Spain (GAP: soluble concentrate, wettable powder; 0.6 kg ai/ha, 0.05 kg ai/hl; one to five applications: PHI, 7 days), Germany (no GAP; uses that of France), France (GAP: 0.075 kg ai/ha; PHI, 7 days), Italy (wettable powder, soluble concentrate; 0.04 kg ai/ha; PHI, 10 days) and the USA (soluble concentrate, water-soluble powder; 2.0 kg ai/ha, 0.06 kg ai/hl terrestrial, 4.8 kg ai/hl aerial; six applications; PHI, 4 days). None of the 13 trials in the USA was conducted according to GAP. Applying the GAP of Spain for Italy, 15 trials in Europe (six in France, three in Germany, three in Italy and three in Spain) were at GAP, and the ranked order of concentrations of residues was: < 0.02, 0.02, 0.03, 0.04 (3), 0.05 (2), 0.07 (2), 0.08, 0.09 (3) and 0.10 mg/kg. The Meeting estimated an STMR value of 0.05 mg/kg and a maximum residue level of 0.2 mg/kg for peaches. The highest residue was estimated as 0.10 mg/kg. The Meeting agreed to withdraw the previous recommendation for peach (5 mg/kg).

Nine supervised trials were conducted on nectarine in the USA, two according to GAP (GAP: soluble concentrate, water-soluble powder; 1.0 kg ai/ha, 1.0 kg ai/hl; three applications; PHI, 1 day), resulting in concentrations of 0.78 and 1.4 mg/kg. The Meeting decided that there were insufficient data to estimate a maximum residue level or STMR value for nectarine from these data. Applying the

European data for peach, the Meeting estimated a maximum residue level of 0.2 mg/kg, an STMR value of 0.05 mg/kg and a highest residue of 0.10 mg/kg for nectarine.

Four trials on apricot were conducted in Italy, all at the GAP of Spain (soluble concentrate, wettable powder; 0.05 kg ai/hl; PHI, 7 days). The ranked order of concentrations of residues was: 0.04 (2), 0.05 and 0.15 mg/kg. The Meeting considered that there were insufficient data from which to estimate a maximum residue level or an STMR value.

Supervised field trials were conducted on plums in Europe (GAP, France: soluble concentrate; 0.075 kg ai/hl; three applications; PHI, 7 days; Germany: none, uses that of France; Spain (stone fruit): soluble concentrate, wettable powder; 0.6 kg ai/ha, 0.05 kg ai/hl; one to five applications; PHI, 7 days). Of the 15 trials, 13 were conducted at GAP, and the ranked order of concentrations of residues was: 0.02 (2), 0.03 (2), 0.06, 0.08 (2), 0.10, 0.11, 0.19, 0.28, 0.34 and 0.51 mg/kg. The Meeting estimated a maximum residue level of 1 mg/kg, an STMR value of 0.08 mg/kg and a highest residue of 0.51 mg/kg for plums.

Pome fruit

Trials on apple and pear were conducted in France (soluble concentrate, 0.075 kg ai/h; three applications; PHI, 7 days), Germany (no GAP; uses that of France), Spain (soluble concentrate, wettable powder; 0.75 kg ai/ha, 0.05 kg ai/hl, one to five applications,; PHI, 7 days), Italy (soluble concentrate, wettable powder; 0.05 kg ai/hl; PHI, 10 days) and Belgium (wettable powder; 0.75 kg ai/ha, 0.05 kg ai/hl; PHI, 21 days). Of the trials on apple, 13 were at GAP (eight in France, two in Italy (GAP of Spain), two in Spain, one in Germany). The ranked order of concentrations of residues was: 0.03, 0.06, 0.08 (3), 0.09 (3), 0.11, 0.13, 0.16 and 0.17 (2) mg/kg.

Supervised field trials on apple were conducted in the USA (water-soluble powder, soluble concentrate; 1.0 kg ai/ha, 2.2 kg ai/hl; five applications; PHI, 14 days). Ten of 34 trials were at GAP, and the ranked order of concentrations of residues was: 0.16, 0.24, 0.25, 0.29, 0.31 (2), 0.34, 0.42, 0.48 and 0.77 mg/kg. The Meeting decided that the European and USA residues were from different populations and could not be combined. Supervised trials on apples were also conducted with thiodicarb, and the ranked order of concentrations of residues was: 0.30, 0.32, 0.40, 0.43, 0.48, 0.61, 0.68, 0.91 (2) and 1.6 mg/kg. The Meeting considered that the data on thiodicarb were from the same population as the data for methomyl and combined them, with a ranked order of concentrations of: 0.16, 0.24, 0.25, 0.30, 0.31(2), 0.32, 0.34, 0.39, 0.40, 0.42, 0.43, 0.48 (2), 0.61, 0.68 (2), 0.77, 0.91 (2), 1.5 and 1.6 mg/kg. The Meeting estimated a maximum residue level of 2 mg/kg, an STMR value of 0.41 mg/kg and a highest residue of 1.6 mg/kg for apple.

Supervised field trials were conducted on pear in Europe. Two trials were conducted in France, two in Belgium and one in Italy. GAP was applied in the trials in France (soluble concentrate; 0.075 kg ai/h; three applications; PHI, 7 days) and Italy (GAP of Spain: soluble concentrate, wettable powder; 0.05 kg ai/hl; five applications,; PHI, 7 days); the ranked order of concentrations of residues was: 0.03, 0.04, 0.11 and 0.18 mg/kg. Six field trials were conducted on pears in the USA, but none was at GAP. The Meeting decided that four trials were insufficient to estimate a maximum residue level or an STMR value for pears but agreed that the data on apple from Europe, with similar GAP and residue values, could be used to support the limited data set for pear. The concentrations in the combined data set, in ranked order, were: 0.03 (2), 0.04, 0.06, 0.08 (3), 0.09 (3), 0.11 (2), 0.13, 0.16, 0.17 (2) and 0.18 mg/kg. The Meeting estimated a maximum residue level of 0.3 mg/kg, an STMR value of 0.09 mg/kg and a highest residue of 0.18 mg/kg for pears.

The Meeting agreed to withdraw the previous recommended MRL for pome fruit (2 mg/kg) and to replace it with the recommendations for apple (2 mg/kg) and pear (0.3 mg/kg).

Berries and small fruit

Supervised field trials on grapes were reported from the USA (GAP: soluble concentrate, water-soluble powder; 1.0 kg ai/ha, 1.1 kg ai/hl; five applications; PHI, 1 day for fresh table grapes, 14 days for wine grapes). Seventeen trials were conducted at GAP. When the grape type (table or wine) was not specified, use on table grapes, with the shorter PHI, was assumed.

Supervised field trials on grapes were reported from France (GAP: soluble concentrate; 0.4 kg ai/ha, 0.05 kg ai/hl; three applications; no PHI), Italy (soluble concentrate, wettable powder; 0.05 kg ai/hl; PHI, 10 days) and Portugal (no GAP; uses that of Italy). Four trials from France were at GAP, with residue concentrations of 0.19, 0.25, 0.26 and 0.29 mg/kg. The results of these trials were combined with those of trials in the USA (foliar), and the ranked order of concentrations of residues was: 0.15, 0.19, 0.25, 0.26, 0.29, 0.54, 0.58, 0.65, 0.78, 0.93, 1.0 (2), 1.2, 1.3, 2.2, 2.3, 2.8, 2.9, 3.5, 4.1 and 5.2 mg/kg. Supervised field trials were also conducted with thiodicarb, giving a ranked order of concentrations of thiodicarb residues of: 0.59 and 0.7 (2) mg/kg. The combined values for methomyl and thiodicarb residues yields a ranked order of: 0.15, 0.19, 0.25, 0.26, 0.29, 0.54, 0.58, 0.59, 0.65, 0.7 (2), 0.78, 0.93, 1.0 (2), 1.2, 1.3, 2.2, 2.3, 2.8, 2.9, 3.5, 4.1 and 5.2 mg/kg. The Meeting estimated an STMR value of 0.86 mg/kg, a highest residue of 5.2 mg/kg and a maximum residue level of 7 mg/kg, which replaces the previous recommendation (5 mg/kg).

Bulb vegetables

Five supervised trials were conducted on onions, bulb in the USA (GAP: 1.0 kg ai/ha, 5.4 kg ai/hl; eight applications; PHI, 7 days). All the trials were at GAP, and the ranked order of concentrations of residues was: < 0.02, 0.056, 0.068, 0.072 and 0.14 mg/kg. The Meeting estimated an STMR value of 0.068 mg/kg, a highest residue of 0.14 mg/kg and a maximum residue level of 0.2 mg/kg, which confirms the existing MRL.

Brassica vegetables

The GAP for cabbage in the USA is soluble concentrate or water-soluble powder formulation at 1.0 kg ai/ha, 1.1 kg ai/hl; 15 applications and a 1-day PHI. Seven trials were conducted at GAP, and the ranked order of concentrations of residues was: 0.086, 0.10, 0.18, 0.27, 0.46, 0.52 and 0.63 mg/kg. Supervised field trials on cabbage with thiodicarb yielded higher values: 0.08 (2), 0.12, 0.53, 0.76, 0.97, 1.2, 1.3, 2.1, 2.7, 2.8, 3.0, 3.1, 3.5, 3.8, 4.3, 4.8, 5.0 and 5.3 mg/kg. The Meeting considered the two sets of data to be from different populations and agreed to use the results for thiodicarb (higher values) for making estimates.

Supervised field trials were conducted on broccoli in the USA, where the GAP is use of the soluble concentrate or water-soluble powder formulation at 1.0 kg ai/ha, 1.1 kg ai/hl; 10 applications and a 3-day PHI. The ranked order of concentrations of residues in the 16 trials at GAP was: 0.09, 0.20, 0.21, 0.35, 0.36, 0.44, 0.45, 0.51, 0.68, 0.70, 0.73, 0.77, 0.96, 1.1, 1.8 and 2.8 mg/kg. Supervised field trials were also conducted on broccoli with thiodicarb, resulting in concentrations of: 1.1, 1.3, 1.6, 1.9, 2.6, 5.0 and 5.6 mg/kg. The Meeting considered the two data sets to be from different populations and agreed to use those for thiodicarb (higher values) for making estimates.

Supervised field trials were conducted on cauliflower in the USA, where the GAP is use of the soluble concentrate or water-soluble powder formulation at 1.0 kg ai/ha, 1.1 kg ai/hl; 10 applications and a PHI of 3 days. Eleven trials were conducted at GAP, and the ranked order of concentrations of residues was: 0.04, 0.18 (2), 0.20, 0.24, 0.51, 0.74, 1.6, 2.0, 3.8 and 5.6 mg/kg. Supervised field trials were also conducted with thiodicarb, resulting in concentrations of: 0.09, 0.16, 0.27, 0.45, 0.64, 0.71 and 2.3 (2) mg/kg. The Meeting considered the two sets of data to correspond to the same population and agreed to combine them for making estimates.

The Meeting noted that GAP for broccoli, cabbage and cauliflower is similar and that the residue concentrations were similar. It therefore decided to combine the values for thiodicarb on cabbage, thiodicarb on broccoli and thiodicarb and methomyl on cauliflower (n = 45), as follows: 0.04, 0.08 (2), 0.09, 0.12, 0.16, 0.18 (2), 0.20, 0.24, 0.27, 0.45, 0.51, 0.53, 0.64, 0.71, 0.74, 0.76, 0.97, 1.1, 1.2, 1.3 (2), 1.6 (2), 1.9, 2.0, 2.1, 2.3 (2), 2.6, 2.7, 2.8, 3.0, 3.1, 3.5, 3.8 (2), 4.3, 4.8, 5.0 (2), 5.3 and 5.6 (2) mg/kg. The Meeting estimated a maximum residue level of 7 mg/kg, an STMR value of 1.3 mg/kg and a highest residue of 5.6 mg/kg for brassica vegetables.

The Meeting agreed to withdraw the previous recommendations for cabbages, head (5 mg/kg) and cauliflower (2 mg/kg), and to replace them by the recommendation for brassica vegetables (7 mg/kg).

Cucurbits

Supervised field trials on cucumbers were conducted in Belgium (wettable powder; 0.5 kg ai/ha, 0.031 kg ai/hl; PHI, 14 days), France (soluble concentrate; 0.3 kg ai/ha; three applications; PHI, 7 days), Greece (soluble concentrate; 0.45 kg ai/ha; one to three applications; PHI, 20 days), Italy (soluble concentrate, wettable powder; 0.04 kg ai/hl; PHI, 10 days) and The Netherlands (soluble concentrate, wettable powder; 0.4 kg ai/ha, 0.025 or 0.008 kg ai/hl; one to three applications; PHI, 3 days). The trials in Belgium and The Netherlands were conducted in glasshouses. The ranked order of concentrations of residues in the four trials conducted at GAP was: < 0.02 (2) and 0.03 (2) mg/kg. Eight trials on cucumber conducted outdoors (two in France, one in Greece and five in Italy) were at the respective GAP, and the ranked order of concentrations of residues was: < 0.02 (8) mg/kg. The Meeting considered that the data from the indoor and outdoor trials were from the same pool and combined them, resulting in a ranked order of concentrations in the 12 trials of: < 0.02 (10) and 0.03 (2) mg/kg.

Field trials on squash, summer were conducted in Belgium (no GAP; uses that of The Netherlands), Greece (wettable powder; 0.45 kg ai/ha; one to three applications; PHI, 15 day s), Italy (no GAP; uses that of France: 0.3 kg ai/ha; three applications; PHI, 7 days) and The Netherlands (soluble concentrate, wettable powder; 0.4 kg ai/hl, 0.025 kg ai/hl [0.08 kg ai/hl for wettable powder]; one to three applications; PHI, 3 days). The trials in Belgium and The Netherlands were conducted in glasshouses. Only one trial, in Belgium, was conducted at GAP, resulting in a residue concentration of < 0.02 mg/kg.

Supervised trials were conducted on watermelon in the USA (GAP: soluble concentrate, water-soluble powder; 1.0 kg ai/ha, 1.1 kg ai/hl; 12 applications; PHI, 3 days). The ranked order of concentrations in the three trials conducted at GAP was < 0.04 (2) and 0.07 mg/kg.

Supervised trials on melons were conducted in Greece (soluble concentrate; 0.45 kg ai/ha; one to three applications; PHI, 20 days), Italy (soluble concentrate, wettable powder; 0.04 kg ai/hl; PHI, 10 days), The Netherlands (soluble concentrate, wettable powder; 0.4 kg ai/ha, 0.025 or 0.08 kg ai/hl; one to three applications; PHI, 3 days) and Spain (no GAP; uses that of Italy). Ten trials (seven in Italy, two in The Netherlands and one in Spain) were at GAP, and the ranked order of concentrations of residues was: < 0.02 (10) mg/kg.

The Meeting noted that the trials on melons, watermelon, summer squash and cucumbers yielded similar results, < 0.02– 0.07 mg/kg, and therefore decided to combine the values and estimate a maximum residue level for the cucurbit group. The ranked order of concentrations was: < 0.02 (21), 0.03 (2), < 0.04 (2) and 0.07 mg/kg. The Meeting estimated a maximum residue level of 0.1 mg/kg, a highest residue of 0.07 mg/kg and an STMR value of 0.02 mg/kg for the cucurbit vegetable group.

The Meeting agreed to withdraw the previous recommendations for cucumber (0.2 mg/kg), melon (0.2 mg/kg), summer squash (0.2 mg/kg) and watermelon (0.2 mg/kg) and to replace them by the recommendation for the cucurbit vegetable group (0.1 mg/kg).

Fruiting vegetables

Supervised trials were conducted on egg plant, tomato and peppers in the USA (GAP: soluble concentrate, water-soluble powder; 1.0 kg ai/ha, 5.4 kg ai/hl; PHI, 3 days for egg plant, 1 day for tomato, 3 days for peppers). One of the trials on egg plant (residue concentration of 0.30 mg/kg), two on tomato (< 0.03 and 0.03 mg/kg) and two on peppers (0.08 and 0.44 mg/kg) were conducted at GAP.

Supervised trials on peppers and tomatoes were conducted in Europe. Trials on tomato were conducted in Belgium (wettable powder; 0.5 kg ai/ha, 0.031 kg ai/hl; PHI, 14 days), Italy (soluble concentrate, wettable powder; 0.04 kg ai/hl; PHI, 10 days), The Netherlands (soluble concentrate, wettable powder; 0.4 kg ai/ha, 0.025 or 0.08 kg ai/hl; one to three applications; PHI, 3 days), Portugal (no GAP; uses that of Spain), and Spain (soluble concentrate, wettable powder; 0.50 kg ai/ha, 0.05 kg ai/hl; one to five applications; PHI, 3 days). Two trials on pepper were reported, one from Italy (soluble concentrate, wettable powder; 0.04 kg ai/hl; PHI, 10 days) and one from The Netherlands (no GAP). The former was conducted at GAP, with a residue concentration of < 0.02 mg/kg. Nine trials on tomato (two in Belgium, four in Italy, two in The Netherlands and one in Spain) and one on peppers were conducted at GAP. The concentration of residues in tomato was < 0.02 (9). Supervised field trials on tomatoes were also conducted with thiodicarb, and the ranked order of concentrations was: 0.05, 0.06, 0.08, 0.09, 0.13, 0.16, 0.18, 0.23 (2), 0.33 and 0.73 mg/kg. The data on methomyl and thiodicarb were considered to represent different populations. Using only the data on thiodicarb (higher values), the Meeting estimated a maximum residue level of 1 mg/kg, an STMR value of 0.16 mg/kg and a highest residue of 0.73 mg/kg. The Meeting estimated a maximum residue level of 1 mg/kg for tomatoes to replace the previous recommendation (2 mg/kg).

The Meeting declined to estimate a maximum residue level or an STMR value for peppers, as there were only three trials at GAP, with concentrations of < 0.02, 0.08 and 0.44 mg/kg.

Sweet corn

Supervised trials were reported from the USA (GAP: soluble concentrate; 0.5 kg ai/ha, 5.4 kg ai/hl; 28 applications; no PHI for maize, 3 days for forage). Fourteen trials were at GAP, and the ranked order of concentrations of residues was: ≤ 0.02 (9), 0.021, 0.03(2), 0.043 and 0.052. Supervised field trials were also conducted with thiodicarb, and the ranked order was: < 0.02, 0.02, < 0.03 (6), < 0.04, 0.04, 0.06, 0.07 (2), 0.08, 0.11, 0.13, 0.22, 0.28, 0.43, 0.54, 0.82 and 1.5 mg/kg. The Meeting ascertained that the two sets of data did not represent the same population and made estimates from the data on thiodicarb (higher values). The Meeting estimated a maximum residue level of 2 mg/kg, an STMR value of 0.065 mg/kg and a highest residue of 1.5 mg/kg. The Meeting agreed to maintain the current recommendation of 2 mg/kg (see report item on thiodcarb).

Leafy vegetables

Supervised field trials were conducted on lettuce, head in the USA (GAP: water-soluble powder, soluble concentrate; 1.0 kg ai/ha, 1.1 kg ai/hl; 15 applications; PHI, 7 days for rates < 0.5 kg ai/ha and 10 days for rates > 0.5 kg ai/ha). All the trials were conducted at the maximum rate with a 10-day PHI. The ranked order of concentrations in the 10 trials at GAP was: 0.18, 0.54, 0.70, 1.2, 1.5, 2.2, 2.3, 3.3, 4.6 and 4.8 mg/kg. The results of supervised trials with thiodicarb on head lettuce resulted in values of : < 0.04 (3), < 0.05, 0.07 (2), 0.09 (2), 0.12, 0.14, 0.19, 0.21, 0.25, 0.34, 0.35, 0.36, 0.42, 0.44, 0.48, 0.49, 0.71, 0.96, 1.1, 1.2, 1.5, 1.7 (2). 1.8, 1.9, 2.2, 2.6, 3.0, 3.2, 6.2, 6.3, 7.7, 10, 13, 17 and 18 mg/kg. The Meeting considered that the two data sets represented different populations and agreed to use those for thiodicarb data (higher concentrations but lower STMR value).

Supervised field trials were conducted on lettuce, leaf in the USA (GAP: water-soluble powder, soluble concentrate; 1.0 kg ai/ha, 1.1 kg ai/hl; eight applications; PHI, 7 days for rates < 0.5 kg ai/ha and 10 days for rates > 0.5 kg ai/ha). All the trials were conducted at the maximum rate, and the ranked order of concentrations of residues in the 10 trials at GAP was: 0.31, 0.62, 1.4, 2.1, 2.5, 2.9, 3.6, 5.5, 5.7 and 6.7 mg/kg.

Supervised field trials were conducted on spinach in the USA (GAP: water-soluble powder, soluble concentrate; 1.0 kg ai/ha, 1.1 kg ai/hl; eight applications; PHI, 7 days). Eight trials were at GAP, and the ranked order of concentrations of residues was: 0.07, 0.34, 0.74, 1.4, 4.1, 4.6 (2) and 5.0 mg/kg. Supervised trials also were conducted with thiodicarb, resulting in concentrations of : 0.04 (2), 0.21, 1.0, 3.2, 3.5, 4.1, 12 and 25 mg/kg. The Meeting considered the two data sets to represent the same population and combined them, resulting in a ranked order of: 0.04 (2), 0.07, 0.21, 0.34, 0.74, 1.0, 1.4, 3.2, 3.5, 4.1 (2), 4.6 (2), 5.0, 12 and 25 mg/kg. The existing MRL is 5 mg/kg.

Supervised trials were conducted on collards with thiodicarb (see report item). The ranked order of concentrations of residues was: 1.5 and 1.8 mg/kg.

The Meeting noted that the ranges of concentrations were similar for leaf lettuce (thiodicarb), spinach (methomyl and thiodicarb), collards (thiodicarb) and head lettuce (thiodicarb) and decided to pool the 69 values to estimate a maximum residue level for leafy vegetables. The ranked order of concentrations was: < 0.04 (3), 0.04 (2), < 0.05, 0.07 (3), 0.09 (2), 0.12, 0.14, 0.19, 0.21 (2), 0.25, 0.31, 0.34 (2), 0.35, 0.36, 0.42, 0.44, 0.48, 0.49, 0.62, 0.71, 0.74, 0.96, 1.0, 1.1, 1.2, 1.4 (2), 1.5 (2), 1.7 (2), 1.8 (2), 1.9, 2.1, 2.2, 2.5, 2.6, 2.9, 3.0, 3.2 (2), 3.5, 3.6, 4.1 (2), 4.6 (2), 5.0, 5.5, 5.7, 6.2, 6.3, 6.7, 7.7, 10, 12, 13, 17, 18 and 25 mg/kg. The Meeting estimated a maximum residue level of 30 mg/kg, an STMR value of 1.4 mg/kg and a highest residue of 25 mg/kg for leafy vegetables.

The Meeting agreed to withdraw the previous recommendations for kale (5 mg/kg), lettuce, head (5 mg/kg), and spinach (5 mg/kg) and to replace them by the recommendation for leafy vegetables (30 mg/kg).

Supervised trials were conducted on succulent beans in the USA (GAP: soluble concentrate, water-soluble powder; 1.0 kg ai/ha, 1.1 kg ai/hl; 10 applications; PHI, 1 day for single use at < 0.56 kg ai/ha and 3 days for single use at > 0.56 kg ai/ha). Six trials were at GAP, and the ranked order of concentrations of residues was: 0.03, 0.05 (2), 0.06, 0.30 and 0.68 mg/kg. The Meeting estimated a maximum residue level of 1 mg/kg, an STMR value of 0.055 mg/kg and a highest residue of 0.68 mg/kg for beans (succulent) or common bean.

Supervised trials were conducted on soya bean (immature seeds) in the USA (GAP: soluble concentrate, water-soluble powder; 1.0 kg ai/ha, 1.1 kg ai/hl; 10 applications; PHI, 1 day). None of the trials was conducted at GAP. The Meeting agreed to withdraw the recommendation for soya bean (immature seed) (0.1 mg/kg).

Supervised trials were conducted on peas (pods and succulent) in the USA (GAP: soluble concentrate, water-soluble powder; 1.0 kg ai/ha, 1.1 kg ai/hl; 10 applications; PHI, 1 day for single use at < 0.56 kg ai/ha and 3 days for single use at > 0.56 kg ai/ha). Eight trials were at GAP, and the ranked order of concentrations of residues was: 0.12, 0.18, 0.19, 0.33, 0.60, 0.83, 1.4 and 4.0. The Meeting estimated a maximum residue level of 5 mg/kg, an STMR value of 0.46 mg/kg and a highest residue of 4.0 mg/kg for peas (pods and succulent). The Meeting agreed to maintain the current recommendation of 5 mg/kg.

Supervised trials were conducted in the USA on beans (dry) (GAP: soluble concentrate, water-soluble powder; 1.0 kg ai/ha, 1.1 kg ai/hl; 10 applications; PHI, 14 days). In the 17 trials at GAP, the ranked order of concentrations of residues was: < 0.02 (15), 0.02 and 0.023 mg/kg. The Meeting

estimated an maximum residue level of 0.05 mg/kg, an STMR value of 0.02 mg/kg and a highest residue of 0.023 mg/kg. The Meeting agreed to withdraw the previous recommendation (0.1 mg/kg) and to replaced it with the recommendation for beans (dry) (0.05 mg/kg).

Root and tuber vegetables

Supervised trials were conducted on potato in the USA (GAP: soluble concentrate, water-soluble powder; 1.0 kg ai/ha; 10 applications; PHI, 6 days). In the nine trials at GAP, the ranked order of concentrations of residues was < 0.02 (9). Supervised field trials were also conducted with thiodicarb; the ranked order of concentrations of residues after foliar application was < 0.007 (2) and < 0.008 (2) mg/kg; and that after granular bait application was < 0.04 mg/kg (11). In all trials, neither thiodicarb nor methomyl was found at the LOQ (0.02 or 0.04 mg/kg). The Meeting therefore estimated a maximum residue level of 0.02(*) mg/kg, an STMR value of 0.00 mg/kg and a highest residue of 0.00 mg/kg. The Meeting agreed to withdraw the previous recommendation of 0.1 mg/kg and to replace it by the recommendation for potato (0.02(*) mg/kg).

Stalk and stem vegetables

Supervised field trials on asparagus were conducted in the USA (GAP: water-soluble powder, soluble concentrate; 1.0 kg ai/ha, 1.1 kg ai/hl; eight applications; PHI, 1 day). In the eight trials at GAP, the rank order of concentrations of residues was: 0.12, 0.14, 0.15, 0.26, 0.40, 0.48, 0.59 and 1.1 mg/kg. The Meeting estimated a maximum residue level of 2 mg/kg, an STMR value of 0.33 mg/kg and a highest residue of 1.1 mg/kg. The Meeting agreed to maintain the current recommendation of 2 mg/kg for asparagus.

Supervised field trials on celery were conducted in the USA (GAP: soluble concentrate, water-soluble powder; 1.0 kg ai/ha, 1.1 kg ai/hl; 10 applications; PHI, 7 days). In the eight trials at GAP, the ranked order of concentrations of residues in untrimmed celery was: < 0.02 (2), 0.09, 0.59, 0.72, 1.8 and 2.0 (2) mg/kg. The Meeting estimated a maximum residue level of 3 mg/kg, an STMR value of 0.66 mg/kg and a highest residue of 2 mg/kg. The Meeting agreed to withdraw the previous recommendation for celery (2 mg/kg) and to replace it by the recommendation for celery (3 mg/kg).

Cereal grains

Supervised field trials were conducted on barley in the USA (GAP: soluble concentrate, water-soluble powder; 0.5 kg ai/ha, 5.4 (soluble concentrate) or 6.0 (water-soluble powder) kg ai/hl; four applications; PHI, 7 days). In the three trials at GAP, the ranked order of concentrations of residues on grain was: 0.12, 0.72 and 1.3 mg/kg (see below).

Supervised field trials were conducted on wheat in the USA (GAP: soluble concentrate, water-soluble powder; 0.5 kg ai/ha, 5.4 kg ai/hl; four applications; PHI, 7 days). In the 15 trials at GAP, the ranked order of concentrations of residues was: < 0.02 (4), 0.02 (2), 0.06, 0.12, 0.14, 0.17 (3), 0.40, 0.69 and 1.1 mg/kg. Supervised field trials were also conducted with application of thiodicarb to barley and wheat, but the GAP was for granular bait use. The concentrations of residues ranged from < 0.02 to 0.06 mg/kg. Foliar application of methomyl was considered the critical use. The Meeting concluded that data on methomyl residues in barley and wheat resulting from identical foliar use were mutually supportive and pooled the data, with the ranked order: < 0.02 (4), 0.02 (2), 0.06, 0.12 (2), 0.14, 0.17 (3), 0.40, 0.69, 0.72, 1.1 and 1.3 mg/kg. The Meeting estimated a maximum residue level of 2 mg/kg, an STMR value of 0.14 mg/kg and a highest residue of 1.3 mg/kg for wheat grain and for barley grain. The Meeting agreed to withdraw the previous recommendations for wheat grain (0.5 mg/kg) and barley grain (0.5 mg/kg) and to replace them with the recommendations for wheat grain (2 mg/kg) and barley grain (2 mg/kg).

Supervised field trials were conducted on oats in the USA (GAP: soluble concentrate, water-soluble powder; 0.5 kg ai/ha, 5.4 kg ai/hl; four applications; PHI, 7 days). In the six trials at GAP, the ranked order of concentrations of residues was < 0.02 (6). The Meeting estimated a maximum residue level of 0.02(*) mg/kg, an STMR value of 0.02 mg/kg and a highest residue of 0.02 mg/kg for oat grain. The Meeting agreed to withdraw the previous recommendation for oat grain (0.5 mg/kg) and to replace it with the recommendation for oat grain (0.02(*) mg/kg).

Field trials on grain sorghum were conducted in the USA (GAP: water-soluble powder, soluble concentrate; 0.5 kg ai/ha, 0,53 kg ai/hl terrestrial, 2.6 kg ai/hl aerial; two applications; PHI, 14 days). In the five trials at GAP, the ranked order of concentrations of residues was: < 0.02 (2), 0.03, 0.07 and 0.1 mg/kg. The Meeting decided that five trials was insufficient to permit estimation of a maximum residue level or an STMR value and agreed to withdraw the recommendation for sorghum (0.2 mg/kg).

Supervised trials were conducted on maize in the USA (GAP: 0.5 kg ai/ha, 1.1 kg ai/hl; 10 applications; PHI, 21 days for ears). In the six trials at GAP, the ranked order of concentrations of residues was < 0.02 (6). The results for sweet corn support the finding of a maximum residue level of 0.05 mg/kg for maize with no PHI. Supervised field trials were also conducted with thiodicarb; all six trials yielded a residue concentration of < 0.1 mg/kg. Estimations were made on the basis of the data for methomyl, at the lower LOQ. The Meeting estimated an STMR value of 0.02 mg/kg and a maximum residue level of 0.02(*) mg/kg for maize grain to replace the previous recommendation (0.05(*) mg/kg).

Oilseed

Supervised trials of cotton seed were conducted in the USA (soluble concentrate, water-soluble powder; 0.5 kg ai/ha east of the Rocky Mountains, 0.67 kg ai/ha in Texas, 0.76 kg ai/ha west of the Rocky Mountains; 8 kg ai/hl (soluble concentrate), 15 kg ai/hl (water-soluble powder); PHI, 15 days for seed). Supervised trials were also conducted in Greece (soluble concentrate; 0.7 kg ai/ha; one to three applications; PHI, 20 days) and Spain (soluble concentrate; 0.4 kg ai/ha, 0.05 kg ai/hl; two to three applications,; PHI, 7 days). One trial from Spain (with a residue concentration of 0.02 mg/kg), one trial from Greece (< 0.02 mg/kg)and six from the USA were conducted at GAP. The ranked order of concentrations of residues was: ≤ 0.02 (5), 0.02 and 0.1 (2) mg/kg. In supervised field trials conducted with thiodicarb, the ranked order of concentrations of residues was: ≤ 0.04 mg/kg (12), < 0.05, 0.05, 0.09 and 0.10 (3) mg/kg. The Meeting considered that the data sets represented the same populations and combined them, with a ranked order of: < 0.02 (5), 0.02, < 0.04 (12), < 0.05, 0.05, 0.09 and 0.1 (5) mg/kg. The Meeting estimated an STMR value of 0.04 mg/kg, a highest residue of 0.1 mg/kg and a maximum residue level of 0.2 mg/kg for cotton seed to replace the previous recommendation (0.5 mg/kg).

Trials on peanut were conducted in the USA (soluble concentrate, water-soluble powder; 1.0 kg ai/ha, 1.1 kg ai/hl; eight applications; PHI, 21 days). The two trials at GAP gave a concentration of < 0.02 (2) mg/kg. The Meeting concluded that two trials were insufficient to estimate a maximum residue level or STMR value and agreed to withdraw the recommendation for peanut (0.1 mg/kg).

Legume animal feeds

Supervised trials were conducted on alfalfa forage (green) in the USA (water-soluble powder, soluble concentrate; 1.0 kg ai/ha, 1.1 kg ai/hl; 10 applications; PHI, 7 days). In the 41 trials at GAP, the ranked order of concentrations of residues in forage was: 0.044, 0.081, 0.10 (2), 0.11, 0.15, 0.25, 0.43, 0.56, 0.57, 0.64, 0.70, 0.98, 1.1, 1.3, 1.5 (2), 1.6, 1.7, 1.8 (2), 1.9, 2.0, 2.1, 2.3 (2), 2.5 (2), 2.6, 3.4, 3.5, 3.6, 3.8, 4.0 (2), 4.2 (2), 4.6, 6.3 and 7.0 (2) mg/kg. Using the default value for dry matter for alfalfa forage (35%), the Meeting estimated an STMR value of 5.1 mg/kg for alfalfa forage and a maximum residue level of 25 mg/kg for alfalfa forage (green) on a dry weight basis. The current MRL is 10 mg/kg for alfalfa forage (green) on a fresh weight basis. The Meeting agreed to withdraw the previous recommendation and to replace it with the recommendation for alfalfa forage (green) (25 mg/kg).

For alfalfa hay, 41 trials were at GAP; the ranked order of concentrations of residues was: 0.12, 0.24, 0.25, 0.26, 0.28 (2), 0.32, 0.41, 0.46, 0.92, 1.1 (3), 1.4, 1.5 (2), 1.8, 1.9, 2.2, 2.4, 2.7, 2.9, 3.3, 3.4 (2), 3.5, 3.7, 3.8, 4.0 (2), 4.6, 5.5, 5.6 (2), 6.2, 7.5, 7.9, 10,14, 15 and 17 mg/kg. The Meeting estimated a maximum residue level of 20 mg/kg, an STMR value of 3.0 mg/kg and a highest residue of 19 mg/kg for alfalfa hay on a dry weight basis from the default value for dry matter value of 89%.

Supervised trials on bean, pea and soya bean forage were conducted in the USA, where the GAP for bean (succulent) is use of the water-soluble powder or soluble concentrate formulation at 1.0 kg ai/ha, 1.1 kg ai/hl, and a maximum of 10 applications. The PHI is 3 days for vines, 7 days for bean hay, 5 days for forage and 14 days for pea hay. One trial on succulent bean forage was at GAP, resulting in a concentration of 4.3 mg/kg. In four trials on pea vines at GAP, the ranked order of concentrations of residues was: 0.34, 1.3, 6.5 and 7.6 mg/kg. In three trials on soya bean (immature) forage at GAP, the concentrations were: 0.08 (2) and 8 mg/kg. The Meeting determined that the values for forage commodities represented the same population and could be combined to yield, in ranked order, concentrations of: 0.08 (2), 0.34, 1.3, 4.3, 6.5, 7.6 and 8 mg/kg. The default value for dry matter of 25% was used. The Meeting estimated a maximum residue level of 40 mg/kg, an STMR value of 11 and a highest residue of 32 mg/kg for pea vines and for soya bean forage. The Meeting agreed to withdraw the recommendations for pea vines (10 mg/kg fresh weight) and soya bean forage (green) and to replace them with the recommendations for pea vines (green) (40 mg/kg) and soya bean forage (green) (40 mg/kg).

Supervised trials were conducted in the USA on beans (dry) (GAP: soluble concentrate, water-soluble powder; 1.0 kg ai/ha, 1.1 kg ai/hl; 10 applications; PHI, 14 days). None of the trials for residues in forage was at GAP. In five trials for hay at GAP, the ranked order of concentrations of residues was: < 0.5 (2), 1.1, 3 and 9 mg/kg. The Meeting estimated a maximum residue level of 10 mg/kg, an STMR value of 1.1 mg/kg and a highest residue of 9 mg/kg for bean hay.

Supervised trials were conducted in the USA for soya bean hay (GAP: soluble concentrate, water-soluble powder; 0.5 kg ai/ha; three applications; PHI, 7 days at < 0.5 kg ai/ha, 12 days at > 0.5 kg ai/ha). In eight trials at GAP, the ranked order of concentrations of residues was: 0.021, 0.033, 0.040, 0.050, 0.056, 0.076, 0.099 and 0.13 mg/kg. The Meeting estimated a maximum residue level of 0.2 mg/kg, an STMR value of 0.060 mg/kg and a highest residue of 0.15 mg/kg for soya bean hay, using the default value for dry matter value of 85%.

Fodder and straw of cereal grains

Supervised field trials on barley were conducted in the USA (GAP: soluble concentrate, water-soluble powder; 0.5 kg ai/ha, 5.4 kg ai/hla (soluble concentrate), 6.0 kg ai/hl (water-soluble powder); four applications; PHI, 7 days). In two trials at GAP, the concentrations of residues in straw were 2.8 and 3.1 mg/kg. Trials were conducted with thiodicarb used as a granular bait, but the concentrations were lower (< 0.04 (6), < 0.2 (2) and 0.24 mg/kg). The values for thiodicarb and methomyl thus appear to represent different populations.

Supervised field trials on wheat were conducted in the USA (GAP: soluble concentrate, water-soluble powder; 0.5 kg ai/ha, 5.4 kg ai/hl; four applications; PHI, 7 days). In the 11 trials for wheat straw conducted at GAP, the ranked order of concentrations of residues was: < 0.02, 0.39, 0.43, 0.69, 2.0 (2), 2.8, 3.7, 4.6, 5.7 and 6.5 mg/kg. In trials conducted with thiodicarb as a granular bait, the concentrations of residues were < 0.02 mg/kg, a different population.

Supervised field trials on oats were conducted in the USA (GAP: soluble concentrate, water-soluble powder; 0.5 kg ai/ha, 5.4 kg ai/hl; four applications; PHI, 7 days). No trials on straw were conducted at GAP.

Supervised field trials were conducted in the USA for sorghum stover (GAP: water-soluble powder, soluble concentrate; 0.5 kg ai/ha, 0.53 kg ai/hl terrestrial, 2.6 kg ai/hl aerial; two applications; PHI, 14 days). In eight trials at GAP, the ranked order of concentrations of residues was: 0.38, 0.50, 0.59, 0.81, 0.93, 1.0, 2.5 and 3.4 mg/kg.

Supervised trials were conducted in the USA for maize fodder (GAP: 0.5 kg ai/ha, 1.1 kg ai/hl; 10 applications; PHI, 3 days for forage, 21 days for fodder). In six trials at GAP for fodder, the ranked order of concentrations of residues was: 0.029, 0.053, 0.094 (2), 0.30, and 0.71 mg/kg.

Supervised field trials were conducted in Japan with thiodicarb on rice straw (GAP: 1.2 kg ai/ha; PHI, 30 days). In four trials at GAP, the ranked order of concentrations of residues was: < 0.5, 0.62, and ≤ 1 (2) mg/kg.

Supervised field trials were conducted in the USA on grain sorghum (GAP: water-soluble powder, soluble concentrate; 0.5 kg ai/ha, 0.53 kg ai/hl terrestrial, 2.6 kg ai/hl aerial; two applications; PHI, 14 days). In nine trials for sorghum hay at GAP, the ranked order of concentrations of residues was: < 0.02 (3), 0.033, 0.035 (2), 0.039, 0.096 and 0.59 mg/kg

The Meeting considered that the values for residues in cereal grain commodities (fodder, stover, straw) represented the same population (except for use of thiodicarb as granular bait on wheat and barley) and combined the values, which, in ranked order, were: < 0.02 (4), 0.029, 0.033, 0.035 (2), 0.039, 0.053, 0.094 (2), 0.096, 0.30, 0.38, 0.39, 0.43, < 0.5, 0.50, 0.59 (2), 0.62, 0.69, 0.71, 0.81, 0.93, < 1 (2), 1.0, 2.0 (2), 2.5, 2.8 (2), 3.1, 3.4, 3.7, 4.6, 5.7 and 6.5 mg/kg. Using a default value for dry matter of 88%, the Meeting estimated a maximum residue level of 10 mg/kg, an STMR value of 0.67 mg/kg and a highest residue of 7.4 mg/kg for cereal grain fodder and straw. The Meeting agreed to withdraw the recommendations for barley straw and fodder, dry (5 mg/kg), maize fodder (50 g/kg fresh weight), and oats straw and fodder, dry (5 mg/kg), and to replace them with the recommendation for cereal grain, straw, fodder (dry), hay (10 mg/kg).

Supervised field trials were conducted on sorghum forage (green) in the USA (GAP: water-soluble powder, soluble concentrate; 0.5 kg ai/ha, 0.53 kg ai/hl terrestrial, 2.6 kg ai/hl aerial; two applications; PHI, 14 days). In nine forage trials at GAP, the ranked order of concentrations of residues was: < 0.02 (3), 0.024, 0.042, 0.046, 0.068, 0.19 and 0.22 mg/kg. Using the default value for dry matter of 35%, the Meeting estimated a maximum residue level of 1 mg/kg, an STMR value of 0.12 mg/kg and a highest residue of 0.63. The Meeting agreed to maintain the current recommendation for sorghum forage (green) (1 mg/kg).

Supervised trials were conducted on sweet corn forage in the USA (GAP: soluble concentrate, 0.5 kg ai/ha, 5.4 kg ai/hl; 28 applications; no PHI for maize or fodder, 3 days for forage). In eight trials for forage at GAP, the ranked order of concentrations of residues was: 2.3, 2.5, 2.7, 2.9, 3.2, 3.3 (2) and 4.8. Supervised field trials were also conducted with thiodicarb; the ranked order of concentrations of residues in forage was: < 0.02, < 0.05, 0.06, 0.16, 0.21, 0.56, 1.1, 2.3, 5.2, 6.9, 11 and 18 mg/kg. The Meeting considered that the two sets of values represented the same population and combined them. They were, in ranked order: < 0.02, < 0.05, 0.06, 0.16, 0.21, 0.56, 1.1, 2.3 (2), 2.5, 2.7, 2.9, 3.2, 3.3 (2), 4.8, 5.2, 6.9, 11 and 18 mg/kg.

Supervised trials were also conducted in the USA on maize forage (GAP: 0.5 kg ai/ha, 1.1 kg ai/; 10 applications; PHI, 3 days for forage, 21 days for fodder). In six trials at GAP for forage, the ranked order of values was: 0.72, 1.0, 1.3, 1.8, 6.6 and 6.9 mg/kg.

The Meeting considered that the data for maize forage were part of the set for sweet corn forage and combined them. The ranked order of concentrations of residues was: < 0.02, < 0.05, 0.06, 0.16, 0.21, 0.56, 0.72, 1.0, 1.1, 1.3, 1.8, 2.3 (2), 2.5, 2.7, 2.9, 3.2, 3.3 (2), 4.8, 5.2, 6.6, 6.9 (2), 11 and 18 mg/kg.

Using the default value for dry matter value of 40%, the Meeting estimated a maximum residue level of 50 mg/kg, an STMR value of 6.0 mg/kg and a highest residue of 45 mg/kg for maize forage on a dry weight basis. The Meeting agreed to withdraw the recommendation for maize forage (50 mg/kg, fresh weight) and to replace it with the recommendation for maize forage (50 mg/kg).

Supervised field trials were conducted on wheat forage in the USA (GAP: soluble concentrate, water-soluble powder; 0.5 kg ai/ha, 5.4 kg ai/hl; four applications; PHI, 7 days). In 17 trials at GAP for forage, the ranked order of concentrations of residues was: 0.02, 0.05, 0.06, 0.12 (2), 0.24, 0.26, 0.37, 0.38, 0.53, 0.57, 0.59, 0.85, 2.7, 3.1 and 4.9 (2)mg/kg. Using the default value for dry matter of 25%, the Meeting estimated an STMR value of 0.38 mg/kg and a highest residue of 20 mg/kg. The Meeting did not estimate a maximum residue limit, as wheat forage is not a recognized commodity.

Unsupported uses

No supervised trials were reported for hops, dry, mint hay, onion, Welsh, peanut forage (green) or pineapple. The Meeting agreed to withdraw the previous recommendations for hops, dry (10 mg/kg), mint hay (2 mg/kg), onion, Welsh (0.5 mg/kg), peanut forage (5 mg/kg) and pineapple (0.2 mg/kg).

Fate of residues during processing

Fifteen studies were reported on processing of 13 raw agricultural commodities. In all the studies, the commodities contained field-incurred residues of methomyl, typically after application rates in excess of GAP. The studies simulated commercial practices, except where consumer practices were indicated. Methomyl occurred in only three matrices: dried orange peel, apple peel and wheat bran, supporting the observation that methomyl has little tendency to translocate. Furthermore, methomyl did not concentrate in oily fractions. Similarly, thiodicarb concentrated in soya bean hulls and sweet corn cannery waste.

The maximum residue levels, STMR values and highest residues given above were multiplied by the relevant processing factor to obtain the maximum residue level (where appropriate), the STMR-P value and the HR-P value for processed commodities of raw agricultural commodities. The results of similar studies with thiodicarb are also included, as appropriate (see the report item on thiodicarb). The calculations are summarized below.

Commodity (mg/kg)	STMR (mg/kg)	HR (mg/kg)	MRL (mg/kg)	Processed commodity	Processing factor	STMR-P (mg/kg)	HR-P (mg/kg)	MRL (mg/kg)
Apple	0.41	1.6	2	Apple juice	0.29[a]	0.12	0.46	
				Apple pomace, wet	0.30[b]	0.12	0.48	
Citrus (orange)	0.17	0.89	1	Citrus juice	0.021	0.004	0.019	
				Citrus pulp, dry	2.9	0.49	2.6	3
Cotton seed	0.04	0.1	0.2	Cotton seed, edible oil	0.16[c]	0.006	0.016	0.04
				Cotton seed, hulls	0.96[d]	0.038	0.096	0.2
				Cotton seed, meal	0.32[e]	0.013	0.032	0.05
Grape	0.86	5.2	6	Wine	0.3[b]	0.26	1.6	
Maize	0.02	0.02	0.02 (*)	Maize, edible oil	0.18	0.004	0.004	0.02 (*)
Soya bean	0.04	0.15	0.2	Soya bean, hulls	3.6[b]	0.14	0.54	1

				Soya bean, meal	1	0.04	0.15	0.2
				Soya bean, oil crude	1	0.04	0.15	0.2
				Soya bean, oil refined	1	0.04	0.15	0.2
Sweet corn	0.065	1.5	2	Cannery waste	78[b]	5.1	120	
Tomato	0.16	0.73	1	Tomato paste	0.04[f]	0.006	0.030	
Wheat grain	0.14	1.3	2	Wheat flour	0.02	0.003	0.026	0.03
				Wheat bran	1.9	0.27	2.5	3
				Wheat germ	0.92	0.13	1.2	2

[a]Thiodicarb factor (0.014 for canned juice) and methomyl factor (0.29 for fresh juice)
[b]Thiodicarb processing study
[c]Average of thiodicarb factor (0.2) and methomyl factor (< 0.12)
[d]Average of thiodicarb factor (1.1) and methomyl factor (0.82)
[e]Average of thiodicarb factor (0.26) and methomyl factor (0.38) [f]Average of thiodicarb factor (0.03) and methomyl factor (0.053)

A study of the results of peeling in a manner similar to that of consumers was conducted with unwashed oranges. The residue reduction factor was 0.2, and this factor was applied to the results of the field trial with citrus (see above).

Residues in animal commodities

Two feeding studies were conducted with lactating dairy cattle, one of which involved radiolabelled methomyl.

Lactating Holstein dairy cows were fed diets containing methomyl for 28 consecutive days at concentrations corresponding to 0, 8.1, 34, or 86 ppm. Milk was collected daily, and tissues were harvested immediately after the last day of treatment. The samples were stored at –70 °C to preclude degradation of methomyl. The compound was not found at the LOQ (0.01 mg/kg) in any tissue or milk sample from cows at any feeding level. The apparent concentrations were similar to those in control samples, < 0.002 – < 0.005 mg/mg, for all samples.

A mixture of methomyl and [^{14}C]methomyl was given orally for 28 consecutive days to lactating dairy cows at a rate of 0, 2, 24 or 80 ppm, as ascertained from actual feed consumption. Milk and tissue samples were stored at –20 °C for up to 2 months before analysis. Studies of stability in storage showed that methomyl was stable in milk and muscle, variably stable in fat (up to 50% loss) and unstable in kidney and liver (> 90% loss over 24 months). Methomyl and methomyl oxime were not found at the LOQ of 0.02 mg/kg in whole milk, cream or skim milk from cows at 24 or 80 ppm. Methomyl was detected in only one sample, a sample of cream from a control animal, at about 0.02 mg/kg. Likewise, neither methomyl nor methomyl oxime was found in tissue samples. However, the storage conditions would have led to degradation of residues in fat, liver and kidney.

Acetonitrile and acetamide were determined in the milk and tissue samples. The maximum concentration of acetonitrile was 0.08 mg/kg in whole milk, while the concentrations in tissues were 0.08 mg/kg in liver, 0.04 mg/kg in kidney, 0.04 mg/kg in muscle and < 0.01–0.01 mg/kg in fat. Studies of stability in storage indicated that as much as 50% of the acetonitrile may have been lost during storage. The concentrations of acetamide in samples of whole milk from cows at 80 ppm contained 2.8–6.6 mg/kg, whereas the concentrations in tissues were 14 mg/kg in liver, 9 mg/kg in kidney, 9 mg/kg in muscle and 5 mg/kg ins subcutaneous fat. Acetamide is endogenous. Determinations of [^{14}C]acetamide showed concentrations attributable to methomyl of < 0.003–0.07 mg/kg in milk, 0.03 mg/kg in muscle and 0.05 mg/kg in liver.

The Meeting concluded that methomyl and methomyl oxime do not bioaccumulate. No residues were detectable in milk or tissues at the concentrations in feed that were studied.

The Meeting estimated the dietary burden of dairy and beef cattle (and poultry) from the diets listed in Appendix IX of the *FAO Manual*. Calculation from maximum residue levels yields the maximum theoretical dietary intake or the level of residues in feed suitable for estimating MRLs for animal commodities. Calculation from STMR values for feed yields estimated STMR values for animal commodities. The diets described are designed to maximize dietary exposure to thiodicarb, and nutritional requirements, are not taken into account. The maximum residue levels for processed commodities were derived from the maximum or highest residue values estimated above for raw agricultural commodities, multiplied by the appropriate concentration or reduction factor from the processing studies. An exception is processed commodities that are considered to be blended, such as sweet corn cannery waste. For these, the STMR value of the raw agricultural commodity is multiplied by the processing factor to obtain the maximum residue level in the processed feed commodity.

Calculation of maximum theoretical dietary burden for animals

Commodity	Maximum or highest residue level (mg/kg)	STMR or STMR-P (mg/kg)	Group	Dry matter (%)	Per cent of diet				Residue contribution (mg/kg)			
					Beef cattle	Dairy cows	Poul-try	Pig	Beef cattle	Dairy cows	Poul-try	Pig
Alfalfa forage	25	0.12	AL	–	70	60	–	–				
Alfalfa hay	20		AL	–	70	60	–	–				
Apple pomace, wet			AB	40	40	20						
Barley grain	2	0.49	GC	88	50	40	75	80				
Cereal grain fodder	10		AS	–	10	10						
Citrus dry pulp		0.013	AB	91	20	20	–	–				
Cotton seed	0.2	0.038	SO	88	25	25	–	–				
Cotton seed meal			SO	89	15	15	20	15				
Cotton seed hulls				90	20	15	–	–				
Maize grain	0.02		GC	88	80	40	80	80				
Maize forage	50		AF	–	40	50	–	–	20	25		
Pea vine	40		AL	–	25	50						
Rape seed forage	0.2	0.04	SO	–	30	30						
Sorghum forage (green)	1	0.14	AF	–	40	50	–	–				
Soya bean meal			VD	92	15	15	40	25				
Soya bean hulls				90	20	20	20				0.03	
Soya bean hay	0.2	0.27	AL	–	30	30	–	–				
Sweet corn cannery waste	5.1			30	35	20	–	–	6.0	3.4		
Wheat bran			CF		59	40						
Wheat grain	2		GC	89	~~50~~ 25	~~40~~ 30	80	80	0.56	0.67	1.8	
Wheat forage	20			–	25	60	–	–				
Wheat straw	10		AS	88	10	10	–	–				
Total					100	100	100		27	29	2.0	

The average daily dietary burden of methomyl for ruminants is a fraction of the maximum daily burden, about 28 mg/kg. The maximum daily burden is expected to yield no quantifiable residues of methomyl in meat, meat by-products or milk, in view of the absence of residues in cows fed at 86 ppm and the absence of methomyl in the study of the nature of the residue in ruminants. Thus, the STMR values for milk, meat and meat by-products are estimated to be 0.000 mg/kg. The highest residue values for meat, edible offal and milk are also estimated to be 0.000 mg/kg; as there is no reasonable expectation that residues will occur. The maximum residue levels for meat, edible offal and milk are estimated to be 0.02(*) mg/kg, the typical LOD. The Meeting agreed to maintain the current recommendations of 0.02(*) mg/kg for milk and for meat (from mammals other than marine mammals).

No study of poultry feeding was provided, but the study of the nature of the residue in poultry, conducted at a concentration equivalent to 45 ppm in feed, showed no methomyl or methomyl oxime in tissues or eggs at a LOD of 0.015 mg/kg. As the study lasted only 3 days, the concentrations of residues may not have reached a plateau in eggs or tissues. A 21-day study with thiodicarb fed at 102 ppm also showed no accumulation of methomyl or thiodicarb. Thus, at a projected dietary intake of 2 mg/kg, no methomyl is anticipated to occur in the tissues or eggs.

The Meeting estimated a maximum residue level of 0.02(*) mg/kg for thiodicarb plus methomyl in eggs, in poultry meat and in edible offal of poultry. The Meeting also estimated highest residues and STMR values for these commodities, each at 0.00 mg/kg.

Dietary risk assessment

Long-term intake

STMR or STMR-P values were estimated by the present Meeting for 39 commodities. When data on consumption were available, these values were used in the estimates of dietary intake.

The dietary intakes in the five GEMS/Food regional diets, on the basis of the new STMR values, represented 1–20% of the ADI (Annex 3). The Meeting concluded that the intake of residues of thiodicarb and methomyl resulting from the uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The IESTI for thiodicarb plus methomyl was calculated for the commodities for which maximum residue levels, STMR values and highest residues were established and for which data on consumption (of large portions and unit weight) were available. The results are shown in Annex 4.

The acute RfD for methomyl is 0.02 mg/kg bw. The IESTI represented 0–7200% of the acute RfD for children and 0–2800 % of the acute RfD for the general population. For children, the 100% of acute RfD was exceeded in: apples (770%), broccoli (1500%), Brussels sprouts (450%), head cabbage (1200%), cauliflower (1700%), celery (310%), watermelon (140%), grapes (1600%), kale (1100%), head lettuce (3000%), leaf lettuce (3800%), spinach (7200%), sweet corn (420%) and tomato (190%). For the general population, the acute RfD was exceeded in: apples (260%), broccoli (810%), Brussels sprouts (200%), head cabbage (320%), cauliflower (590%), grapes (470%), kale (670%), head lettuce (2000%), leaf lettuce (1500%), spinach (2800%) and sweet corn (140%).

The information provided to the Meeting precluded an estimate that the acute dietary intake of methomyl plus thiodicarb from the consumption of apples, broccoli, Brussels sprouts, head cabbage, cauliflower, celery (children only), watermelon (children only), grapes, kale, head lettuce, leaf lettuce, spinach, sweet corn and tomato (children only) would be below the acute RfD. The Meeting concluded that the short-term intake of residues of methomyl plus thiodicarb from uses other than on the 14 commodities that have been considered by the JMPR is unlikely to present a public health concern.

4.19 METHOPRENE (147) AND *S*-METHOPRENE

Toxicology

Methoprene is the common name for isopropyl-(2*E*,4*E*,7*R*,*S*)-11-methoxy-3,7,11-trimethyl dodeca-2,4-dienoate. It is a racemic mixture of two enantiomers (R and S in a ratio of 1:1). The activity of the compound as a juvenile hormone is restricted to the S-enantiomer. The identity of the compound was given by the 1984 JMPR in its evaluation of residues, and the purity of methoprene was stated to be 92–95%. Methoprene was first evaluated by the 1984 JMPR, when a temporary ADI of 0–0.06 mg/kg bw was established on the basis of a NOAEL of 25 mg/kg bw per day in rats and a NOAEL of 12.5 mg/kg bw per day in dogs, with safety factors of 400 and 200, respectively. The 1984 JMPR

asked for a 6-month study in dogs treated in the diet, adequate studies of developmental toxicity, and a two-generation (two litters per generation) study of reproductive toxicity in rats. No new information became available, but the 1987 JMPR, noting that the data on metabolism and kinetics indicated that the compound was completely metabolized, considered it unlikely that it would reach the conceptus and that long-term studies in dogs would not provide further information. On the basis of these considerations, the 1987 JMPR established an ADI of 0–0.1 mg/kg bw. The evaluations of the 1984 and 1987 JMPR were based on the racemic mixture.

Methoprene was considered by the present Meeting within the periodic review programme of the CCPR. The sponsor that submitted data informed the present Meeting that the methoprene formulations that it markets are based on the biologically active enantiomer *S*-methoprene. The Meeting was also informed that other companies continue to market the racemic mixture. The present Meeting reviewed the available database, consisting of the original studies with the racemate and new studies on the kinetics, acute toxicity after oral and dermal administration and inhalation, dermal and ocular irritation, dermal sensitization and mutagenicity with *S*-methoprene. Three decisions were taken with respect to the database on methoprene:

- In the reports of studies performed before 1984, it was not clear whether the racemate or *S*-methoprene had been tested. Therefore, studies performed before 1980 (the year in which the manufacturing procedure for *S*-methoprene was established) were considered to have been performed with the racemate.
- Since the older studies were performed with (technical-grade) racemic methoprene of varying purity (69-96%), the doses used in these studies were corrected accordingly.
- Studies performed by the Industrial BioTest Laboratory were submitted, but as they had not been validated in accordance with the policy outlined in section 3.1 of the report of the 1981 JMPR, these studies were not evaluated. These studies were also not included in the 1984 evaluation.

The absorption, distribution, excretion, and metabolism of racemic methoprene have been studied in mice, rats, guinea-pigs, cows, and chickens given single doses. No study of metabolism after repeated doses was available.

After administration of single oral doses of methoprene, the radiolabel was relatively rapidly absorbed and excreted in urine, faeces, and expired air. Further, about 8% of the radiolabel administered to a cow was excreted in milk 7 days after dosing, and up to 19% of radiolabel administered to chickens was excreted in eggs 14 days after dosing. In most species investigated, the bulk of the radiolabel was excreted within 5 days or less, and the remainder was incorporated into tissues.

Substantial enterohepatic circulation occurs in rats, and a small percentage of intact, unabsorbed methoprene was found in faeces, with none in urine or bile, after its administration. Methoprene is probably extensively metabolized in rats, as a large portion of the radiolabel was excreted with CO_2. After a single oral dose to rats, the peak plasma concentration, 1.6% of the administered radiolabel, was reached by 6 h; the level declined slowly, with a half-time of about 48 h. Whole-body autoradiography and tissue analysis showed that most of a single labelled dose was located in organs concerned with absorption, biotransformation, and excretion. A relatively high concentration of radiolabel was found in adrenal cortex, lachrymal glands, and adipose tissue after 48 h.

Studies in guinea-pigs, cattle, and chickens showed that racemic methoprene was extensively metabolized to polar conjugates (glucuronides), which were excreted in the urine and faeces, and that the C5-labelled molecule underwent rapid α and β oxidation to produce CO_2 and acetate, which was incorporated into natural products such as triglycerides, bile acids, and cholesterol found in tissues, milk, and eggs.

The pharmacokinetics of *S*-methoprene was investigated for 7–8 h in blood and fat of rats given a single oral or intravenous dose. The clearance of *S*-methoprene was relatively rapid after intravenous administration of 10 mg/kg bw. After oral administration of 10 or 1000 mg/kg bw, *S*-methoprene was rapidly absorbed, and the maximum concentration of parent compound in blood was reached 2 h after dosing. In fat, the concentration of unchanged methoprene reached a plateau 3–4 h after intravenous and 4-6 h after oral administration, and then very slowly declined. Because of this slow decline, methoprene may build up in fat after repeated dosing. Most of the radiolabel in fat was unchanged methoprene, whereas in blood methoprene had been degraded rapidly to other radiolabelled compounds.

The racemate and *S*-methoprene showed little acute toxicity. The LD_{50} values for *S*-methoprene were > 5000 mg/kg bw (oral, rat) and > 2000 mg/kg bw (dermal, rabbit), and those of the racemate were > 24 000 mg/kg bw (oral, rat) and > 3400 mg/kg bw (oral, dog). The LD_{50} for the racemate after intraperitoneal administration in rats was 3300 mg/kg bw. WHO has classified methoprene as 'unlikely to present acute hazard in normal use'. The racemate and *S*-methoprene were not irritating to the eye or skin of rabbits. In a limited test in guinea-pigs, the racemate appeared to have no sensitizing properties. In a study with a formulation containing 20% *S*-methoprene, skin sensitization was seen; however, it was unclear whether the effect was due to *S*-methoprene or to another compound in the formulation.

Several studies of the toxicity of repeated doses of racemic methoprene given by oral or dermal application or inhalation were available. The design and reporting of these studies did not meet current guidelines, and the studies of dermal application or inhalation were considered inadequate for evaluation. The studies by oral administration could be used to deduce the toxicological profile of methoprene, and, despite their shortcomings, most were considered suitable for use in risk assessment.

Studies in which mice (78 weeks), rats (14 or 90 days, 104 weeks), and dogs (14 or 90 days) were exposed to racemic methoprene in the diet showed that the compound has little toxic potential. Some effects were found on food intake and body weight, but the main effect was to increase the weight of the liver relative to body weight (in rats at doses (5000 ppm; in dogs at doses (1000 ppm). This effect was not always associated with histopathological changes. In the 90-day study in dogs treated in the diet, the NOAEL was 500 ppm, equivalent to 8.6 mg/kg bw per day. In the 2-year study in rats treated in the diet at 5000 ppm, the highest dose tested, increased absolute and relative liver weights and an increased incidence of hepatic lesions such as bile-duct proliferation and portal lymphocyte infiltration were observed in male rats. The NOAEL was 1000 ppm, equivalent to 44 mg/kg bw per day. Minor histopathological changes in the kidneys observed in the 90-day feeding study in rats were considered of no significance for human risk assessment. In the 78-week study of carcinogenicity in mice, hepatic lesions characterized by pigment deposition in the cytoplasm of parenchymal cells were seen at 1000 and 2500 ppm, with increased incidence and severity at the highest dose. Focal accumulations of macrophages with brownish foamy cytoplasm were found in survivors of each sex at 2500 ppm, and an increased frequency of amyloidosis of the intestine was seen in females at this dose. No adverse effects (the brownish pigment was considered not to be of toxicological relevance) were observed at 1000 ppm, equivalent to 130 mg/kg bw per day.

No increase in the incidence of tumours at any site was seen in either the 78-week study of carcinogenicity in mice or the 2-year study of toxicity and carcinogenicity in rats treated in the diet.

Racemic methoprene did not induce chromosomal aberrations in Chinese hamster ovary cells in vitro. No increase in the frequency of reverse mutations in *Salmonella typhimurium* was observed. The Meeting noted that only a limited range of concentrations were tested. No definitive conclusion can be drawn about the genotoxic potential of the racemate.

S-Methoprene did not induce reverse mutations in *S. typhimurium* or mitotic crossing-over, gene conversion, or reverse mutations in *Saccharomyces cerevisiae*. On the basis of the negative results in a limited range of studies for genotoxicity and the results of the studies of carcinogenicity with methoprene, the Meeting concluded that methoprene was unlikely to pose a carcinogenic risk to humans.

In a three-generation study of reproductive toxicity with racemic methoprene in rats, the total weight gain of animals of each sex in the F_0 and F_1 generations during the growth period was slightly decreased, the mean weight of pups in the F_2 and F_3 litters was reduced, and the mean number of pups in the F_3 litters born dead per litter was increased at a dose of 2500 ppm. The NOAEL was 500 ppm, equivalent to 29 mg/kg bw per day.

In a study of developmental toxicity in which mice were treated on days 7–14 of gestation with racemic methoprene, no toxicologically relevant effects were observed in dams or fetuses at any dose; the NOAEL was 570 mg/kg bw per day, the highest dose tested. In the same experiment, several dams were allowed to litter and rear their pups until weaning; the pups of five litters at each dose were killed at weaning, and the remaining litters were observed for 7 additional weeks. Effects on organ weights were observed in pups at the highest dose. The NOAEL for toxicity to offspring was 190 mg/kg bw per day. In a study of developmental toxicity in which rabbits were treated on days 7–18 of gestation with racemic methoprene, the NOAEL for maternal, embryo-, and fetotoxicity was 190 mg/kg bw per day, on the basis of reduced weight gain and an increased frequency of abortions among the does and an increased percentage of fetal deaths at 1900 mg/kg bw per day, the highest dose tested. The shortcoming of the study - mice and rabbits were treated for 2 and 1 day less than that required in the relevant test guideline - was not considered critical for evaluating end-points of developmental toxicity. All the developmental effects were seen at very high doses or only postnatally. Therefore, the Meeting considered that additional studies were not necessary and concluded that methoprene is not teratogenic.

Several plant metabolites of methoprene showed little acute toxicity when administered orally.

Racemic methoprene

The Meeting reaffirmed the basis of the ADI for racemic methoprene established in 1987, but lowered the value to 0–0.09 mg/kg bw to correct for the purity of the racemate tested. The basis for the ADI was the NOAEL of 500 ppm, equivalent to 8.6 mg/kg bw per day (corrected for purity), in the 90-day study in dogs and a safety factor of 100.

The LD_{50} for racemic methoprene given orally was > 2000 mg/kg bw, and no toxic signs were seen at this dose. In studies with repeated oral doses (including studies of teratogenicity), racemic methoprene did not induce signs indicative of acute toxicity. The Meeting concluded that allocation of an acute reference dose was unnecessary.

S-*Methoprene*

No bridging studies with repeated doses were available for *S*-methoprene. The Meeting therefore made the conservative assumption that, in the absence of any information to the contrary, all the toxicity of the racemate was due to the *S*-enantiomer. On this basis, the Meeting established an ADI for *S*-methoprene of 0-0.05 mg/kg bw, equal to one-half the ADI for the racemate (which is a 1:1 mixture of the R and S enantiomers).

A toxicological monograph was prepared.

Levels relevant to risk assessment of racemic methoprene
Levels relevant to risk assessment of racemic methoprene
Levels relevant to risk assessment of racemic methoprene
Levels relevant to risk assessment of racemic methoprene
Levels relevant to risk assessment of racemic methoprene
Levels relevant to risk assessment of racemic methoprene

Species	Study	Effect	NOAEL[a]	LOAEL[A]
Mouse	Developmental toxicity (expanded)	Maternal toxicity	570 mg/kg bw per day[b]	
		Embryo- and fetotoxicity	570 mg/kg bw per day[b]	---
		Offspring toxicity	190 mg/kg bw per day	570 mg/kg bw per day
Rat	Long-term toxicity and carcinogenicity	Toxicity	1000 ppm, equivalent to 44 mg/kg bw per day	5000 ppm, equivalent to 220 mg/kg bw per day
	Reproductive toxicity	Parental and offspring toxicity	500 ppm, equivalent to 29 mg/kg bw per day	2500 ppm, equivalent to 140 mg/kg bw per day
Rabbit	Developmental toxicity	Maternal toxicity	190 mg/kg bw per day	1900 mg/kg bw per day
		Embryo- and fetotoxicity	190 mg/kg bw per day	1900 mg/kg bw per day
Dog	90-day study of toxicity		500 ppm, equivalent to 8.6 mg/kg bw per day	5000 ppm, equivalent to 86 mg/kg bw per day

[a] Dose of racemic methoprene corrected for purity when expressed as mg/kg bw per day
[b] Highest dose tested

Estimate of acceptable daily intake for humans

0–0.09 mg/kg bw (racemic methoprene)
0–0.05 mg/kg bw (*S*-methoprene)

Estimate of acute reference dose

Unnecessary (racemic methoprene and *S*-methoprene)

Studies that would provide information useful for continued evaluation of both compounds

- toxicity of repeated doses in rats (*S*-methoprene)
- developmental toxicity in rats (*S*-methoprene)
- skin sensitization (*S*-methoprene and racemic methoprene)
- gene mutation in mammalian cells (racemic methoprene)
- observations in humans

List of end-points relevant for setting guidance values for dietary and non-dietary exposure[a]

Absorption, distribution, excretion, and metabolism in mammals	
Rate and extent of oral absorption:	Rapid and extensive
Dermal absorption	No data
Distribution:	Mainly in organs concerned with absorption, biotransformation, and excretion
Potential for accumulation[b]:	Long half-times of total radiolabelled compounds (metabolites) in blood and of parent in fat
Rate and extent of excretion:	Bulk of radiolabel excreted within 5 days; significant proportion exhaled; remaining radiolabel incorporated into tissues
Metabolism in animals	Very extensive: rapid oxidation to CO_2 and acetate, which is reincorporated into natural products
Toxicologically significant compounds	Methoprene
Acute toxicity[c]	

Rat, LD_{50}, oral	> 5000 mg/kg bw
Rat, LD_{50}, dermal	> 2000 mg/kg bw
Rat, LC_{50}, inhalation	No data
Skin irritation	Not irritating
Eye irritation	Not irritating
Skin sensitization	No reliable data available
Short-term toxicity	
Target / critical effect	Body-weight gain; effect on liver

Lowest relevant oral NOAEL	8.6 mg/kg bw per day (90 days, dogs)
Lowest relevant dermal NOAEL	No reliable data available
Lowest relevant inhalation NOAEL	No reliable data available
Genotoxicity[c]	Weight of evidence suggests no genotoxic concern
Long-term toxicity and carcinogenicity	
Target/critical effect	Body-weight gain; effect on liver
Lowest relevant NOAEL	44 mg/kg bw per day (2 years, rats)
Carcinogenicity	No carcinogenic potential (mice, rats)
Reproductive toxicity	
Reproduction target / critical effect	Reduced pup weight in F_2 and F_3 litters; reduced number of live F_3 pups at birth
Lowest relevant (reproductive) NOAEL	29 mg/kg bw per day
Developmental target / critical effect	Offspring toxicity
Lowest relevant developmental NOAEL	190 mg/kg bw per day (mouse)
Neurotoxicity / Delayed neurotoxicity	
Acute neurotoxicity; NOAEL	No concern from other studies
90-day neurotoxicity; NOAEL	No concern from other studies
Delayed neuropathy	No concern from other studies
Other toxicological studies; observations in humans	No data
Medical data	No data

Summary	Value	Study	Safety factor
ADI methoprene	0.09 mg/kg bw	90 days, dogs	100
ADI *S*-methoprene	0.05 mg/kg bw	0.5 x ADI of racemic methoprene	
Acute reference dose	Unnecessary		

[a] Relevant end-points relate to racemic methoprene, unless otherwise stated in a footnote.
[b] *S*-Methoprene
[c] Racemic methoprene and *S*-methoprene

Dietary risk assessment

The theoretical maximum daily intakes of racemic methoprene and *S*-methoprene in the five GEMS/Food regional diets, on the basis of existing MRLs, represented 10–70% of the ADI (Annex 4). The Meeting concluded that the intake of residues of methoprene resulting from uses that have been considered by the JMPR is unlikely to present a public health risk.

4.20 PHOSALONE (060)

Toxicology

Phosalone was evaluated toxicologically by the JMPR in 1972, 1993 and 1997. The 1997 JMPR allocated an ADI of 0–0.02 mg/kg bw. The compound was re-evaluated by the present Meeting to consider the

need to establish an acute RfD. Other studies to underpin maintenance of the ADI were submitted and were evaluated by the Committee.

The LD_{50} in rats treated orally is approximately 150 mg/kg bw, and WHO has classified phosalone as moderately hazardous.

Phosalone is an organophosphate ester, and virtually all its toxic actions are mediated by cholinesterase inhibition.

After preliminary studies had shown that peak effects occur at about 6 h, neurotoxicity was studied in rats given phosalone by gavage at a single dose of 0, 10, 25, or 60 mg/kg bw. No deaths were observed. Abnormal clinical signs were seen on the day of treatment with the highest dose. Changes in the functional observational battery (FOB) were seen at the highest dose and, with one exception, on day 1 only. The NOAEL was 25 mg/kg bw on the basis of clinical signs and decreased erythrocyte and brain cholinesterase activity at 60 mg/kg bw.

The Meeting also reviewed studies which were not relevant to establishment of an acute RfD but which were nevertheless relevant to continuation of the current ADI. In a study of acute toxicity in rats exposed by inhalation for 4 h, the LC_{50} was 2.1 mg/l in males and 1.3 mg/l in females. In a 13-week study of neurotoxicity, rats received phosalone in the diet at a concentration of 50, 150, or 600 ppm for 13 weeks; satellite groups of rats received phosalone at the same dietary concentrations for 4 or 8 weeks. The NOAEL was 50 ppm, equal to 3.9 mg/kg bw per day, on the basis of reduced brain cholinesterase activity at the next highest dose (150 ppm, equal to 12 mg/kg bw per day). A study of DNA repair in rat hepatocytes *in vitro* gave negative results. The Meeting concluded that these studies supported continuation of the current ADI.

After considering previous evaluations of phosalone and the new data, the Meeting established an acute RfD of 0.3 mg/kg bw on the basis of the NOAEL of 25 mg/kg bw in the study of acute toxicity in rats treated by gavage and a safety factor of 100.

An addendum to the toxicological monograph was prepared.

Dietary risk assessment

Short-term intake

The IESTI for phosalone was calculated for the commodities for which MRLs have been recommended, STMR and highest residue vaLues have been estimated and data on consumption of large portion sizes and unit weights were available. The results are shown in Annex 4.

The calculated short-term intakes were less than 100% of the acute RfD for children and for the general population. The Meeting concluded that the intake of residues of phosalone resulting from uses that have been considered by JMPR is unlikely to present a public health concern.

4.21 PIPERONYL BUTOXIDE (062)

Residue and analytical aspects

Piperonyl butoxide is a synergist used to prolong the effects of insecticides. The compound was reviewed by the 1992 JMPR for both residues and toxicology. As some critical data were not submitted, in particular studies on metabolism in plants and animals, and as the studies of stability and processing that were received related only to commercially stored wheat and wheat products, withdrawal of all the MRLs was recommended. At its Twenty-sixth Session (1994), the CCPR decided to withdraw the CXLs for cereal grains and for all other commodities (ALINORM 95/24), except for wheat, which was advanced to step 5/8. The 1995 JMPR established an ADI of 0–0.2 mg/kg bw per day.

At its Twenty-ninth Session, the CCPR scheduled piperonyl butoxide for periodic review at the 1999 JMPR, but at its Thirtieth Session it re-scheduled the review for 2000 (ALINORM 99/24 App.VII). The compound was reviewed by the current Meeting within the CCPR periodic review programme.

The Meeting received information from the manufacturer on physical and chemical properties, metabolism and environmental fate, analytical methods, stability in freezer storage, registered uses, the results of supervised trials on pre- and post-harvest uses, studies of processing, studies of animal transfer, residues in food in commerce and national residue limits. The Australian Government provided information on registered uses and national residue limits.

Metabolism

Animals

Three studies were conducted on metabolism in rats. In the first study, rats were dosed with [^{14}C]piperonyl butoxide labelled in the glycol side-chain at a single dose of 50 or 500 mg/kg bw or repeated doses of 50 mg/kg bw per day. Seven days after treatment, 27–38% of the radiolabel had been excreted in urine, 55–66% in faeces and 0.89–1.5% in carcass and tissues, with no specific trends by sex or dose. The highest concentration of residue was found in the gastrointestinal tract (≤ 2.0 mg/kg). Piperonyl butoxide was detected only in urine from female rats dosed with 50 mg/kg bw, and eight metabolites were identified (representing 0.8–6.7% of the administered dose). Piperonyl butoxide can be metabolized at the propyl side-chain, the glycolate side-chain and the dioxole ring. A product of cyclization of the propyl and glycolate chain (lactone of 6-methoxy-1,3-benzodioxol-5-yl acetic acid) was the main compound in male rat urine (5.2–6.8%). In faeces, piperonyl butoxide accounted for 2.2–31% of the administered dose. Of the four metabolites detected, 4-{[[2-(hydroxymethoxy)ethoxy]ethoxy]methyl}-5-propyl-1,2-benzenediol, a catechol with an intact glycolate chain, was the main one, representing 9.4–26% of the administered dose.

In a second study, formulated [^{14}C]piperonyl butoxide applied to discs of skin excised from rats showed a potential for adsorption through skin. After 24 h, 31% of the radiolabel was recovered in the skin homogenate. In a third study, rats received a single dose of ring-labelled piperonyl butoxide at a dose of 50 or 500 mg/kg bw. Most of the radiolabel was eliminated within the first 48 h after dosing, primarily in the faeces. During the 7 days of collection, 11–23% of the administered dose was found in urine and 70–85% in faeces, with a mean of 97% in the excreta of animals at the high dose and 98% in the excreta of those at the low dose. The carcass accounted for 0.28–0.44% of the administered dose. The metabolite profiles in excreta were similar at the two doses, piperonyl butoxide being metabolized at the dioxole ring to produce either a catechol or a substituted anisole moiety, and at the glycolate side-chain. At the glycolate side-chain, metabolism occurred by hydroxylation at the terminal carbon, oxidation to acid, followed by successive losses of the acetate moiety to form alcohols and acids. At least 15 metabolites were identified in excreta of both male and female rats, the main metabolite being 4-{[[2-(hydroxymethoxy)ethoxy]ethoxy}-methyl-5-propyl-1,2-benzenediol, representing 19% of the administered dose.

One goat received a dermal application of a 10% solution of [^{14}C]piperonyl butoxide uniformly labelled in the benzene ring for 5 days, and two other goats were given feed containing 10 or 100 ppm for

5 days. The radiolabel was excreted rapidly by the orally dosed goats and more slowly by the dermally dosed goat. Within 22 h after administration of the last dose, most of the dose had been excreted in urine (73% and 79% after oral and 44% after dermal administration) and faeces (22% and 22% after oral and 8.9% after dermal administration). The amounts excreted in milk were similar throughout the study, with all dose regimens: 0.33% of the applied dose was found in milk of orally dosed goats and 0.53% in milk of the dermally dosed goat. Little radiolabel was found in muscle, and radiolabel was concentrated in the fat of dermally dosed animal (0.20 mg/kg) and in the liver of the orally dosed animals (0.36 and 2.0 mg/kg at the low and high doses, respectively). The same metabolite profiles were found in tissues and urine. Piperonyl butoxide was detected at > 0.02 mg/kg only in liver and fat from the animals given the high oral dose (0.12 and 0.13 mg/kg) and in fat from the dermally treated animal (0.16 mg/kg). It was metabolized primarily at the glycolate side-chain. Two metabolites were detected in milk, at concentrations of 0.001–0.016 mg/kg, which had a carboxylic acid moiety at C-2 or C-4 of the glycolate chain (1-(6-propyl-1,3-benzodioxol-5-yl)-2-oxabutan-4-oic acid and 2-{2-[(6-propyl-1,3-benzodioxol-5-yl)methoxy]ethoxy}acetic acid). In kidney, the metabolites were found at concentrations of 0.001–0.045 mg/kg, and the alcohol precursor of the carboxylic acid at C-4 (2-{2-[(6-propyl-1,3-benzodioxol-5-yl)methoxy]ethoxy}ethanol) was detected. In liver, a catechol of the latter metabolite (4-{[2-(hydroxymethoxy)ethoxy]methyl}-5-propyl-1,2-benzenediol) was detected at 0.14 mg/kg.

In two studies, laying hens received [^{14}C]piperonyl butoxide uniformly labelled in the benzene ring for 5 consecutive days by dermal application at a dose of 14 mg/g under an occluded patch of 2.5 x 530 cm or in the feed at 10 or 100 ppm. Excreta from hens dosed dermally contained 59% of the applied radiolabel, and those from the hens dosed orally at the low and high doses contained 89% and 94%, respectively. In eggs, the concentration of radiolabel was higher in the white during the first 48 h (up to 0.63 mg/kg) and then concentrated in the yolk (≤ 1.7 mg/kg at the higher oral dose). In tissues, the least radiolabel was found in muscle (0.002–0.124 mg/k) and the most in fat (0.13–4.8 mg/kg). The concentrations in kidney and liver were 0.11–1.6 mg/kg. At the end of the study, piperonyl butoxide was found in eggs and tissues at 0.006–1.2 mg/kg (the latter in egg yolk from hens given the high oral dose), but not in liver or kidney from hens given the low oral dose. No metabolites were found in egg white or fat. Of the four metabolites found in egg yolk, liver, kidney and thigh muscle (1-(6-propyl-1,3-benzodioxol-5-yl)-2-oxabutan-4-oic acid, 2-{2-[(6-propyl-1,3-benzodioxol-5-yl)methoxy]ethoxy}ethanol, 2-{2-[(6-propyl-1,3-benzodioxol-5-yl)methoxy]ethoxy}acetic acid and 4-{[2-(hydroxymethoxy ethoxy] methyl}-5-propyl-1,2-benzenediol), the last predominated, reaching 0.19 mg/kg in kidney from animals at the high oral dose.

Thus, in animals, piperonyl butoxide can be metabolized at the glycolate side-chain, through hydroxylation at the terminal carbon, oxidation to acid, followed by successive losses of the acetate moiety to form alcohols and acids, which can be conjugated; at the propyl side-chain, through cyclization with the hydrolysed glycolate chain; and through opening of the dioxole ring. The main residue in animal tissues, egg and milk is piperonyl butoxide.

Plants

The behavior of [^{14}C]piperonyl butoxide labelled in the glycolate chain was studied after foliar application to cotton, potato and lettuce, leaf at the maximum rate of 0.56 kg ai/ha. Only minimal uptake or translocation of parent or degradates occurred in cotton and potato. The concentration of TRR found in potato tubers was 0.076% of that found in the leaves (617 mg/kg) 8 days after the fourth and last application. Cotton leaves collected 5 weeks after the fifth application had 142 mg/kg of total radiolabel. Hulls, lint and seed from cotton bolls collected 16 days after the sixth and last application contained 5, 0.4 and 0.3% of the radiolabel found in leaves. Piperonyl butoxide was not detected in potato tubers. The concentrations in cotton products ranged from 0.047 in lint to 1.23 mg/kg TRR in hulls, corresponding to 0.2–5% of that found in leaves (26.3 mg/g). In lettuce leaves, piperonyl butoxide was responsible for 51% of TRR on the day of the fifth application, but the percentage dropped to 24.4% after 10 days.

The aqueous fraction of the lettuce extract at day 0 (24.2% of TRR) contained at least three conjugated metabolites, two of which were identified, and a small amount of piperonyl butoxide (1.5% TRR). An aqueous extract from plants on day 10 contained five identified metabolites at concentrations of 0.2–2.0 mg/kg (0.9–7.6% TRR), consisting of conjugated alcohols formed after hydrolysis and truncation of the glycosate side-chain, with an intact dioxole ring.

Potato leaves contained at least seven degradates of high to moderate polarity, none of which represented more than 3% TRR. About 82% of the TRR was extracted into organic solvent, and more than 30 degradates were present, each at < 0.02 mg/kg (4% TRR). The metabolite profile was different in potato leaves and tubers. The degradates in post-extraction solids of potato tubers were characterized as highly polar materials, probably the products of oxidation of one or both side-chains to benzyl alcohols or carboxylic acids and of opening of the dioxole ring to a catechol structure.

Cotton leaves contained 11 or more degradates soluble in organic solvents; the predominant one (7.5% TRR) was similar to compounds found in lettuce, with one to three oxygen atoms remaining in the glycolate side-chain. The metabolites observed in the leaves were not observed in hulls, seeds or lint. In cotton seed, parent piperonyl butoxide was the only residue soluble in organic solvents. Mild acid hydrolysis of the post-extraction solids released almost 50% of the TRR, which presented two minor peaks (< 0.05 mg/kg) on the HPLC and a third, comprising 45% TRR (0.12 mg/kg), with characteristics similar to those in potato tubers. Cotton lint extract also contained a highly polar material that eluted at the HPLC solvent front (80% TRR, 0.19 mg/kg), which may have been the same dioxole ring-opened metabolite found in potato tubers and cotton seed, except that it was not bound. Cotton hulls contained five degradates soluble in organic solvents (0.1% TRR). The predominant degradate released by mild acid hydrolysis of the post-extraction solids was 1-(6-propyl-1,3-benzodioxol-5-yl)-2-oxabutan-4-oic acid (5.1% TRR).

Thus, piperonyl butoxide is metabolized in plants in a manner similar to that in animals, except that more polar metabolites are formed, which are fully degraded molecules resulting from hydrolysis of the glycolate side-chain, oxidation of the propyl side-chain and opening of the dioxole ring. The main residue found in lettuce, potato and cotton leaves was piperonyl butoxide, and minimal translocation occurred to potato tubers and cotton products.

Environmental fate

Soil

A 2-mm layer of a sandy loam soil treated with [phenyl ring-^{14}C]piperonyl butoxide at a rate equivalent to 10 kg ai/ha was exposed to artificial sunlight for ≤ 15 days (corresponding to 41 days of natural sunlight) or kept in the dark. The half-time in both soils was 1–3 days. Four degradates were identified, resulting from loss of the glycolate side-chain and oxidation of the resulting benzyl alcohol to the corresponding aldehyde and acid. The concentration of hydroxymethyl dihydrosafrole, a benzyl alcohol, reached a peak at day 3 (63 and 44% of the applied radiolabel in unirradiated and irradiated soil, respectively) and fell to 1.9 and 3.1% after 15 days. Hydroxymethyl dihydrosafrole was oxidized to an acid (6-propyl-,3-benzodioxol-5-carboxylic acid) which accumulated in unexposed soil after 15 days (49% of applied radiolabel). More decomposition and oxidation of the phenyl ring, observed as formation of CO_2, occurred in irradiated soil (28%) than in the control dark soil (1.3%). In another experiment, piperonyl butoxide incubated in the dark for 242 days degraded with a half-time of approximately 14 days, in a pathway similar to that discussed above. Two additional metabolites with oxidized propyl side-chains were detected at 0.1–5.8% of the applied radiolabel during the incubation period. More than one-half the applied piperonyl butoxide had been mineralized to CO_2 by 242 days.

Terrestrial dissipation of piperonyl butoxide was studied in soil treated at rate of 5.2 kg ai/ha in the USA. The half-times were 4.3 in California and Georgia and 3.5 in Michigan. At 15 cm depth, the

concentration of piperonyl butoxide after 14 days was 0.11–0.22 mg/kg and fell to < 0.10 mg/kg after 30 days of application. No parent compound was detected at any site in soil collected at depths below 15 cm.

Water–sediment systems

A solution of 1 mg/L radiolabelled piperonyl butoxide was stable when incubated at 25 °C in the drak for 30 days at pH 5, 7 or 9 in sterile aqueous buffers (97–100 % of the applied radiolabel recovered). In another experiment, a 10 mg/L solution of [^{14}C]piperonyl butoxide (at pH 7) exposed to natural sunlight for 84 h degraded with a half-time of 8.4 h. Two main photoproducts were observed: hydroxymethyl dihydrosafrole (22% and 48% of the applied radiolabel after 4 and 84 h, respectively) and its aldehyde oxidation product (3,4-methylenedioxy-6-propylbenzyl aldehyde; 5.7–11% of the applied radiolabel). At least five other minor degradates were found, each representing < 10% of the applied radiolabel. Unexposed samples contained ≤ 2% of radiolabel associated with metabolites.

Radiolabelled piperonyl butoxide in a sandy loam soil water–sediment system incubated under aerobic conditions in the dark (10 mg/kg sediment or 3.2 (g/ml of water) degraded slowly, and 72% of the piperonyl butoxide remained after 30 days. Under anaerobic conditions, 91% of the parent compound was still present after 181 days. In both systems, it degraded to hydroxymethyl dihydrosafrole and further to 3,4-methylenedioxy-6-propylbenzyl aldehyde and acid, which represented ≤ 3.8% of the applied radiolabel.

The adsorption and desorption characteristics of piperonyl butoxide radiolabelled in the phenyl ring were assessed in sand, clay loam, sandy loam and silt loam soils at a concentration of 0.4, 2, 3 or 4 mg/l. The systems were equilibrated for 24 h at 25 °C in darkness at a soil:solution ratio of 1:10. Piperonyl butoxide showed low to moderate mobility in sandy loam, clay loam and silt loam (K_a, 8.4, 12 and 30, respectively) and high mobility in sanyd soil (K_a, 0.98). The K_{oc} values ranged from 399 in sand to 830 in silt loam. A K_d value was not determined for sandy soil, but in the other soils it ranged from 8.2 to 42 after the first desorption step and from 6.3 to 95 after the second.

The leaching behaviour of [^{14}C]piperonyl butoxide was investigated in sand, silt loam, sandy loam and clay loam soils after application at a rate equivalent to 5 kg ai/ha to the top of 30-cm columns (1 mg/column) and eluted with 0.01 mol/L calcium chloride. Piperonyl butoxide did not leach readily into loam soils (0.2–1.3% of the applied radiolabel in the leachate), but it was highly mobile in sandy soil (74% in the leachate), with a distribution coefficient of 0.42 ml/g. When the experiment was conducted with a sandy loam soil aged for 18 days and treated with [^{14}C]piperonyl butoxide, 33% of the applied radiolabel remained in the top of the column (up to 5 cm) and 14% was recovered in the leachate. The three degradates found (hydroxymethyl dihydrosafrole, 3,4-methylenedioxy-6-propylbenzyl aldehyde and the acid) were more mobile than the parent compound, being detected at 20–25 cm of the column. An extract of the aged soil contained 45% of the applied radiolabel as piperonyl butoxide.

Methods of analysis

One method for determining residues of piperonyl butoxide and its metabolites in raw and processed plant commodities involves extraction with acetonitrile, partition of piperonyl butoxide into petroleum ether and analysis by HPLC with fluorescence detection. The more polar metabolites remain in the aqueous phase, which is subjected to mild acid hydrolysis to convert the metabolites quantitatively to hydroxymethyl dihydrosafrole, which is extracted and analysed by HPLC with fluorescence detection. The LOQ for piperonyl butoxide and for total metabolites was 0.10 mg/kg, with an average recovery of 91–94%. In grapes and cranberries, < 70% of metabolites were recovered. In another method, the extract containing piperonyl butoxide was brominated and cleaned up by liquid–solid partition, and the eluate was analysed by GC with ECD. The LOQ for piperonyl butoxide was 0.10 mg/kg, and average recovery was 56% in beans to 67% in peanuts. Other solvents can be used to extract piperonyl butoxide from wheat and the milled fraction, including methanol, hexane and ethyl acetate.

In the method used to determine residues of piperonyl butoxide in milk, eggs and tissues, samples were extracted with acetonitrile, the fat was removed, and piperonyl butoxide was partitioned into hexane. The hexane solution was cleaned up on silica gel with solid-phase extraction, and piperonyl butoxide was determined by GC–MS. The LOQ was validated at 0.05 mg/kg for tissues (liver, kidney, muscle and fat), with recovery of 70–108%. The recovery at 0.01 and 0.05 mg/kg from milk was 67–120%, and that from eggs was 71–104%.

Stability of residues in stored analytical samples

Piperonyl butoxide at 1.0 mg/kg was stable in samples stored frozen in the dark for up to 12 months. In potato tubers and chips, leaf lettuce, broccoli, cucumber, grapes, orange fruit, molasses, juice and dry pulp, tomato fruit, juice, puree, dry and wet pomace, succulent beans pod and vine, cotton seed, oil and soapstock and beans, 70–108% of the added piperonyl butoxide remained after a 12-month storage. In potato granules, potato wet peel and cotton meal, these values varied from 53 to 68%. When piperonyl butoxide was added to sweets, meat, bread, sugar and peanuts at a concentration of 0.2 mg/kg, 50–69% remained after 12 months of frozen storage.

Definition of the residue

On the day of application, piperonyl butoxide accounted for 51% of the TRR in lettuce, two metabolites being formed in approximately equal amounts and accounting for 24% of the radiolabel. After 10 days, the concentration of piperonyl butoxide had decreased by half, and at least 10 metabolites were formed, each representing < 10% of the TRR. Piperonyl butoxide was not translocated to potato tubers or cotton products when applied to the leaves of these plants. Some highly polar material was found in cotton seed and in lint, representing 44 and 80% TRR, respectively. Although these metabolites were not identified, they were highly degraded compounds and, owing to their high polarity, would probably not accumulate in animals if ingested. Although no studies of metabolism in stored plant commodities were conducted, the Meeting agreed that piperonyl butoxide is degraded mainly by photolysis and considered that such studies were not necessary, as the residues are very stable in cereal grains in storage. No major metabolite was found in edible animal commodities. The main compound in both plant and animal commodities is piperonyl butoxide.

The Meeting agreed that the residue definition for compliance with MRL and for estimating dietary intake in plant and animal commodities continues to be piperonyl butoxide.

Piperonyl butoxide has a log P_{ow} of 4.6 and is concentrated in the fat of animals dosed orally and dermally. The Meeting concluded that piperonyl butoxide is fat-soluble.

Results of supervised trials

Pre-harvest trials were conducted in crops in various regions of the USA between 1992 and 1996, with 10–12 applications of pyrethrins containing piperonyl butoxide, according to maximum GAP for piperonyl butoxide (0.56 kg/ha; no PHI).

Citrus

Seven supervised trials were conducted on citrus. The concentrations of residues of piperonyl butoxide in lemon were 3.1 and 1.7 mg/kg, those in oranges were 0.90, 0.98 and 1.0 mg/kg and those in grapefruit were 0.49 and 1.4 mg/kg. The concentrations in citrus were, in ranked order (median underlined): 0.49, 0.90, 0.98, 1.0, 1.4, 1.7 and 3.1 mg/kg. Although there were fewer trials on citrus fruits than would be required for a major crop, piperonyl butoxide is used to only a minor extent as a synergist in pre-harvest treatment in pyrethrin formulations. Recommendations for pyrethrins in citrus were made by the 2000 JMPR on the basis of trials conducted with a pyrethrin–piperonyl butoxide formulation. Therefore, the

Meeting agreed to recommend a maximum residue level of 5 mg/kg and a STMR of 1.0 mg/kg for piperonyl butoxide in citrus.

Berries and small fruits

Seven supervised trials were conducted on berries and small fruits. The concentrations of residues of piperonyl butoxide were 2.8 mg/kg in blackberry, 5.0 and 5.0 mg/kg in blueberry, 4.2 mg/kg in cranberry, 9.6 mg/kg in grapes and 3.0 and 3.1 in strawberry. As insufficient data from trials performed according to GAP were submitted, the Meeting agreed not recommend a maximum residue level for piperonyl butoxide in berries, strawberry and grapes. There is no current recommendation for pyrethrins in berries and small fruits.

Brassica vegetables

Three supervised trials were conducted on broccoli, giving rise to concentrations of residues of piperonyl butoxide of 0.69, 1.7 and 2.3 mg/kg. In three trials conducted on cabbage, the concentrations were 0.09, 0.23 and 0.46 mg/kg, while those in cabbage with wrapper leaves were 1.1, 6.4 and 2.7 mg/kg. As insufficient data from trials performed according to GAP were submitted, the Meeting agreed not recommend a maximum residue level for piperonyl butoxide in broccoli and cabbage. There is no current recommendation for pyrethrins in broccoli and cabbage.

Curcubits

Eight supervised trials were conducted on curcubits. The concentrations of residues of piperonyl butoxide were 0.83 and 0.61 mg/kg in cantaloupe, 0.07 and 0.68 mg/kg in cucumber and 0.10, 0.20, 0.25 and 0.27 mg/kg in squash. The Meeting agreed that the data on residues in curcubits could be combined as 0.07, 0.10, 0.20, 0.25, 0.27 0.61, 0.68 and 0.83 mg/kg, and estimated a maximum residue level of 1 mg/kg and a STMR of 0.26 mg/kg for piperonyl butoxide in curcubits.

Peppers and tomato

In three supervised trials conducted on peppers, the concentrations of residues of piperonyl butoxide were 0.39, 0.59 and 1.4 mg/kg. In three trials conducted in tomato, the values were 0.37, 0.76 and 1.0 mg/kg. Although there were fewer trials on peppers and tomato than required for these crops, the Meeting agreed to consider the data sufficient to recommend maximum residue levels, for the reasons outlined for citrus fruits. The data for peppers and tomato were combined, in ranked order, as 0.37, 0.39, 0.59, 0.76, 1.0 and 1.4 mg/kg. The Meeting estimated a maximum residue level of 2 mg/kg and a STMR of 0.675 mg/kg for piperonyl butoxide in peppers and tomato.

Leafy vegetables

Eleven supervised trials were conducted on leafy vegetables. In lettuce, head, the concentrations of residues of piperonyl butoxide were 0.54 and 0.35 mg/kg ; when the wrapper leaves were attached, the values were 5.0 and 3.6 mg/kg. Lettuce, leaf contained concentrations of 19 and 23 mg/kg, mustard greens contained 37 and 38 mg/kg, radish leaves (crowns with leaves) contained 38 mg/kg and spinach contained 32 and 39 mg/kg. The concentrations in mustard greens, radish leaves and spinach are within the same range and provide mutual support. They were, in ranked order: 32, 37, 38 (2) and 39 mg/kg. The Meeting recommended a maximum residue level of 50 mg/kg and a STMR of 38 mg/kg for piperonyl butoxide in mustard greens, radish leaves, leaf lettuce and spinach.

Legume vegetables

Two supervised trials were conducted on succulent beans, giving concentrations of piperonyl butoxide in pods of 0.34 and 2.2 mg/kg: In two trials conducted in succulent peas, the values were 2.2 and 5.5 mg/kg. As insufficient data from trials performed according to GAP were submitted, the Meeting agreed not recommend a maximum residue level for piperonyl butoxide in succulent beans and peas.

Root and tuber vegetables

In one supervised trial conducted on carrot, the concentration of residues of piperonyl butoxide in roots was 1.1 mg/kg. Three trials conducted on potato gave values in tubers of < 0.10 (2) and 0.11 mg/kg, one trial on radish gave a value in roots of 0.34 mg/kg and two trials conducted on sugar beet gave concentrations in roots of < 0.10 mg/kg. In a study of metabolism conducted with labelled piperonyl butoxide on potato at maximum GAP, no residues were detected in tubers. Although there were fewer trials on root and tuber vegetables than would be required for this group, the Meeting agreed to consider the data sufficient to recommend residue levels, for the reasons outlined for citrus fruits. As only one trial was conducted on carrots, giving a much higher value than for the other commodities in the group, the Meeting agreed to combine the values for all commodities except carrots. Those are, in ranked order: < 0.10 (3), 0.11 and 0.34 mg/kg. The Meeting estimated a maximum residue level of 0.5 mg/kg and a STMR of 0.10 mg/kg for piperonyl butoxide in root and tuber vegetables, except carrots.

Pulses

In two supervised field trials on dry beans and two on dry peas at GAP rate, the concentrations of piperonyl butoxide residues in seed were 0.10 and 0.11 mg/kg in beans and 0.27 and 0.57 mg/kg in peas. As insufficient data from trials performed according to GAP were submitted, the Meeting agreed not recommend a maximum residue level for piperonyl butoxide in pulses due to pre-harvest use.

Celery

In two supervised trials on celery, the concentrations of residues of piperonyl butoxide were 17 and 23 mg/kg in untrimmed leaf stalk and 0.98 and 2.3 mg/kg in the petiole. As insufficient data from trials performed according to GAP were submitted, the Meeting agreed not recommend a maximum residue level for piperonyl butoxide in celery.

Mustard seed

One supervised trial was conducted on mustard seed, which gave a concentration of piperonyl butoxide residues of 2.1 mg/kg. As insufficient data from trials performed according to GAP were submitted, the Meeting agreed not recommend a maximum residue level for piperonyl butoxide in mustard seeds.

Cotton seed

In five supervised trials conducted on cotton seed, the concentrations of residues of piperonyl butoxide were < 0.10 (2), 0.10 (2) and 0.21 mg/kg. As insufficient data from trials performed according to GAP were submitted, the Meeting agreed not recommend a maximum residue level for piperonyl butoxide in cotton seed. There is no current recommendation for pyrethrins in cotton seed.

Animal feed

In four trials conducted on succulent or dry beans, the concentrations of residues in vine were 16 (2), 26 and 28 mg/kg. In hay samples dried for 2–6 days in the open air, the values were 11, 14, 21 and 42 mg/kg, and those in forage were 14 and 25 mg/kg. In four trials on succulent or dry pea, the concentrations in vine were 26, 29, 47 and 96 mg/kg. In hay samples dried for up to 14 days in the field or in a greenhouse, the values were 3.7, 38, 48 and 153 mg/kg, and those in forage were 31 and 42 mg/kg.

The Meeting agreed that the data on residues in bean vines represent the same population as those for pea vines and could be used to support a recommendation for pea vines. The concentrations were, in ranked order: 16 (2), 26 (2), 28, 29, 47 and 96 mg/kg. When the median (27 mg/kg) and the maximum values (96 mg/kg) were corrected for moisture content (75%, *FAO Manual*, p. 125), the values were 108 mg/kg and 384 mg/kg, respectively, in dry matter. The Meeting recommended a maximum residue level of 400 mg/kg and a STMR of 108 mg/kg for piperonyl butoxide in pea vines, green (dry basis).

The Meeting agreed that the data on residues in bean and pea hay represented a single population and could be combined, in ranked order, as 3.8, 11, 14, 21, 38, 42, 48 and 153 mg/kg. The median (17.5 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 and 174 mg/kg, respectively, on a dried base. The Meeting estimated a maximum residue level of 200 mg/kg and a STMR of 19.9 mg/kg for piperonyl butoxide in bean hay and pea hay or fodder.

As insufficient data from trials performed according to GAP were submitted, the Meeting agreed not recommend a maximum residue level for piperonyl butoxide in pea and bean forage.

In five supervised trials conducted on cotton forage, the concentrations of residues of piperonyl butoxide were 20, 28, 30 (2) and 37 mg/kg. As insufficient data from trials performed according to GAP were submitted, the Meeting agreed not recommend a maximum residue level for piperonyl butoxide in cotton forage.

In two trials conducted with sugar beet leaf, the concentrations of residues of piperonyl butoxide in crowns with leaves attached were 37 and 12 mg/kg. As insufficient data from trials performed according to GAP were submitted, the Meeting agreed not recommend a maximum residue level for piperonyl butoxide in sugar beet leaves.

Post-harvest treatment

Trials were conducted in which navy beans in cloth bags underwent treatment with up to 10 applications of piperonyl butoxide at the label rate in a warehouse by a space spray (0.25 kg ai/1000 m^3) and a contact spray (0.3 kg ai/100 m^2). One bag was collected for analysis after each application, for a total of 10 bags from each treatment. The concentrations of residues were < 0.05 (2) (LOD), < 0.10 (3) (LOQ), 0.10, 0.13 (2), 0.16 and 0.17 mg/kg in samples collected after the space spray treatment and < 0.05 (10) mg/kg in samples after the contact spray treatment. The concentrations of residues after post-harvest use were, in ranked order, < 0.05 (12), < 0.10 (3), 0.10, 0.13 (2), 0.16 and 0.17 mg/kg.

The Meeting estimated a maximum residue level of 0.2 mg/kg, an STMR value of 0.05 and a highest residue of 0.17 mg/kg for piperonyl butoxide in pulses after post-harvest use.

Trials were conducted with harvested peanuts in cloth bags treated in a warehouse with 10 applications at the label rate by a space spray (0.25 kg ai/1000 m^3) and a contact spray (0.3 kg ai/100 m^2). One bag was collected for analysis after each application, for a total of 10 bags from each treatment. The concentrations of residues in samples collected after each space spray treatment were < 0.10 (3), 0.20, 0.24, 0.28, 0.29, 0.36 and 0.54 (2) mg/kg, while those after contact spray treatment were < 0.05 (6) and < 0.10 (4) mg/kg. The concentrations after post-harvest use were, in ranked order: < 0.05 (6), ≤ 0.10 (7), 0.20, 0.24, 0.28, 0.29, 0.36 and 0.54 (2) mg/kg.

The Meeting estimated a maximum residue level of 1 mg/kg and an STMR value of 0.10 mg/kg for piperonyl butoxide in peanuts after post-harvest treatment.

Trials were conducted with prunes treated in a warehouse with 10 applications at the label rate by a space spray (0.25 kg ai/1000 m^3) or a contact spray (0.3 kg ai/100 m^2). One bag was collected for analysis after each application, for a total of 10 bags from each treatment. The concentrations of residues in samples collected after each space spray treatment were < 0.05 (5), < 0.10 (4) and 0.11 mg/kg, while those after contact spray were < 0.05 (6) and < 0.10 (4) mg/kg. The concentrations of residues after post-harvest use were, in ranked order, ≤ 0.05 (11), < 0.10 (8) and 0.11 mg/kg.

The Meeting agreed that the values for residues in prunes could be extended, and estimated a maximum residue level of 0.2 mg/kg and an STMR value of 0.05 mg/kg for piperonyl butoxide in dried fruits after post-harvest treatment.

Post-harvest trials were conducted on cacao beans, raisins and wheat flour in Germany during 1993–94 with eight space spray applications of pyrethrum–piperonyl butoxide formulation containing piperonyl butoxide at 21.3 g/1000 m^3 at 14-day intervals, or two applications of piperonyl butoxide at 128 g/1000 m^3. Samples were taken on days 0, 14, 30, 60 and 90 after treatment. In Germany, GAP for space spray treatment of stored products consists of 0.375–132 g ai/1000 m^3.

Two trials were conducted on cacao beans in jute sacks. At the lower rate, the concentrations of residues in beans 0 and 14 days after the last application were 0.21 and 0.25 mg/kg and then fell to 0.08 mg/kg at day 90. At the higher rate, the concentrations varied from 0.52 mg/kg on day 0 to 0.75 mg/kg on day 30. In one trial conducted at the higher rate (128 g ai/1000 m^3) on raisins in stored polythene and cardboard, the concentration was < 0.01 mg/kg at all sampling times. In one trial on wheat flour at the same rate, the concentrations ranged from 0.12 mg/kg at day 14 to 0.46 mg/kg at day 60.

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. The maximum residue level, STMR value and highest residue for raisins are covered by the recommendations for dried fruits after post-harvest treatment.

Two trials were conducted on wheat in Germany. The concentrations in grain after the lower rate of treatment (21.3 g/1000 m^3) varied from 0.71 mg/kg after 30 days to 2.5 mg/kg on day 0. Samples taken after the higher rate of treatment (128 g/1000 m^3) contained concentrations of 1.3 mg/kg on day 30 and 2.2 mg/kg on day 0.

In the USA, there are two further approved post-harvest uses for piperonyl butoxide as a pyrethrin formulation on stored grains: direct treatment of grain as it is carried to a silo (11.1–26 mg a.i./kg of grain) or application to grain in storage (0.12–0.24 kg ai/100 m^2). A series of trials was conducted in the USA in 1959 with various formulations of piperonyl butoxide applied to wheat at various rates as it was transferred to the bins. Up to five bins were treated at each application rate, and samples were taken 3–25 months after application. In three trials conducted at maximum GAP, the highest concentrations of piperonyl butoxide residues in all bins were 12, 17 and 25 mg/kg. One trial at lower rate gave similar results (maximum, 12 mg/kg), and the highest value in one trial conducted at a rate below GAP was 5.2 mg/kg.

Although trials were conducted on wheat in the USA according to GAP in 1959–61, full reports were not provided. The concentrations of piperonyl butoxide residues during storage for up to 12 months ranged from 4.1 to 13 mg/kg.

In Australia, piperonyl butoxide can be used on grain in various insecticide formulations for post-harvest treatment at a rate of 2.4–8.5 mg ai/kg of grain. In a series of trials conducted in 1978–79, treated wheat was sampled after up to 9 months of storage. In nine trials conducted at maximum GAP, the highest concentrations during sampling were 3.4, 8.0, 7.1, 7.2, 6.2, 9.1, 7.5 (2) and 8.0 mg/kg. In 10 trials conducted at a lower GAP rate or at a higher rate, the concentrations ranged from 2.4 to 16 mg/kg.

In 31 trials conducted in Australia in 1981–82, wheat treated with piperonyl butoxide at 10 mg/kg of grain in various formulations was sampled up to 9 months after treatment. The highest concentrations of residues found were 5.7 (2), 7.9 (3), 4.2 (2), 7.3 (3), 5.3, 5.0, 7.0 (2), 4.5, 7.8 (2), 5.2, 4.8, 7.5, 8.1, 8.2, 10 (3), 8.6, 9.2, 11, 8.0, 9.4 and 30 mg/kg. In four further trials conducted under the same conditions, treated wheat was sampled after 10–31 months of storage. The highest concentrations during this period were 7.3, 6.7 and 5.9 (2) mg/kg.

In a series of 13 trials conducted in Australia in 1979–80, wheat grain treated with various piperonyl butoxide formulations at 10 mg ai/kg of grain were sampled after up to 9 months of storage. The highest concentrations were 9.7 (2), 8.6, 7.7, 8.7, 8.9, 9.3, 9.5, 10 (2), 7.3, 8.4 and 14 mg/kg. In two other trials conducted at lower GAP the concentrations were 4.5 and 2.3 mg/kg.

In three trials conducted in Australia in 1998 at 8 mg ai/kg of grain in various formulations, the highest concentrations of piperonyl butoxide residues found during a 9-month storage period were 13, 16 and 5.4 mg/kg. In a trial conducted at a lower GAP, the concentration was 1.7 mg/kg. Although another 27 trials were conducted between 1990 and 1998, at rates of 4–10.7 mg ai/kg of grain, full reports of the studies were not provided. The highest concentrations found in each trial ranged from 1.5 to 8.9 mg/kg.

In Italy, piperonyl butoxide can be used after harvest in various formulations at a rate of 2.3–12.5 mg ai/kg of grain. In 18 trials conducted at various locations in Italy at a rate of 2.5, 5.0 or 10 mg/kg, samples were taken after up to 12 months of storage. The concentrations of residues in the trial at the highest GAP rate were 13, 3.9, 5.2, 4.2, 3.9 and 4.5 mg/kg. The highest concentrations in trials conducted at lower rates were 0.37–8.7 mg/kg.

Six post-harvest trials were conducted on barley in Australia in 1992–96 according to maximum GAP (6.33–8 mg ai/kg of grain) in three formulations. The grain was stored for up to 6.5 months. The highest concentrations of piperonyl butoxide residues were, in ranked order, 0.9, 6.0, 6.4, 6.5, 6.6 and 7.2 mg/kg. One trial at a lower rate gave values within the same range, but a full report of the study was not provided.

In 30 trials on maize in the USA conducted in 1952–57 with dust and spray formulation at rates of 10.4–29.4 mg ai/kg of grain, samples were taken after 1–50 months of storage. The highest concentrations of piperonyl butoxide found during storage in samples from the 10 trials conducted according to maximum GAP were 12, 11, 4.0, 8.0, 7.0, 8.0, 25, 6.0, 9.0 and 13 mg/kg, while those in trials conducted at lower GAP rates were 1–21 mg/kg. In another study, for which a full report was not provided, conducted at maximum GAP, the highest concentration found during 12 months of storage was 10 mg/kg.

Trials were conducted in maize with three concentrations of piperonyl butoxide applied by surface spray (49.7–149 g ai/m^2) at various frequencies of application. Three months after treatment, 25–41% of the total applied remained in the maize; after 6 months, this value had dropped to 11–13%.

In Italy, two trials were conducted on maize at the lowest and highest GAP rates, and samples were taken for analysis after up to 6 months of storage. The highest concentrations of piperonyl butoxide found were 1.3 mg/kg at the lowest GAP rate and 4.1 mg/kg at the highest rate.

In two trials conducted on sorghum in Australia at maximum GAP, the concentrations of piperonyl butoxide residues on day 0 were 2.9 and 10 mg/kg; these were reduced after 3 months of storage. Two trials at lower and higher rates gave highest values of 0.50 and 20 mg/kg. In another trial conducted at maximum GAP, the highest concentration found during a 6-month storage period was 9.7 mg/kg. A full report of this trial was not provided.

GAP for post-harvest use of piperonyl butoxide on cereal grains is 10 mg/kg of grain in Australia, ≤ 12.5 mg/kg of grain in Italy and ≤ 26 mg/kg of grain in the USA. The Meeting agreed that the estimates should be derived from the critical GAP, that of the USA. The concentrations of residues in trials conducted according to GAP in the USA (10 trials on wheat, three on maize) were, in ranked order: 4.0, 6.0, 7.0, 8.0 (2), 11, 12 (2), 8.0, 9.0, 13 and 25 mg/kg. The Meeting estimated a maximum residue level of 30 mg/kg and a STMR value of 11 mg/kg for piperonyl butoxide in cereal grains after post-harvest treatment.

Fate of residues during processing

A series of studies was conducted on processing of orange, grapes, tomato, beans, potato, sugar beets and cotton that had been treated with at least 10 applications at five times the GAP rate. Samples were collected on the day of the last application, except for cotton, samples of which were collected after 14 days. Bulk samples were processed into the required products by procedures that simulated commercial practice.

Three orange plots were treated and one bulk sample consisting of one-third of each treated plot was processed. The concentration of piperonyl butoxide residues in orange was 9.4 mg/kg. The residues concentrated in orange dry pulp and orange oil, with processing factors of 5.7 and 15. In orange molasses, the concentration of residues was reduced by a processing factor of 0.53, and no residue was found in orange juice (processing factor, < 0.01). On the basis of the recommended maximum residue level of 5 mg/kg and the STMR value of 1.0 mg/kg, the Meeting estimated an STMR-P value of 5.7 mg/kg and a maximum residue level of 0.05 mg/kg in orange dried pulp and an STMR-P value of 0.01 mg/kg in orange juice.

Three tomato plots were treated, and one bulk sample consisting of one-third of each treated plot was processed. The concentration of residues in tomato was 8.5 mg/kg, and was found in wet and dry pomace, with processing factors of 5.9 and 34, respectively. The concentrations of residues in tomato purée and juice were reduced, with processing factors of 0.33 and 0.15, respectively. On the basis of the recommended maximum residue level of 2 mg/kg and the STMR value of 0.675 mg/kg in tomato, the Meeting estimated a maximum residue level of 0.3 mg/kg and an STMR-P value of 0.10 mg/kg for tomato juice and a STMR-P of 0.223 mg/kg for tomato purée.

Three grape plots were treated, and samples were collected for processing. The concentrations of residues in fruit were 14 (2) and 11 mg/kg. In all samples, the concentration increased in raisin, raisin waste and wet and dry grape pomace, giving average processing factors of 1.1, 2.3, 2.1 and 5.5, respectively. The concentration in juice decreased to 0.22–0.24 mg/kg, giving a processing factor of 0.02. As no STMR value was recommended for grapes, the Meeting could not estimate a STMR-P value for grape products.

Samples from three treated potato plots contained no detectable residues (< 0.10 mg/kg), and no residues were found in granules or chips. The residues were concentrated in wet potato peel, giving an average processing factor > 1.5. On the basis of the STMR value of 0.10 mg/kg recommended for root and tuber vegetables, the Meeting estimated a STMR-P value for wet potato peel of 0.15 mg/kg.

The concentration of residues in sugar beet root in one treated plot was 0.08 mg/kg. The concentration increased after processing to dry pulp, with a processing factor of 3.44. No residues were detected in sugar or molasses (< 0.10 mg/kg), giving an estimated processing factor for both commodities of < 1.2.

In one treated plot of succulent bean, the concentration of residues in pods was 8.0 mg/kg. The residues concentrated in cannery waste, with a processing factor of 6.4.

Three treated cotton plots had concentrations of residues in seed of 0.10 mg/kg (3). Each sample was processed, and the residues were found mainly in hulls with an average processing factor of 1.1, in crude oil with an average processing factor of 6.3, in refined oil with an average processing factor of 20 and in soapstock with an average processing factor of 3.8. Residues were not detected in cotton meal (< 0.10 mg/kg). As no STMR value was recommended for cotton, the Meeting could not estimate a STMR-P value for cotton products.

Various studies were conducted on processing of wheat at various locations. In three studies conducted in Australia, wheat treated with piperonyl butoxide at 8.0 mg ai/kg of grain was processed into bread and bran. The concentrations of residues in grain were 16 and 14 (2) mg/kg and residues were found mainly in bran, giving processing factors of 2.85, 1.5 and 2 (average, 2.1); the values were reduced in bread, with average processing factors of 0.015 and 0.03 (average, 0.225). No residues were detected in one bread sample. No information of the processing or analytical method was provided.

In a series of 12 studies in Australia, wheat was treated at a 15 mg ai/kg of grain, stored for 3 months and processed to bran and flour. The concentration of residues decreased after cleaning in flour and short and low-grade middlings, with average processing factors of 0.82, 0.42, 0.56 and 0.56, respectively. In bran, the concentration increased, with an average processing factor of 1.7. A full report of the studies was not provided.

Eighteen processing studies were conducted in Italy with wheat treated at various rates and stored for 45 or 180 days. The processing factors of cleaned, decorticated grain ranged from 0.27 to > 1.8 (average, 0.549) and from < 0.27 to 1.33 (average, 0.506), respectively. On average, the concentrations of residues in bran increase, with an average processing factor of 1.3 (< 0.02–3.1). In all studies, the concentrations of residues in flour decreased, with an average processing factor of 0.285, ranging from < 0.24 to 0.78.

In one study conducted in Australia, treated wheat was processed to bran, pollard, germ, gluten, flour, wholemeal bread and white bread at various extraction rates. Piperonyl butoxide residues were determined 1 month after processing. The residues concentrated in bran with processing factors of 4.2 and 4.3, in pollard with a processing factor of 2.7, in germ with a processing factor of 2.6 and in gluten with a processing factor of 1.8. The concentration decreased in flour with processing factors of 0.30 and 0.23, in wholemeal bread with a processing factor of 0.51 and in white bread with processing factors of 0.19 and 0.20.

In one study conducted in Australia, wheat treated with piperonyl butoxide at 8 mg ai/kg of grain was stored for 1, 3 or 6 months and processed to bran, pollard, germ, gluten, meal, flour and bread. Two flour extraction rates and a 1:1 blend of the two were used. The concentrations of residues increased in bran, pollard, germ and gluten, with average processing factors of 3.95 (n = 6), 2.3 (n = 3), 3.3 (n = 5) and 1.57 (n = 3), respectively. In meal, flour and bread, the concentrations decreased with average processing factors of 0.85 (n = 3), 0.3 (n = 6) and 0.36 (n = 9), respectively, from wheat wholemeal to white bread.

Wheat treated with two formulations at application rates of 10 and 13 mg/kg of grain and stored for up to 24 weeks was processed in three commercial mills (50 t per sample) and a pilot mill (1 t per sample). The concentrations of residues increased in bran with processing factors of 3.1–4.8 (average, 4.1; n = 10), in germ with processing factors of 2.1–4.3 (average, 3.2; n = 10) and in pollard with processing factors of 1.8–5.5 (average, 2.8; n = 6). On average, the concentration increased in wholemeal, with processing factors of 0.48–2.8 (average, 1.3; n = 9), but decreased in flour, with processing factors of 0.27–1.1 (average, 0.53; n = 10).

Wheat treated with piperonyl butoxide at 10 mg/kg of grain was stored for 2 or 4 h and processed to bran, pollard, germ, meal, flour and bread. The concentration of residues increased in bran, pollard and germ, with average processing factors of 3.8, 2.6 and 2.6, respectively. The concentrations decreased in flour, meal, wholemeal bread and white bread, with processing factors of 0.22, 0.78, 0.41and 0.11, respectively.

Five processing studies were conducted in Australia with wheat treated at the GAP rate or higher and stored for 1–26 weeks. The concentrations of residues increased in bran with an average processing factor of 3.8 (3.33–4.7, n = 4), in germ with an average processing factor of 2.2 (1.12–2.89, n = 4) and in gluten with a processing factor of 1.4. The concentrations decrease in flour with an average processing

factor of 0.34 (0.24–0.51, *n* = 5), in bread (white pan, wholemeal, flat Arabic and steamed) with average processing factors of 0.19–0.36 (average, 0.47) and in noodles (yellow alkaline and white) with average processing factors of 0.24 and 0.28. On average, the concentrations of residues decreased in wheat wholemeal, with processing factors of 0.61–1.29 (*n* = 5; average, 0.98).

In summary, the concentrations of piperonyl butoxide residues increased in wheat bran, with an average processing factor of 3.5 (*n* = 42), in germ with an average processing factor of 2.8 (*n* = 20), in pollard with an average processing factor of 2.6 (*n* = 10) and in gluten with an average processing factor of 1.5 (*n* = 4). The concentrations decreased in wheat flour with an average processing factor of 0.32 (*n* = 42), in wheat wholemeal with an average processing factor of 0.98 (*n* = 18), in bread with an average processing factor of 0.32 (*n* = 18) and in noodles, with an average processing factor of 0.26 (*n* = 2).

On the basis of the processing factors derived and the recommended MRL of 30 mg/kg and the STMR value of 11 mg/kg for cereal grains, the Meeting estimated a maximum residue level of 100 mg/kg and an STMR-P value of 38.5 mg/kg for wheat bran; a maximum residue level of 10 mg/kg and an STMR-P value of 3.5 mg/kg for wheat flour; a maximum residue level of 30 mg/kg and an STMR-P value of 10.8 mg/kg for wheat wholemeal 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.

In Italy, six processing studies were conducted on maize treated with piperonyl butoxide at two rates and stored for 42 or 182 days. Degermination was conducted in the laboratory under conditions that matched the industrial procedure, by starch processing (wet conditions) and mill processing (dry conditions). The concentrations of residues in germ and oil decreased, with average processing factors of < 0.3 and < 2.7, respectively (*n* = 6). On the basis of the recommended MRL and the STMR value for cereal grains, the Meeting recommended a maximum residue level of 80 mg/kg and an STMR-P value of 29.7 mg/kg for maize oil, crude.

Two processing studies were conducted in France on dried and undried cargo rice treated with piperonyl butoxide at 2.5 mg/kg of grain, but only a short summary of the study was provided.

Cocoa beans and soya beans were treated with piperonyl butoxide formulations at 7.5 or 10 mg ai/kg and stored for up to 1 year. Samples were then processed and analysed. The processing factors were 0.15–0.85 (average, 0.58; *n* = 10) for roasted cocoa beans and < 0.15–0.53 (average, < 0.20; *n* = 6) for chocolate paste. The concentration of residues increased in soya oil, with processing factors of 6.18, 22 and 13 (average, 13.9), and decreased in soya cake, with processing factors of 0.86, 0.75 and 0.10 (average, 0.57). Only a summary of the studies was provided.

Residues in animal commodities

Dietary burden of farm animals

The Meeting estimated the dietary burden of piperonyl butoxide residues in cows and poultry on the basis of the diets listed in Appendix IX of the *FAO Manual* (FAO, 1997; pp. 121–127) and the maximum residue levels and STMR values estimated by the current Meeting.

Estimate of maximum dietary burden of farm animals

Commodity	Group	Residues (mg/kg)	Basis	Dry matter (%)	Residues, dry weight (mg/kg)	% of diet	Residue contribution (mg/kg)

		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	20	10	–	1.2	0.6	–
Potato peel, wet	AB	0.15	STMR-P	20	0.27			–			–
Sorghum	GC	30	MRL	86	34.2	5		20	1.7		27.4
Wheat	GC	30	MRL	89	33.3						
Wheat bran	GC	100	MRL	89	111	50	40	80	55.5	44.4	88.8
Rice	GC	30	MRL	88	33.6						
Maize	GC	30	MRL	88	33.6						
Pea vines	AL	400	MRL	–	400	25	50	–	100	200	–
Pea hay	AL	200	MRL	–	200						–
					Total	100	100	100	158	245	116

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	20	10	–	1.2	0.6	–
Potato peel, wet	AB	0.15	STMR-P	20	0.27			–			–
Sorghum	GC	11	STMR	86	12.5	5		20	0.6		2.5
Wheat	GC	11	STMR	89	12.2						
Wheat bran	GC	38.5	STMR	89	42.7	50	40	80	21.3	17.1	34.2
Rice	GC	11	STMR	88	12.3						
Maize	GC	11	STMR	88	12.3						
Pea vines	AL	108	STMR	–	108	25	50	–	27	54	–
Pea hay	AL	19.9	STMR	–	19.9			–			
					Total	100	100	100	50.1	71.7	36.7

Feeding and dermal application to animals

Cows were given diets containing piperonyl butoxide at a concentration of 100, 300, 900 or 3000 mg/kg (dry weight basis) once daily for 28–30 consecutive days. The average concentration of residues in milk from three cows at 100 and 300 ppm remained approximately constant thoroughout the dosing period within ranges of < 0.01–0.02 mg/kg and 0.03–0.07 mg/kg, respectively. The concentrations in milk reached a plateau rapidly at higher doses. The average concentration of piperonyl butoxide in milk from cows at 900 ppm was 0.41 mg/kg, and that in milk from cows at the highest dose was 6.2 mg/kg. The residues in all treated animals were concentrated in liver and fat, and none were detected in kidney or muscle at the lower dose. In liver, the mean concentration ranged from 0.14 mg/kg at 100 ppm to 12 mg/kg at 300 ppm. The concentrations in animals at 100 ppm and 3000 ppm were 0.21 and 146 mg/kg in fat, 0.08 and 10 mg/kg in kidney and 0.05 and 7.6 mg/kg in muscle.

In Costa Rica and the USA, piperonyl butoxide may be sprayed directly onto livestock and poultry at a rate of 0.42–8.9 g ai/animal. Three cows were treated dermally twice daily for 28 consecutive days at a maximum GAP dose of 2.28 g/day (3.78 mg/kg bw per day). The average concentration of

residues in milk was 0.06 mg/kg on the first day and increased to 0.14 mg/kg on day 3, 0.12 mg/kg on day 7 and 0.16 mg/kg on day 27.

Laying hens were given diets containing 20.4, 61.2 or 196 ppm piperonyl butoxide equivalents. The concentrations of residues in eggs from hens at 61.2 ppm reached a plateau on day 7, at 0.16–0.21 mg/kg on days 7–21 and an increase on day 27. Residues were detected in liver only at the highest dietary level (at a concentration of 0.13 mg/kg). In muscle, residues were present in hens at the two higher dietary levels at mean concentrations of 0.09 and 0.74 mg/kg, respectively. The mean concentration in fat ranged was 0.30 mg/kg at the lowest dietary level and 12 mg/kg at the highest.

Laying hens exposed dermally for 28 consecutive days to piperonyl butoxide at a GAP application rate of 37.8 g/1000 m^3 had residues in their eggs from day 3, at a concentration of 0.02 mg/kg, which increased steadily up to day 27 (0.46 mg/kg) and did not reach a plateau. The average concentrations in tissues ranged from 0.96 mg/kg in muscle to 3.0 mg/kg in fat.

Maximum residue levels

The maximum calculated dietary burden of piperonyl butoxide for cattle was 158 mg/kg for beef cattle and 245 mg/kg for dairy cows. The highest dietary burden was used to estimate the maximum residue level in milk and tissues of cattle. The mean intake calculated for dairy cattle (71.7 mg/kg) was higher than that for beef cattle (50.1 mg/kg) and was used to estimate the STMR value for milk and cattle tissue. The calculated maximum and mean intakes of piperonyl butoxide for poultry, 116 mg/kg and 36.7 mg/kg, respectively, were used to estimate the maximum residue level and STMR value, respectively.

The highest concentrations of residues in tissues in the feeding studies and the mean value in milk after the plateau were used to estimate the maximum residue level. For eggs, the highest and the mean values at day 27 were used to calculate the maximum residue level and the STMR value, respectively. For cattle, the values at the calculated dietary burden (254 mg/kg) were estimated by interpolation of values for residues found at 100 and 300 ppm in feed. For poultry, these values (at a dietary burden of 116 mg/kg) were estimated by interpolation of concentrations found at 61.2 and 196 ppm. The mean concentrations of residues in tissues, milk and eggs were used to estimate the STMR value. For cattle, the concentration of residue at the calculated dietary burden (71.7 mg/kg) was estimated by 'proportioning' residues found at 100 ppm. For poultry, the concentration at 36.7 mg/kg was estimated by interpolation of data at 20.4 and 61.7 ppm.

The mean concentration of residue in milk after dermal treatment was used to estimate the maximum residue level and the STMR value for cattle milk. The highest and median concentrations of residues in eggs at day 27 (no plateau reached) were used to estimate the maximum residue level and the STMR value, respectively, in eggs, and the highest and median concentrations in tissues were used to estimate the maximum residue level and the STMR value, respectively, for both cattle and poultry.

Residues in cattle milk and tissues from animals treated orally

Dose (ppm) *Interpolated* / actual	Piperonyl butoxide concentration (mg/kg)							
	Milk (mean)	Liver		Kidney		Muscle		Fat	
		Highest	Mean	Highest	Mean	Highest	Mean	Highest	Mean

MRL										
245 /	*0.037* /	*0.71* /		*0.11* /		*0.0* /		*1.57* /		
100	0.01	0.15		< 0.05		< 0.05		0.42		
300	0.04	0.73		0.14		0.05		1.7		
STMR										
71.7 /	(0.007)		(0.10)		(<0.04)		(<0.04)		(0.15)	
100	0.01		0.14		<0.05		<0.05		0.21	

Residues in cattle milk and tissues from animals treated dermally

Piperonyl butoxide concentration (mg/kg)								
Milk (mean)	Liver		Kidney		Muscle		Fat	
	Highest	Median	Highest	Median	Highest	Median	Highest	Median
0.14	*0.14*	*0.03*	*0.21*	*0.21*	*0.21*	*0.16*	*2.7*	*2.6*

The Meeting estimated a maximum residue level of 1 mg/kg and an STMR value of 0.10 mg/kg for piperonyl butoxide in cattle liver, on the basis of the data from the feeding study. The concentrations of residues in milk, kidney, muscle and fat after dermal treatment were higher than those in the feeding study and were used in the estimations. The Meeting estimated a maximum residue level for piperonyl butoxide of 0.2 mg/kg in cattle milk, 0.3 mg/kg in cattle kidney and 5 mg/kg in cattle meat (fat).

The STMR concept is designed for supervised field trials on crops to obtain a typical residue value when a pesticide is used at maximum GAP and is not applicable to a trial with a single direct treatment. The Meeting agreed that, in this case, a typical residue value can be derived from the median concentrations in tissues and in milk. The Meeting estimated values for typical piperonyl butoxide residues after direct use (at maximum label conditions) of 0.14 mg/kg in cattle milk, 0.21 mg/kg in cattle kidney and 0.16 mg/kg in cattle meat. These values can be used in the same way as STMR values for estimating the effect of long-term dietary intake on residue concentrations in tissues and of long-term and short-term intake on concentrations in milk.

Residues in poultry products from poultry treated orally

Dose (ppm) *Interpolated* / actual	Piperonyl butoxide (mg/kg)							
	Eggs		Liver		Muscle		Fat	
	Highest	Mean	Highest	Mean	Highest	Mean	Highest	Mean
MRL	*0.55* /		*< 0.02* /		*0.06* /		*1.14* /	
116 /	0.35		–		< 0.05		0.38	
61.2	1.0		< 0.05		0.12		1.7	
196								
STMR								
36.7 /		*0.18* /		< 0.045 /		*0.035* /		*0.90* /
20.4		0.03		–		< 0.05		0.30
61.2		0.23		< 0.05		0.09		1.3

Residues in poultry products from poultry treated dermally

Piperonyl butoxide (mg/kg)									
Eggs		Liver		Skin		Muscle		Fat	
Highest	Median	Highest	Median	Highest	Median	Highest	Median	Highest	Median
0.79	*0.36*	*0.44*	*0.26*	*8.3*	*3.8*	*1.2*	*1.0*	*5.0*	*2.0*

The concentrations of residues in eggs and tissues from poultry treated dermally are higher than those from poultry fed piperonyl butoxide and were used in the estimations. The Meeting estimated a maximum residue level of 1 mg/kg for piperonyl butoxide in eggs, 10 mg/kg in poultry edible offal (based on liver and skin) and 5 mg/kg for poultry meat (fat).

The Meeting estimated values for typical piperonyl butoxide residues after direct use (at maximum label concentration) of 0.36 mg/kg in eggs, 2.03 mg/kg in poultry edible offal (mean of 0.26 and 3.8 mg/kg) and of 1.0 mg/kg in poultry meat. These values can be used in the same way as STMR values for estimating long-term dietary intake of piperonyl butoxide.

Dietary risk assessment

Long-term intake

Currently, the ADI for piperonyl butoxide is 0.2 mg/kg bw. IEDIs were calculated for commodities for human consumption for which STMR values had been estimated by the present Meeting. The results are shown in Annex 3.

The IEDIs for the five GEMS/Food regional diets, on the basis of the estimated STMRs, ranged from 20 to 40% of the ADI. The Meeting concluded that the long-term intake of residues of piperonyl butoxide resulting from its uses that have been considered by the JMPR is unlikely to present a public heath concern.

Short-term intake

The 2001 JMPR concluded that an acute RfD for piperonyl butoxide was unnecessary. The Meeting therefore concluded that short-term dietary intake of piperonyl butoxide residues is unlikely to present a risk to consumers.

4.22 PROCHLORAZ (142)

Toxicology

Prochloraz (*N*-propyl-*N*-[2-(2,4,6-trichlorophenoxy)ethyl]-1*H*-imidazole-1-carboxamide) is a broad-spectrum fungicide. It acts by inhibiting ergosterol biosynthesis. Its toxicity was first evaluated by the

Meeting in 1983, when an ADI of 0–0.01 mg/kg bw was established on the basis of a NOAEL of 0.9 mg/kg bw per day in a 2-year study in dogs and a NOAEL of 1.3 mg/kg bw per day in a 2-year study in rats. Since that time, several studies have been conducted: on the absorption, distribution, metabolism, and excretion of prochloraz; on its ability to irritate the skin and eye; on developmental toxicity in rabbits; and on the toxicity of plant metabolites. Prochloraz was re-evaluated within the periodic review programme of the Codex Committee on Pesticide Residues.

After oral administration to rats, prochloraz was rapidly and completely excreted in urine and faeces. There was a noticeable sex difference, faecal excretion predominating in females. After administration of a single oral dose of 5 mg/kg bw [^{14}C]prochloraz to male and female rats with cannulated bile ducts, the radiolabel was recovered quantitatively, with no apparent sex difference. Prochloraz was well absorbed, a mean of 74% of the dose being recovered in the bile, urine, cage washings, and carcass. Biliary excretion was the major route of elimination. After an oral dose of 5 mg/kg bw, the tissue concentrations were very low; only the liver contained > 0.1 mg/kg 96 h after dosing. By 96 h after a dose of 100 mg/kg bw, the concentrations in liver, kidneys, blood, and plasma of animals of each sex and in the lungs and adrenals of females were > 1 mg/kg.

The main metabolic pathway at both doses involved cleavage of the imidazole ring and initial loss of small fragments, to give *N*-formyl-*N'*-2-(2,4,6-trichlorophenoxy)ethylurea and *N*-propyl-*N*-2-(2,4,6-trichlorophenoxy)ethylurea, which, together with a considerable quantity of unchanged prochloraz, were the main compounds found in the faeces. Further metabolism yielded the phenoxy ethylurea, which was excreted mainly in the faeces or further metabolized to the phenoxyethanol and then to the acid. These latter compounds were excreted mainly in the urine in free or conjugated forms, and trichlorophenoxyacetic acid was the main metabolite in urine. A small amount of this acid may be further metabolized to trichlorophenol, which was also excreted in the urine. A minor metabolic pathway involves aromatic hydroxylation.

Prochloraz has low acute toxicity. The LD_{50} in rats treated orally was 1600–2400 mg/kg bw, and the main toxic effects were reversible central nervous system depression and gastrointestinal irritation. WHO has classified prochloraz as "slightly hazardous". The LD_{50} after dermal application was > 2100 mg/kg bw in rats and > 3000 mg/kg bw in rabbits, and the LC_{50} in rats exposed by inhalation for 4 h was > 2.2 mg/l of air, the highest achievable concentration. The substance was not irritating to the skin of rabbits after a 4-h exposure, was not irritating to the eyes of rabbits, and did not sensitize the skin of guinea-pigs in a Magnusson and Kligman maximization test.

In short-term studies in mice, rats, and dogs, the liver was the principal target organ. Prochloraz is a potent inducer of the hepatic microsomal mixed-function oxidase system of rats and mice after oral administration. The spectrum of induction was similar to that caused by phenobarbital, with increased content and activity of cytochrome P450 enzymes. In a 14-day range-finding study in dogs given 40 mg/kg bw per day, serum alkaline phosphatase activity increased progressively from day 3 throughout treatment. The NOAEL for the increase in alkaline phosphatase activity at day 3 was 10 mg/kg bw per day. In 13-week studies, liver weights were increased in all three species; this response was considered to reflect induction of the hepatic mixed-function oxidase system. In mice and rats, hepatocyte enlargement was observed, with periportal fat infiltration and glycogen loss in mice. No histopathological changes were observed in the liver in dogs. In all studies, the effect was dose-related and showed partial reversal after a 4-week recovery period. Dogs also had decreased weights of the prostate and testis. The NOAELs were 6 mg/kg bw per day in mice and 2.3 mg/kg bw per day in dogs, but no NOAEL could be identified in rats, as at the lowest dose, 6 mg/kg bw per day, increased liver weights, and occasional signs of intoxication (increased salivation, diarrhoea) were observed.

In long-term studies in mice and rats and in a 2-year study in dogs, the liver was again the principal target organ. The NOAELs were 1.3 mg/kg bw per day in rats and 0.9 mg/kg bw per day in dogs; no carcinogenic effect was observed in rats. In the study in mice, an increased incidence of liver

adenomas and carcinomas was found in both males and females at concentrations ≥ 325 ppm. No significant difference from controls was found in the number of liver tumours in animals of either sex at 78 ppm, equal to 7.5 mg/kg bw per day, which was therefore the NOAEL. Prochloraz was hepatocarcinogenic in mice.

A comprehensive range of studies of genotoxicity gave consistently negative results, except for a weakly positive response in a test for sister chromatid exchange in Chinese hamster ovary cells in vitro in both the presence and the absence of an exogenous metabolic activation system. The Meeting concluded that prochloraz is unlikely to be genotoxic.

Investigation of the effects of prochloraz on the initiation and promotion stages of hepatocarcinogenesis in rats suggested that the substance acts as a weak tumour promoter but does not initiate the process. It was a weak, rodent-specific hepatocarcinogen, with a mode of action similar to that of phenobarbital. The Meeting concluded that the increased incidence of tumours observed in the liver was a threshold phenomenon that was species-specific, and that prochloraz was therefore unlikely to pose a carcinogenic risk to humans.

In a two-generation study of reproductive toxicity in rats, reproductive performance was affected only at a concentration of 625 ppm in the diet, as indicated by total litter loss in a few females, reduced mean litter size at birth, higher pup mortality rates at birth, and impaired growth of the offspring; furthermore, parental toxicity was observed. The NOAEL for parental and offspring toxicity was 38 ppm, equal to 3.1 mg/kg bw per day in the parents. Prochloraz was not teratogenic in either rats or rabbits. In a study of developmental toxicity in rats, a dose of 100 mg/kg bw per day was toxic in dams, embryos, and fetuses. The NOAELs were 6 mg/kg bw per day for maternal toxicity and 25 mg/kg bw per day for developmental toxicity. In a study of developmental toxicity in rabbits, both maternal toxicity and embryotoxicity were seen at 160 mg/kg bw per day; the NOAEL for both maternal and fetal toxicity was 40 mg/kg bw per day.

Prochloraz did not affect plasma or erythrocyte cholinesterase activity in rats or dogs.

In a comparative study of the acute toxicity of prochloraz and the plant metabolites *N*-propyl-*N*-2-(2,4,6-trichlorophenoxy)ethylurea and *N*-formyl-*N'*-2-(2,4,6-trichlorophenoxy)-ethylurea in rats treated orally, the signs of toxicity were qualitatively similar, but prochloraz was more acutely toxic than either of the metabolites. Trichlorophenol was also less acutely toxic than prochloraz. In dogs, *N*-formyl-*N'*-2-(2,4,6-trichlorophenoxy)ethylurea and trichlorophenol were less acutely toxic than prochloraz, and *N*-propyl-*N*-2-(2,4,6-trichlorophenoxy)ethylurea elicited a similar toxic response at the same dose. Neither *N*-propyl-*N*-2-(2,4,6-trichlorophenoxy)ethylurea nor *N*-formyl-*N'*-2-(2,4,6-trichlorophenoxy)ethylurea induced reverse mutation in *Salmonella typhimurium*.

Since the initial synthesis of prochloraz in 1974 and its commercial introduction in 1980, only a few cases of skin and eye irritation have been reported in humans heavily exposed to products containing prochloraz.

The Meeting concluded that the existing database was adequate to characterize the potential hazards of prochloraz to fetuses, infants, and children.

The Meeting confirmed the ADI of 0–0.01 mg/kg bw established in 1983, on the basis of a NOAEL for effects on the liver of 0.9 mg/kg bw per day in a 2-year study in dogs, a NOAEL of 1.3 mg/kg bw per day in a 2-year study in rats, and a safety factor of 100.

The Meeting established an acute reference dose of 0.1 mg/kg bw, on the basis of a NOAEL of 10 mg/kg bw per day for effects on the liver at day 3 (increased serum alkaline phosphatase activity) in a 14-day study in dogs, and a safety factor of 100.

A toxicological monograph was prepared.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Mouse	2-year studies of toxicity and carcinogenicity[a]	Toxicity	78 ppm, equal to 7.5 mg/kg bw per day	325 ppm, equal to 33 mg/kg bw per day
		Carcinogenicity	78 ppm, equal to 7.5 mg/kg bw per day	325 ppm, equal to 33 mg/kg bw per day
Rat	2-year studies of toxicity and carcinogenicity[a]	Toxicity	38 ppm, equal to 1.3 mg/kg bw per day	150 ppm, equal to 5.1 mg/kg bw per day
		Carcinogenicity	625 ppm, equal to 28 mg/kg bw per day[c]	–
	Multigeneration study of reproductive toxicity[a]	Parental toxicity	38 ppm, equal to 3.1 mg/kg bw per day	150 ppm, equal to 13 mg/kg bw per day
		Offspring toxicity	38 ppm, equal to 3.7 mg/kg bw per day	150 ppm, equal to 16 mg/kg bw per day
	Study of developmental toxicity[b]	Maternal toxicity	6 mg/kg bw per day	25 mg/kg bw per day
		Embryo/fetotoxicity	25 mg/kg bw per day	100 mg/kg bw per day
Rabbit	Study of developmental toxicity[b]	Maternal toxicity	40 mg/kg bw per day	160 mg/kg bw per day
		Embryo and fetotoxicity	40 mg/kg bw per day	160 mg/kg bw per day
Dog	14-day study of toxicity[b,d]	Toxicity	10 mg/kg bw per day[e]	40 mg/kg bw per day[e]
	2-year study of toxicity[a]	Toxicity	30 ppm, equal to 0.90 mg/kg bw per day	135 ppm, equal to 4.1 mg/kg bw per day

[a]Diet
[b]Gavage
[c]Highest dose tested
[d]This study was used to establish the acute reference dose.
[e]Based on an increase in alkaline phosphatase activity at day 3

Estimate of acceptable daily intake for humans

0–0.01 mg/kg bw

Estimate of acute reference dose

0.1 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 prochloraz

Absorption, distribution, excretion and metabolism in mammals	
Rate and extent of oral absorption	Rapidly and well absorbed; mean of 74% at low dose (bile duct-cannulated rats)
Dermal absorption	Poor; < 2% in pigs
Distribution	Rapid and extensive. At high dose, liver, kidneys, blood, and plasma of males and females and lungs and adrenals of females had concentrations > 1 mg/kg 96 h after dosing.
Potential for accumulation	None

Rate and extent of excretion	Rapid and complete, significant sex difference, faecal excretion predominating in females (70% *vs* 59% in males at low dose). Urinary excretion: 65% in males, 41% in females at high dose.
Metabolism in animals	Major pathway: cleavage of imidazole ring and initial loss of small fragments. Further metabolism yields the urea, which is excreted in faeces or further metabolized to the phenoxyethanol and then to the acid, which is excreted in urine in free and conjugated forms. A small amount may be further metabolized to the trichlorophenol. Minor metabolic pathway involves aromatic hydroxylation.
Toxicologically significant compounds	Prochloraz
Acute toxicity	
Rat, LD_{50}, oral	1600 mg/kg bw
Rat, LD_{50} , dermal	> 2100 mg/kg bw
Rat, LC_{50}, inhalation	> 2.2 mg/l of air (4 h)
Rabbit, skin irritation	Not irritating (4 h)
Rabbit, eye irritation	Not irritating
Guinea-pig, skin sensitization (test method)	Not sensitizing (Magnusson and Kligman)
Short-term studies of toxicity	
Target/critical effect	Liver: increased weight (rats, mice, dogs), hepatocyte enlargement (rats, mice), periportal fat infiltration and glycogen loss (mice) Prostate and testis: decreased weight (dogs)
Lowest relevant oral NOAEL	10 mg/kg bw per day (dogs, 14 days, NOAEL based on increase in alkaline phosphatase activity at day 3) 2.3 mg/kg bw per day (dogs, 90 days)
Lowest relevant dermal NOAEL	No data
Lowest relevant inhalation NOAEL	No data
Genotoxicity	No genotoxic potential
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	Liver (mice, rats, dogs), prostate (dogs)
Lowest relevant NOAEL	0.90 mg/kg bw per day (dogs), 1.3 mg/kg bw per day (rats)
Carcinogenicity	Not carcinogenic in rats Increased incidence of liver adenomas and carcinomas in mice
Reproductive toxicity	
Reproduction target/critical effect	Decreased litter size, increased pup mortality rate, and impaired growth of pups at parentally toxic dose
Lowest relevant reproductive NOAEL	3.1 mg/kg bw per day
Developmental target/critical effect	Embryo and fetotoxicity at maternally toxic dose
Lowest relevant developmental NOAEL	Maternal toxicity: 6 mg/kg bw per day Developmental toxicity: 25 mg/kg bw per day (rats)
Neurotoxicity/delayed neurotoxicity	No concern from other studies
Mechanistic studies	Potent inducer of hepatic microsomal monooxygenase system in rats and mice after oral administration, with spectrum of induction similar to that caused by phenobarbital Weak tumour promoter but not an initiator
Medical data	Few cases of skin and eye irritation after heavy exposure to products containing prochloraz

Summary	**Value**	**Study**	**Safety factor**
ADI	0–0.01 mg/kg bw	2 years, dogs and rats, toxicity	100

Acute RfD	0.1 mg/kg bw	14 days, dogs, toxicity	100

Dietary risk assessment

The theoretical maximum daily intakes from the five GEMS/Food regional diets, on the basis of existing MRLs, represented 30–140% of the ADI (Annex 4). The dietary intake estimates will be refined further during the periodic review of residues of prochloraz.

4.23 PYRIPROXYFEN (200)

Assessment of a proposal for its direct addition to drinking-water for mosquito control

Pyriproxyfen is the common name for 4-phenoxyphenyl(*R*,*S*)-2-(2-pyridyloxy)propyl ether. Residues and toxicity of the compound were evaluated by the 1999 JMPR, which established an ADI of 0-0.1 mg/kg bw on the basis of a 1-year study in dogs. In 2000, the WHO Pesticide Evaluation Scheme evaluated use of a 0.5% granule formulation of pyriproxyfen for mosquito control.

The present Meeting was requested to evaluate the toxicological aspects of the proposed direct addition of pyriproxyfen to drinking-water for the control of *Aedes aegypti*, the vector of dengue fever and dengue haemorrhagic fever. The Meeting also considered the formulation evaluated by the WHO Pesticide Evaluation Scheme (WHOPES).

The pyriproxyfen formulation referred to JMPR by WHOPES contains 0.5% w/w active ingredient, 1.0% emulsifiers, and 3.0% solvent, the remaining constituents being clay and silica. The emulsifier is composed of polyoxyethylene nonylphenol ether, polyoxyethylene alkyl ethers, branched dodecylbenzene sulfonic acid salts, and benzene dialkyl derivatives. The solvent is a mixture of linear alkyl benzene derivatives.

It is proposed that drinking-water stored in jars and other small containers inside and outside the home, rooftop storage tanks, rainwater collection tanks, ground-level reservoirs and cisterns, and drinking-water to which chlorine has been added as a disinfectant be treated with the pyriproxyfen formulation at a concentration of 0.01 mg ai/l. Addition to water supply sources such as reservoirs, streams, and springs is also foreseen. Government specialists and/or pest control operators would be the main users of the formulation, but it might also be distributed to householders to carry out treatment by themselves.

An analytical method based on gas chromatography with a nitrogen-phosphorus detector is available for determining pyriproxyfen at the target concentration of 0.01 mg ai/l. This method could be used for water samples collected and shipped to the laboratory under proper documented storage and handling procedures. No information was available on a method for water analysis that would be suitable for use on-site in the field.

At the target concentration, an assumed extreme drinking-water consumption of 10 l/day, and a body weight of 60 kg, the intake of pyriproxyfen would be approximately 0.002 mg/kg bw per day, or 2% of the ADI of 0–0.1 mg/kg bw. The Meeting concluded that intake of pyriproxyfen at this level would not present an appreciable toxicological risk.

At the target concentration of 0.01 mg ai/l, the expected concentrations of the emulsifiers and solvent would be 0.02 mg/l and 0.06 mg/l, respectively. As only limited information was available to the

Meeting, a comprehensive toxicological evaluation of the emulsifiers and solvents could not be performed. These compounds belong, however, to chemical classes the members of which are widely

used in existing household and agricultural products. The Meeting noted that, even with an extreme daily water consumption of 10 l/day, the intake of each of these chemicals would not exceed 0.01 mg/kg bw per day.

Given the low estimated consumption, the existing widespread use, the low acute toxicity, and the toxicological profile of these types of compounds, the Meeting concluded on the basis of the limited data available that their use in products intended for addition to drinking-water at the levels proposed was unlikely to raise toxicological concerns.

The Meeting noted, however, that considerably more toxicological information than that provided was likely to be available on these emulsifiers and solvents or related compounds. Evaluation of such information might allow an improved risk assessment of these constituents. The Meeting further noted that WHO and national authorities responsible for registering or authorizing specific products for direct addition to drinking-water should assess the risks of the non-active constituents, in conjunction with risk–benefit analyses.

4.24 SPINOSAD (203)

Toxicology

Spinosad is the ISO approved name for a mixture of compounds formed as a fermentation product of the soil organism *Saccharopolyspora spinosa.* The mixture comprises approximately 10 related chemicals, with proteinaceous, carbohydrate, and inorganic salt compounds derived from the fermentation process. Two closely related compounds, spinosyn A and spinosyn D, in a ratio of approximately 6 or 7:1, represent about 88% of the composition of spinosad and are responsible for most of its insecticidal activity. Spinosyn A and spinosyn D differ only in respect to substitution of a hydrogen by a methyl group at a non-metabolically labile position. The remainder of spinosad is made up of a number of closely related spinosyns, which differ in the location of other minor substitutions at various sites around the molecule.

Spinosad, an insecticide which acts by causing rapid excitation of the insect nervous system, is a new insecticidal compound and has not previously been evaluated by JMPR.

The pharmacokinetics and metabolism of the two principal constituents of spinosad, spinosyn A and D, are very similar. Oral administration of spinosyn A or D to rats resulted in rapid but incomplete absorption of > 70% of the dose. Peak blood concentrations of radiolabel were achieved 1 h after administration of 10 mg/kg bw and 2–6 h after administration of 100 mg/kg bw. This delay in achieving peak blood concentrations is likely to reflect saturation of absorption at higher doses. Elimination occurs primarily in the faeces (70–90%) via the bile, and < 10% was recovered from urine. Most of the administered radiolabel was recovered within 24 h. The half-times for spinosyn A and D radiolabel were 25–42 h and 29–33 h, respectively. A large proportion of the material excreted in the faeces had been absorbed and eliminated in the bile, primarily as glutathione conjugates of *N*- and *O*-demethylated spinosyns A and D. Excretion as exhaled $^{14}CO_2$ was negligible. The highest concentrations of tissue residues were identified in fat, liver, kidneys, and lymph nodes. Although the concentrations in the thyroid were not high in comparison with many other tissues shortly after administration of spinosyn A or D, the rate of decline was slow and ultimately resulted in higher concentrations in the thyroid than in other tissues, where the decline was more rapid. Absorbed spinosyn A and D were extensively biotransformed, with glutathione conjugates of *N*- or *O*-demethylated spinosyn A or D as the predominant metabolites.

Technical-grade spinosad had little acute toxicity after oral or dermal administration or inhalation; the LD_{50} values after oral administration were consistently > 2000 mg/kg bw and generally ≥ 5000 mg/kg bw in rats and mice. In one study, however, four of five male rats died after administration of 5000 mg/kg bw by gavage. The LD_{50} in rabbits treated dermally was > 5000 mg/kg bw, and the LC_{50} after inhalation in rats was > 5.2 mg/l.

Spinosad was not irritating to the skin of rabbits and not sensitizing to the skin of guinea-pigs. It caused slight eye irritation in rabbits, which resolved within 48 h.

An extensive range of effects was observed in both short- and long-term studies with repeated doses, and the effects were similar in mice, rats, and dogs.

In short-term studies in mice, rats, and dogs, tissue vacuolation was a consistent observation at the LOAEL. In mice, the overall NOAEL in the 90-day study was 6 mg/kg bw per day, and increased liver weight was also observed at the LOAEL. In rats, the overall NOAEL was 8.6 mg/kg bw per day in three 90-day studies and 21 mg/kg bw per day in two 28-day studies, with increased liver weights again observed at the LOAEL in the 90-day studies. In dogs, the LOAEL in a 28-day study was the lowest dose tested, 6.5 mg/kg bw per day; the NOAEL in a 90-day study was 4.9 mg/kg bw per day; and the NOAEL in a 12-month study was 2.7 mg/kg bw per day. Increased thyroid weights were observed in the 28- and 90-day studies in dogs at and above the LOAEL, in addition to tissue vacuolation. In dogs, however, the lymphatic system was more sensitive to vacuolation than the thyroid, the lymphatic lesions occurring at the LOAEL in both the 90-day and 12-month studies.

In long-term studies in mice and rats, tissue vacuolation and other histological alterations were again observed at and above the LOAEL. In mice, the lungs, lymph nodes, stomach, and tongue were the main organs affected at doses above the NOAEL of 11 mg/kg bw per day. The main histological findings were chronic inflammation, hyperplasia, and hyperkeratosis of the stomach, vacuolation of the parathyroid, pancreas, ovaries, and epididymal epithelial cells, and myopathy of the tongue. In rats, the NOAEL in the 2-year study was 2.4 mg/kg bw per day. The primary organ affected at the LOAEL of 9.5 mg/kg bw per day was the thyroid; the lungs, liver, larynx, and bone marrow were affected at higher doses. Vacuolation was limited to the epithelial cells of the thyroid gland, and inflammation was observed in the thyroid, lung, and larynx. Bone-marrow hyperplasia and slight dilatation of liver sinusoids were also observed.

Strong similarities in other toxic effects were found between species and in the short- and the long-term studies. At the higher doses used in all studies with repeated doses, spinosad was toxic in multiple organs of mice, rats, and dogs, resulting in increased serum activity of liver, muscle, and cardiac enzymes (alanine aminotransferase, alkaline phosphatase, aspartate aminotransferase, and creatinine phosphokinase), microcytic hypochromic anaemia, and increased spleen, thyroid, and liver weights. The histological alterations in a wide range of organs were similar in all species tested, the predominant lesions being cellular vacuolation, inflammatory changes (including necrosis), histiocytosis, regenerative and degenerative changes, increased haematopoiesis, and skeletal myopathy. In the long-term study in rats, the thyroid was the most sensitive organ overall, effects occurring at lower doses than in other organs and resolving more slowly after withdrawal of treatment.

Vacuolation in the thyroid, the most sensitive toxicological end-point overall, was seen in both short- and long-term studies in rats and was shown to be reversible in two studies: a 28-day study in males fed diets containing concentrations equal to doses of up to 120 mg/kg bw per day and a 13-week study in rats of each sex fed diets containing concentrations equal to up to 40-50 mg/kg bw per day.

Selected tissues from rats and mice in the short-term studies were examined by electron microscopy, and the vacuolation was found to be associated with cytoplasmic lamellar inclusion bodies,

reflecting a lysosomal storage disorder. While such disorders may arise through a variety of mechanisms which prevent degradation of cell constituents that are usually processed in the lysosomes, spinosad probably acts through a largely physicochemical mechanism associated with its cationic amphiphilic structure (having both lipophilic and hydrophilic properties in one molecule).

A comparison of spinosad, spinosyn A, and spinosyn D in a 28-day study in rats treated in the diet revealed notable differences in the toxicological profiles of spinosyn A and D. The toxicological effects of spinosyn A were closely similar to those of spinosad, but spinosyn D failed to produce most of the haematological and clinical chemical alterations seen with spinosad or spinosyn A. Consequently, minor variations in the relative proportions of spinosyn A and D in the technical-grade active ingredient are unlikely to alter its toxicological profile significantly.

In long-term studies in mice and rats treated in the diet at doses up to 51 and 49 mg/kg bw per day, respectively, there was no evidence that spinosad is carcinogenic.

Spinosad gave negative results in an adequate range of assays for genotoxicity in vivo and in vitro. The Meeting concluded that spinosad is not genotoxic.

Given the absence of both genotoxicity in appropriate short-term tests and carcinogenicity in long-term studies in rats and mice, the Meeting concluded that spinosad is unlikely to pose a carcinogenic risk to humans.

The reproductive toxicity of spinosad was investigated in a two-generation study in rats. The reproductive effects, a reduced number of pups per litter, and clinical alterations in F_{1a} and F_2 pups, reported only at a dietary concentration adjusted to deliver a constant dose of 100 mg/kg bw per day, the highest dose tested, were attributed to nonspecific parental toxicity rather than to a specific toxic effect on the reproductive system. A reduction in the number of pups per litter was observed in each of three generations of pups at 100 mg/kg bw per day. As a similar finding was not observed at 200 mg/kg bw per day in the study of developmental toxicity in rats, the reduction in pup number per litter may reflect preimplantation losses. The NOAEL for reproductive toxicity was 10 mg/kg bw per day.

In a study of developmental toxicity in rats, dams were given doses up to 200 mg/kg bw per day. Slightly reduced maternal body-weight gain was observed at the highest dose. Unilateral microphthalmia was found at external examination in two fetuses in separate litters at 200 mg/kg bw per day and in one at 50 mg/kg bw per day. Although this is a rare spontaneous malformation in rats, it was discounted as a cluster effect incidental to treatment, for two reasons. First, a similar incidence of this malformation occurred randomly in control and other groups in studies conducted in the same laboratory with the same strain of rat over a number of years; secondly, it occurred in the absence of other developmental effects which normally accompany a treatment-related increase in the incidence of malformation. The absence of ocular malformations in the study of reproductive toxicity at doses up to 100 mg/kg bw per day provides further support for this conclusion. On this basis, the NOAEL for maternal toxicity in rats was 50 mg/kg bw per day, and that for developmental toxicity was 200 mg/kg bw per day, the highest dose tested. In a study of developmental toxicity in rabbits, the does were given spinosad on days 7-19 of gestation at doses up to 50 mg/kg bw per day, with no evidence of embryo or fetal effects, despite maternal toxicity, consisting of weight loss, abortion, and clinical signs at the highest dose. The NOAEL for maternal toxicity was 10 mg/kg bw per day, and that for embryo and fetal toxicity was 50 mg/kg bw per day, the highest dose tested.

Neurotoxicity was investigated in rats by giving them a single dose of up to 2000 mg/kg bw, doses up to 43 mg/kg bw per day for 3 months, or doses up to 49 mg/kg bw per day for 12 months. Comprehensive behavioural and histopathological investigations revealed no evidence of neurotoxicity.

The Meeting concluded that the existing database was adequate to characterize the potential hazards of spinosad to fetuses, infants, and children.

The most sensitive overall toxicological end-point was thyroid vacuolation in rats treated in the diet in a 2-year study. The Meeting established an ADI of 0-0.02 mg/kg bw on the basis of the NOAEL of 2.4 mg/kg bw per day in this study and a 100-fold safety factor.

Spinosad has little acute toxicity. In studies with repeated doses, no acute toxicological alerts were observed that might indicate the need for establishing an acute reference 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	80 ppm, equal to 11 mg/kg bw per day	360 ppm equal to 51 mg/kg bw per day
		Carcinogenicity	360 ppm equal to 51mg/kg bw per day[b]	–
Rat	2-year study of toxicity and carcinogenicity[a]	Toxicity	50 ppm, equal to 2.4 mg/kg bw per day	200 ppm equal to 9.5 mg/kg bw per day
		Carcinogenicity	200 ppm equal to 9.5 mg/kg bw per day[b]	–
	12-month study of neurotoxicity[a]	Neurotoxicity	1000 ppm, equal to 49 mg/kg bw per day[b]	–
	Two-generation study of reproductive toxicity[a]	Parental and offspring toxicity	10 mg/kg bw per day	100 mg/kg bw per day
	Study of developmental toxicity[c]	Maternal toxicity	50 mg/kg bw per day	200 mg/kg bw per day
		Embryo- and fetal toxicity	200 mg/kg bw per day[cb]	–
Rabbit	Study of developmental toxicity[c]	Maternal toxicity	10 mg/kg bw per day	50 mg/kg bw per day
		Embryo- and fetal toxicity	50 mg/kg bw per day[b]	–
Dog	12-month study of toxicity[a]	Toxicity	100/120 ppm, equal to 2.7 mg/kg bw per day	300 ppm, equal to 8.2 mg/kg bw per day

[a]Diet
[b]Highest dose tested
[c]Gavage

Estimate of acceptable daily intake for humans

0–0.02 mg/kg bw

Estimate of acute reference dose

Unnecessary

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

Observations in humans
Further investigation of the mechanism of tissue vacuolation

Relevant end-points for setting guidance values for dietary and non-dietary exposure

Absorption, distribution, excretion, and metabolism in mammals	
Spinosyn A	
Rate and extent of oral absorption	> 70%
Dermal absorption	< 1% after 24 h in rats
Distribution	Rapid; highest concentrations of residues in kidney, lymph nodes, fat, and thyroid at 168 h
Rate and extent of excretion	Rapid, largely complete within 24 h; faeces, > 80%; urine, 6–10%
Potential for accumulation	Limited, but decline in thyroid tissue is slow and prolonged
Metabolism in mammals	Large proportion eliminated unchanged in faeces. Biliary and urinary metabolites primarily glutathione conjugates of spinosyn A and N- and O-demethylated spinosyn A
Spinosyn D	
Rate and extent of oral absorption	> 70%
Distribution	Rapid; highest concentrations of residues in kidney, lymph nodes, fat, and thyroid at 168 h
Rate and extent of excretion	Rapid, largely complete within 24 h; faeces, > 80%; urine, 6–10%
Potential for accumulation	Limited, but decline in thyroid tissue is slow and prolonged
Metabolism in mammals	Large proportion eliminated unchanged in the faeces. Biliary and urinary metabolites primarily glutathione conjugates of spinosyn D and N- and O-demethylated spinosyn D
Toxicologically significant compounds	Spinosyns A, D
Acute toxicity	
Spinosad	
$LD_{50,}$ oral	Spinosad: > 5000 mg/kg bw, mice and female rats > 2000-< 5000 mg/kg bw, male rats Spinosyn A:D (46:50): males, 4400 mg/kg bw; females, > 5000 mg/kg bw
LD_{50}, dermal	Spinosad: > 5000 mg/kg bw, rabbit Spinosyn A:D (46:50): males and females, > 5000 mg/kg bw
LC_{50}, inhalation	> 5.2 mg/l, rats
Dermal irritation	Not irritating, rabbits
Ocular irritation	Slight, rabbits
Dermal sensitization	Not sensitizing, guinea-pigs
Short-term toxicity	
Target/critical effect	Many tissues, vacuolation; thyroid, increased weight; liver, increased aspartate aminotransferase activity
Lowest relevant oral NOAEL	2.7 mg/kg bw per day
Lowest relevant dermal NOAEL	> 1000 mg/kg bw per day (rabbits, 21 days)
Lowest relevant inhalational NOAEL	> 9.5 mg/m^3 (rats, 14 days)
Long-term toxicity and carcinogenicity	
Target/critical effect	Mice, rats, and dogs; many tissues, vacuolation and associated alterations in clinical chemical parameters; anaemia
Lowest relevant NOAEL	2-year study, rats, 2.4 mg/kg bw per day
Carcinogenicity	Not carcinogenic, mice, rats
Genotoxicity	Not genotoxic
Reproductive toxicity	
Reproductive target/critical effect	Reduced number of pups per litter, clinical signs in rat pups secondary to maternal toxicity
Lowest relevant reproductive NOAEL	10 mg/kg bw per day in a two-generation study in rats
Developmental target/critical effect	No developmental effects in rats or rabbits
Lowest relevant developmental NOAEL	50 mg/kg bw per day, rabbits
Neurotoxicity/Delayed neurotoxicity	No evidence of neurotoxicity in a 12-month study in rats at doses up to 49 mg/kg bw per day

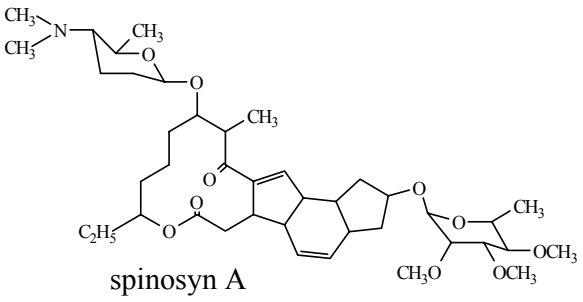
Medical data	No data

Summary	Value	Study	Safety factor
ADI	0–0.02 mg/kg bw	2 years, rats	100
Acute RfD	Unnecessary		

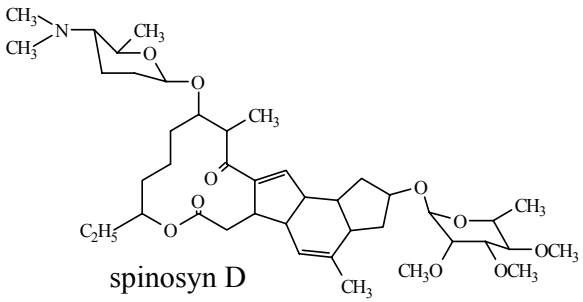
Residue and analytical aspects

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

Spinosad is a naturally derived fermentation product, which has demonstrated insect control activity against a large number of pests, including members of the insect orders Lepidoptera, Coleoptera and Thysanoptera. The product contains a mixture of two structurally similar molecules which are both active insecticidally and have been designated spinosyn A and spinosyn D. *N*-Demethyl-spinosyn A is called spinosyn B, and the analagous product from spinosyn D is called spinosyn B of D.



spinosyn A



spinosyn D

The Meeting received extensive information on the metabolism and environmental fate of spinosad, methods of analysis for residues, stability in freezer storage, national registered use patterns, the results of supervised trials, direct animal treatments, farm animal feeding studies, the fate of residues in processing and national MRLs.

Metabolism

Animals

Spinosyns A and D, reasonably uniformly radiolabelled at 23 carbons in the aglycone ring system, were used in studies of metabolism and environment fate. The amino and rhamnose sugars did not contain the ^{14}C label.

When lactating goats were dosed orally with [^{14}C]spinosyn A or [^{14}C]spinosyn D at the equivalent of 10 ppm in the feed for 3 consecutive days, a considerable portion of the residue (45% spinosyn A and 20% spinosyn D) transferred to tissues and milk. Excretion occurred mainly via the faeces. The parent compounds (spinosyns A and D) were major components of the residue in tissues and milk and constituted an especially high percentage of the total residue in fat (86 and 85%) and milk (71 and 81%). The concentrations of spinosyn A in fat and milk were 3.1 and 0.45 mg/kg, respectively. A number of metabolites were identified and were most prevalent in kidney and liver. The metabolites resulted from *N*-demethylation and hydroxylation of the macrolide ring.

Most of a dose of [^{14}C]spinosyn A (69%) or [^{14}C]spinosyn D (82%) appeared in the excreta of laying hens dosed at the equivalent of 10 ppm in feed for 5 consecutive days. The concentrations in eggs were apparently still increasing at the end of the study. The highest concentrations occurred in fat, parent compound constituting most of the residue; spinosyns A and D constituted 81% and 79% of the fat residue, respectively, at concentrations of 1.8 and 0.81 mg/kg. The parent compounds were also the main or important constituents of the residue in muscle and eggs. Substantial metabolism occurred in liver, where the metabolites were identified as deriving from *N*-demethylation, *O*-demethylation and loss of the forosamine sugar moiety.

When goats were treated dermally once along the backline with [^{14}C]spinosyns A or [^{14}C]spinosyn D, more residue was found in liver and fat than in other tissues. The parent compound was the predominant component of the residue, particularly in fat and milk. The metabolites were produced by *N*-demethylation and hydroxylation of the macrolide ring, a process also identified after oral dosing. The concentrations of residues in milk reached a peak 40–70 h after treatment.

Plants

The Meeting received information on the fate of spinosyns after foliar application to apples, cabbage, tomatoes, turnips, grapes and cotton. The residues of spinosad on fruits, vegetables and other crops are usually at the surface, and the main primary degradation step is photolysis.

Apple trees were sprayed with [^{14}C]spinosyn A or [^{14}C]spinosyn D, one branch being protected from the spray and some apples being protected from light immediately after spraying. The total amount of radiolabel in the apples decreased by about half during the 42 days of sampling, most likely because of growth dilution. The residue occurred mostly on the surface; even after 42 days, about 60% of the remaining residue could be rinsed from the surface. The concentrations of parent spinosyns A and D declined quickly (more than 50% during the first 3 days). The only metabolites that were characterized were spinosyn B and spinosyn B of D, both resulting from *N*-demethylation of the parent compound. The nature of the radiolabelled residues was extensively investigated: they were shown to be polar and to have multiple components. Fractions taken on day 14 from apples sprayed with spinosyn A had low sensitivity in the spinosyn immunoassay, suggesting that the residues did not contain structures similar to those to which the immunoassay is sensitive (spinosyns A, B, C, E, F, K or pseudoaglycone of A).

Both spinosyns A and D were more persistent on apples kept from the light, indicating that photolysis is a major process of degradation. The radiolabelled residues on apples protected from spraying represented only 1.3% of those on apples that had been sprayed directly on day 42, indicating that translocation was minimal. The radiolabel was shown to be incorporated into structural carbohydrates in both treated and untreated leaves.

When grapes were treated separately with [^{14}C]spinosyn A and [^{14}C]spinosyn D, a high percentage of residue was found on the surface, even when aged. When the grapes reached maturity (49 days after treatment), spinosyn A accounted for about 35% of its residue and spinosyn D for 22%. Other components of the residue were polar and numerous and were probably products of photolysis. Hydroxy-spinosyn A and hydroxy-spinosyn D were tentatively identified in the residues.

After cabbage was treated with [^{14}C]spinosyn A and [^{14}C]spinosyn D, the parent compounds disappeared rapidly, most likely by photolysis, and accounted for only 10 and 13% of the residue 3 days after treatment. In a study in which cabbages were treated with [^{14}C]spinosyn A, spinosyns B and K were identified in the residue, which also comprised numerous polar compounds and some incorporation of radiolabel into natural compounds.

When tomato plants were treated four times with [^{14}C]spinosyn A 0 and 3 days before harvest, spinosyn A accounted for 65%and 24% of the radiolabel in the fruit. A portion of the tomatoes (TRR, 0.080 mg/kg as spinosyn A) was processed to juice and seeds plus peel. The concentrations of residue in

the juice (TRR, 0.048 mg/kg as spinosyn A) and seeds plus peel (TRR, 0.28 mg/kg as spinosyn A) indicated that most of the radiolabelled residue was on the surface.

Turnip plants were treated with [^{14}C]spinosyn A and [^{14}C]spinosyn D, and the leaves and roots were subsequently sampled for analysis. By day 10, the parent compounds constituted a minor proportion of the radiolabelled residue in the foliage; however, the residues of parent compounds that reached the root and were protected from sunlight were more persistent. By day 24, the concentrations of parent compound were higher in the roots (A: leaf and root, 0.075 and 0.084 mg/kg; D: leaf and root, 0.016 and 0.036 mg/kg) than in the foliage and constituted a much higher percentage of the total radiolabel in the roots. Spinosyns B, K and B of D, which are products of photolysis, appeared as components of the residue in leaf and root from day 0.

Cotton plants were treated five times with [^{14}C]spinosyn A and [^{14}C]spinosyn D. Cotton seed and fibre were collected from the plots 48 or 49 days after the final treatment and were ginned to separate seed from fibre. The concentrations of radiolabel were 0.29 mg/kg in seed and 0.22 mg/kg in fibre after spinosyn A treatment and 0.11 and 0.075 mg/kg (seed and fibre) after spinosyn D treatment. Despite persistent attempts to identify spinosyn-related compounds, none were identified in cottonseed. Further attempts on separated fractions of the seeds showed that at least some of the radiolabel had become incorporated into natural compounds; the other residues had multiple components and were highly polar. The radiolabel in the fibre was incorporated into cellulose.

Environmental fate

Soil

The losses of spinosad by volatilization from soil and foliar surfaces were too small to be observed at 20 °C in a wind tunnel with air flowing at 1–1.5 m/s.

When [^{14}C]spinosyn A and [^{14}C]spinosyn D on a soil surface were exposed to sunlight in August–September at 39.8° N, the initial disappearance half-lives were 17 and 7 days, respectively. Subsequent disappearance was slow (estimated half-lives > 100 days), indicating that the residues had become absorbed into the soil particles and unavailable for exposure to UV radiation. Spinosyns B and B of D were identified as photoproducts. In another study, spinosyn B was shown to be the primary photoproduct of spinosyn A. Spinosyns A and B disappeared with a half-life of about 20 days. Other photoproducts were characterized as parent compound with a hydroxyl attached to the macrolide ring and an *N*-demethyl derivative, also hydroxylated on the macrolide ring.

Spinosyns A and D were quite persistent under aerobic soil conditions at 20 °C in the dark, with estimated half-lives of 40–75 days and 65–85 days, respectively, in four different soils. Spinosyn B and spinosyn B of D were the main soil metabolites and were more persistent than the parent compounds, with concentrations exceeding those of the parents after 56 days. The amount of mineralization of spinosyn A ranged from 5.8% within 1 year in a sandy silt to 26% within 6 months in a sandy loam, while that of spinosyn D ranged from 4.8% to 25% within 8 months. In another study of aerobic soil metabolism, additional metabolites of spinosyn A were characterized as a hydroxy-spinosyn A and a hydroxy-spinosyn B.

In a series of studies of soil adsorption and desorption, spinosyn A and its metabolite spinosyn B were rated as unlikely to leach in most agricultural soils.

The leaching behaviour of fresh, microbially aged and photolytically aged [^{14}C]spinosyn A and [^{14}C]spinosyn D in soil columns was tested on a loamy sand. The fresh residues were not leached at all.

Some products of aging were leached down the column and into the leachate. The compounds could not be fully identified but were substantially modified from the starting spinosyns.

In a study of confined rotational crops, lettuce, radish and wheat seed were sown into a soil that had been treated 30, 120 and 365 days previously with [^{14}C]spinosyn A at 1.1 kg ai/ha. Radiolabel was present in lettuce leaf, radish root and leaf and wheat forage from crops grown to maturity. No spinosyns or closely related metabolites were identified in the crops. At least some of the radiolabel had been incorporated into natural compounds.

Spinosyn A residues disappeared very quickly (> 70% within 1 day) in field studies of dissipation on a silty clay and a sandy loam. Three metabolites were formed at low concentrations, which declined within 2 months to undetectable levels. Very little of the residue penetrated below the top 15 cm. The mineralization half-life was about 7 months at both sites.

Water–sediment systems

In a study of photolysis, [^{14}C]spinosyn A and [^{14}C]spinosyn D dissolved in sterile pH 7 buffers at 2 mg/l in borosilicate glass tubes were subjected to natural sunlight at 39.9° N in summer. The disappearance half-lives for spinosyns A and D were 22.3 and 19.7 h of sunlight, respectively. The photoproducts were characterized as parent compounds with changes such as saturation of a double-bond and addition of a water molecule. The disappearance half-life for spinosyns A and D in pond water was 4.3 h. The photodegradates were identified as spinosyn B and spinosyn B of D.

In a study of anaerobic sediment water, [^{14}C]spinosyn A and [^{14}C]spinosyn D rapidly became attached to the sediment and were relatively persistent (50% decrease within 6 months). Little mineralization occurred (< 2% within 1 year). The main metabolites were spinosyn B (from A) and spinosyn B of D (from D).

Spinosad in the form of a diluted suspension concentrate formulation was applied to the surface of an aquatic microcosm (1200-l open tank) at a nominal rate of 0.10 kg ai/ha. The concentrations of residues declined rapidly in the water, with a half-life of 1–2 days. Small amounts of spinosyn A reached the sediment, generally accounting for only about 10–15% of that applied. The results suggest that spinosad dissipates principally by degradation (photolysis) and then by adsorption to the sediment.

Methods of analysis

Methods for the analysis of residues of the spinosyns fall into two main categories: HPLC and immunoassay. The methods have been extensively validated on a wide range of substrates.

The HPLC methods, after an extraction specific to the matrix, follow a reasonably standard clean-up, with determination based on UV or MS detection. These methods allow measurement of the individual spinosyns and provide data on spinosyns A, D, K, B and B of D in residue trials. Spinosyn A usually contributes most of the residue, and some HPLC methods are designed to concentrate on spinosyns A and D. The LOQ for most substrates was 0.01 mg/kg.

Immunoassay methods, again after an extraction designed for the matrix, may or may not require clean-up before the final colorimetric determination. The method is specific and represents the sum of the spinosyns and their metabolites. When the HPLC and immunoassay methods were tested side-by-side, the agreement was usually good. The method is based on a commercially available test kit in which the antibody is sensitive to several spinosyns. A portion of a cleaned-up sample extract is incubated with enzyme-conjugated spinosad and magnetic particles coated with antibodies specific to spinosad. The spinosad in the sample and enzyme-conjugated spinosad compete for antibody sites on the magnetic particles. When a magnetic field is applied to the particles at the end of the incubation period, the

spinosad and enzyme-conjugated spinosad bound to antibodies on the particles are held in the sample tube by the magnetic field, while the unbound reagents are decanted. A coloured product, produced by incubating the antibody-bound enzyme conjugate with hydrogen peroxide and 3,3′,5,5′-tetramethylbenzidine, is measured by its absorbance at 450 nm. The assay is sensitive to spinosyn analogues with little or no modification to the trimethylpyranosyl ring, but it is relatively insensitive to analogues or degradates in which the trimethylpyranosyl ring has been modified or is missing. The LOQ for most substrates was 0.01 mg/kg.

Stability of residues in stored analytical samples

Stability in freezer storage was tested for a range of representative substrates. Residues of spinosyns A, D, K, B and B of D were generally stable for the intervals tested:

(iv) 18 months: grapes, peppers, strawberries, wine (estimated 30% decrease in spinosyn D residues in wine within 12 months)
(v) 12 months: tomatoes, cabbage, cotton seed, potato, maize grain, sweet corn forage, sweet corn stover
(vi) 6 months: apples, almond kernels, almond hulls, celery, spinach; incurred residues in liver, kidney, muscle and fat.
(vii) 5 months: milk
(viii) 3 months: apple juice

Definition of the residue

Spinosad is a mixture of spinosyn A and spinosyn D. After it has been applied to crops, the closely related compounds spinosyn B, spinosyn K and spinosyn B of D are formed, principally by photolysis. HPLC methods can be used to measure all these compounds separately, whereas immunoassay allows measurement of these spinosyns and also some other metabolites. Spinosyn A constitutes approximately 85% of the residue initially and in practice represents most of the spinosyn residue; in 482 of 624 (77%) measurements in the residue trials, spinosyn A constituted ≥ 70% of the measured residue. Spinosyn A and spinosyn D together generally constitute more than 90% of the total spinosyn residue.

Spinosyns A and D were major identifiable components of the residue in fat, muscle, kidney, liver and milk of goats dosed orally or treated dermally with spinosyns A and D.

In some trials the residue was measured by the immunoassay method; the residue so measured may be considered sufficiently close to the sum of spinosyn A and spinosyn D for the purpose of estimating maximum resodues levels or dietary intake.

The log P_{ow} of 4 and 4.5 (pH 7) and the studies of animal metabolism indicate that spinosyns A and D should be described as soluble in body fat. However, spinosad residues are incompletely partitioned into the fat of milk. In the study with direct treatment of dairy cows, the ratio of residue in cream to that in milk was 4.2 (mean of 119 observations). In the feeding study in dairy cows, the concentrations of residue in cream were three to five times those in milk.

The Meeting recommended that spinosad be described as fat-soluble for the purposes of residues in meat but not for residues in milk.

The Meeting was aware that national governments had already adopted the sum of spinosyn A and spinosyn D as the residue definition for spinosad.

The Meeting recommended that the residue definition for compliance with MRLs and for estimation of dietary intake be the sum of spinosyn A and spinosyn D.

The proposed definition of the residue for compliance with MRLs and for estimation of dietary intake is the sum of spinosyn A and spinosyn D. The residue is fat-soluble, but residues in milk should be measured in whole milk.

Results of supervised trials

The results of supervised trials were available for use of spinosad on almonds, apples, blueberries, brassica vegetables, celery, citrus, cotton, cucurbits, egg plant, grapes, Japanese radish, kiwifruit, leafy vegetables, legume vegetables, lettuce, maize, navy beans, peppers, potatoes, sorghum, soya beans, stone fruit, strawberries, sweet corn, tomatoes and wheat. No relevant GAP was available to evaluate the data for blueberries, egg plant, grapes, navy beans and strawberries, and only those trials with relevant GAP are discussed below.

The residue definition for spinosad requires addition of residues of spinosyns A and D. In this calculation, when the concentration of residue of spinosyn D was below the LOQ, it was assumed to be zero, except when the concentrations of residues of both spinosyns A and D were below the LOQ. In that case, the total was taken as below the LOQ, which is a reasonable assumption because the concentration of spinosyn D is usually much lower than that of spinosyn A. For example:

Spinosyn A	Spinosyn D	Sum of spinosyns A and D
0.59	0.082	0.67
0.052	< 0.01	0.052
< 0.01	< 0.01	< 0.01

When residues had been measured in a sample by both HPLC and immunoassay, the results from the HPLC method were preferentially chosen for evaluation.

Citrus

Spinosad is registered in the USA for use on citrus fruits at 0.18 kg ai/ha with a PHI of 1 day. The concentrations of residues resulting from trials in the USA in 1996 that met those conditions were: grapefruit, 0.013, 0.021, 0.03, 0.061, 0.086 and 0.19 mg/kg; lemon, 0.021, 0.037, 0.056 and 0.14 mg/kg; and oranges, 0.01, 0.017, 0.031, 0.044, 0.046, 0.053, 0.053, 0.07, 0.11, 0.13, 0.14, 0.14 and 0.15 mg/kg. The residues in the three fruits appeared to be from the same population and were therefore evaluated together. The concentrations of spinosad residues in citrus in 23 trials that matched GAP in the USA, in ranked order (median underlined), were: 0.01, 0.013, 0.017, 0.021, 0.021, 0.03, 0.031, 0.037, 0.044, 0.046, 0.053 (2), 0.056, 0.061, 0.07, 0.086, 0.11, 0.13, 0.14 (3), 0.15 and 0.19 mg/kg.

The Meeting estimated a maximum residue level of 0.3 mg/kg and an STMR value of 0.053 mg/kg for spinosad in citrus whole fruit.

Six samples of orange from the trials were peeled, and residues were measured in the peeled oranges. In five of the peeled oranges, the concentrations of residues were < 0.01 mg/kg (0.017, 0.031, 0.046, 0.053 and 0.20 mg/kg in the whole oranges). In one peeled orange (0.14 mg/kg in the whole orange), the concentration was 0.01 mg/kg, and this finding was taken as evidence that the concentrations in the edible portion were usually below the LOQ but occasionally reached 0.01 mg/kg.

The Meeting estimated an STMR value for spinosad in citrus edible portion of 0.01 mg/kg.

Apple

In Japan, spinosad is registered for use on apple at a spray concentration of 0.01 kg ai/hl and harvesting 3 days after the final application. In two trials in Japan that matched GAP, the concentrations of residues of spinosyn A were 0.03 and 0.17 mg/kg.

GAP in the USA permits application of spinosad at 0.18 kg ai/ha on apples with a PHI of 7 days. The concentrations of spinosad residues, in ranked order, in apples from 32 trials that matched GAP were: < 0.01 (8), 0.01 (4), 0.014, 0.015 (2), 0.016, 0.017, 0.020, 0.024 (3), 0.025, 0.028, 0.032, 0.033 (2), 0.036, 0.041 (2), 0.045, 0.078 and 0.080 mg/kg.

The results of the Japanese trials were not included in the evaluation because they probably did not represent the same population as those from the USA. The Meeting estimated a maximum residue level of 0.1 mg/kg and an STMR value of 0.0165 mg/kg for spinosad in apples.

Stone fruits

The results of trials in Japan on peach could not be evaluated because the results were for peel and flesh rather than fruit. Trials on nectarine in Chile could not be evaluated because the conditions did not match GAP.

GAP in the USA permits application of spinosad at 0.14 kg ai/ha with harvesting 7 days after the final application for cherries, plums and prunes or 14 days for peach, nectarine and apricot. The concentrations of residues, in ranked order, from eight trials on cherry that met GAP in the USA were: < 0.02, 0.023, 0.03, 0.04, 0.06, 0.083 and 0.11 (2) mg/kg; those in seven trials on peach were: < 0.02 (3), 0.03, 0.05 and 0.055 (2) mg/kg; and those in five trials on plum were: < 0.02 (5) mg/kg.

The Meeting agreed that cherries, peaches and plums represent the stone fruit group and that cherries and peaches would usually have the highest concentrations of residues in the group. Therefore, a maximum residue level could be recommended for stone fruit. The concentrations in ranked order in the 20 trials (median underlined) were: < 0.02 (9), 0.023, 0.03 (2), 0.04, 0.05, 0.055 (2), 0.06, 0.083 and 0.11 (2) mg/kg. The Meeting estimated a maximum residue level of 0.2 mg/kg and an STMR value of 0.0265 mg/kg for spinosad in stone fruits.

Kiwifruit

GAP in New Zealand permits application of spinosad at a spray concentration of 0.0048 kg ai/hl and harvesting 120 days after the final application on kiwifruit. In seven trials in New Zealand in 1998–99 which matched the application rate and with PHIs of 118–142 days, the concentrations of spinosad residues, in ranked order, were: < 0.01 (3) 0.02 (2) and < 0.05 (2) mg/kg.

The Meeting estimated a maximum residue level of 0.05 mg/kg and an STMR value of 0.02 mg/kg for spinosad in kiwifruit.

Brassica vegetables

Spinosad is registered in Australia for use on broccoli, cauliflower, cabbage and Brussels sprouts at 0.096 kg ai/ha with a PHI of 3 days. In trials in Australia that matched GAP conditions, the concentrations of spinosad residues were: 0.06, 0.08 and 0.39 mg/kg in broccoli; 0.02 mg/kg in cauliflower; < 0.01 mg/kg in cabbage; and 0.02 and 0.03 mg/kg in Brussels sprouts.

Spinosad is registered in New Zealand for use on brassica vegetables at 0.048 kg ai/ha with a PHI of 3 days. In trials in New Zealand that matched GAP, the concentrations were: 0.02 mg/kg in cauliflower and < 0.01 mg/kg in cabbage.

Spinosad is registered in Japan for use on cabbage at a spray concentration of 0.01 kg ai/hl and a PHI of 3 days. In trials in Japan that matched GAP conditions, the concentrations of spinosad residues in cabbage were: < 0.01 and 0.01 mg/kg.

In the USA, spinosad is registered for use on cole crops at 0.18 kg ai/ha with a 1-day PHI. In trials in the USA that matched GAP (0.15 kg ai/ha is sufficiently close to 0.18 kg ai/ha) for cole crops, the concentrations of spinosad residues were: 0.12, 0.16, 0.19, 0.35, 0.36, 0.39, 0.44 and 0.53 mg/kg in broccoli and 0.01, 0.02, 0.053, 0.080, 0.088, 0.37, 0.95 and 1.1 mg/kg in cabbage.

The data from the USA appeared to represent a different population from those from Australia, Japan and New Zealand. The Meeting agreed that the data from the USA for cabbage and broccoli represented the same population and could be combined for brassica vegetables. The concentrations of spinosad residues in brassica vegetables from the 16 trials in the USA, in ranked order, were: 0.01, 0.02, 0.053, 0.080, 0.088, 0.12, 0.16, 0.19, 0.35, 0.36, 0.37, 0.39, 0.44, 0.53, 0.95 and 1.1 mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg and an STMR value of 0.27 mg/kg for spinosad in brassica vegetables.

Cucurbits

Spinosad is registered in the USA for use on cucumbers at 0.14 kg ai/ha with a 1-day PHI. In six trials that matched GAP, the concentrations of spinosad residues in cucumbers, in ranked order, were: 0.01, 0.024, 0.046, 0.052, 0.053 and 0.059 mg/kg.

Spinosad is registered in the USA for use on cucurbit vegetables other than cucumbers at 0.14 kg ai/ha with a 3-day PHI. In six trials in the USA that matched GAP, the concentrations of spinosad residues in musk melons, in ranked order, were: 0.036, 0.045, 0.054, 0.092, 0.12 and 0.16 mg/kg. In three trials in the USA that matched GAP, the concentrations of spinosad residues in summer squash were: < 0.01, 0.024 and 0.038 mg/kg.

The Meeting agreed to pool the data to support an MRL for cucurbit vegetables, as follows (ranked order): < 0.01, 0.01, 0.024 (2), 0.036, 0.038, 0.045, 0.046, 0.052, 0.053, 0.054, 0.059, 0.092, 0.12 and 0.16 mg/kg. The Meeting estimated a maximum residue level of 0.2 mg/kg and an STMR value of 0.046 mg/kg for spinosad in cucurbit vegetables.

Tomato

In Argentina, spinosad is registered for use on tomato at 0.11 kg ai/ha with harvesting permitted 3 days after the final application. In six trials in Argentina that matched GAP conditions, the concentrations of spinosad residues were: 0.01, 0.02, 0.06 (2), 0.17 and 0.21 mg/kg.

In Australia, spinosad is registered for use on tomato at 0.096 kg ai/ha with harvesting permitted 1 day after the final application. In five trials in Australia that matched GAP conditions, the concentrations of spinosad residues were: 0.02, 0.03 (3) and 0.04 mg/kg. In a trial in New Zealand that matched Australian GAP, the concentration of spinosad residues was 0.04 mg/kg.

GAP in New Zealand for use of spinosad on tomato requires a 3-day PHI after application at 0.048 kg ai/ha. The concentration of spinosad residues in a trial that matched GAP in New Zealand was < 0.01 mg/kg.

Spinosad is registered in the USA for use on fruiting vegetables, including tomato, at 0.18 kg ai/ha with harvesting permitted 1 day after the final application. The concentrations of spinosad residues

in 18 trials that matched GAP (0.15 kg ai/ha is sufficiently close to 0.18 kg ai/ha), in ranked order, were: < 0.01 (2), 0.013, 0.02 (3), 0.023, 0.024, 0.026, 0.03 (3), 0.04 (2), 0.062, 0.086 and 0.11 (2) mg/kg.

As the data on tomato appeared to represent the same population, except for that from New Zealand where the GAP application rate was lower, they may be combined for evaluation. The concentrations of spinosad residues in tomatoes in the 30 trials, in ranked order, were: < 0.01 (2), 0.01, 0.013, 0.02 (5), 0.023, 0.024, 0.026, 0.03 (6), 0.04 (4), 0.06 (2), 0.062, 0.086, 0.11(2), 0.17 and 0.21 mg/kg. The Meeting estimated a maximum residue level of 0.3 mg/kg and an STMR value of 0.03 mg/kg for spinosad in tomato.

Peppers

In Australia, spinosad is registered for use on peppers at 0.096 kg ai/ha with harvesting permitted 1 day after the final application. In two trials in Australia that matched GAP conditions, the concentrations of spinosad residues on sweet peppers were 0.04 and 0.12 mg/kg.

Spinosad is registered in the USA for use on fruiting vegetables, including peppers, at 0.18 kg ai/ha with harvesting permitted 1 day after the final application. The concentrations of spinosad residues in eight trials that matched GAP (0.15 kg ai/ha is sufficiently close to 0.18 kg ai/ha) in hot and sweet peppers, in ranked order, were: 0.02, 0.03, 0.05 (2), 0.062, 0.073, 0.14 and 0.17 mg/kg.

The Meeting agreed to combine the data on peppers from Australia and the USA, as follows: 0.02, 0.03, 0.04, 0.05 (2) 0.062, 0.073, 0.12, 0.14 and 0.17 mg/kg. The Meeting estimated a maximum residue level of 0.3 mg/kg and an STMR value of 0.056 mg/kg for spinosad in peppers.

Sweet corn

In the USA, spinosad is registered for use on sweet corn at 0.11 kg ai/ha with harvesting permitted 1 day after the final application. In nine trials in USA that matched GAP conditions, the concentrations of spinosad residues on sweet corn were below the LOQ (0.01 mg/kg). The Meeting estimated a maximum residue level of 0.01* and an STMR value of 0.01 mg/kg for spinosad in sweet corn.

Leafy vegetables

In the USA, spinosad is registered for use on cole crops, including mustard greens, at 0.18 kg ai/ha with a 1-day PHI. In trials in the USA that matched GAP (0.15 kg ai/ha is sufficiently close to 0.18 kg ai/ha) for cole crops, the concentrations of spinosad residues in mustard greens were: 0.040, 1.0, 3.5, 4.0, 5.0, 5.5, 5.6 and 5.7 mg/kg.

Australian GAP permits an application rate of 0.096 kg ai/ha and a 3-day PHI for use of spinosad on lettuce. In three trials in Australia that matched GAP conditions, the concentrations of spinosad residues in head lettuce were: 0.21, 1.1 and 1.7 mg/kg.

Spinosad is registered in Australia for use on Chinese cabbage at 0.096 kg ai/ha with a PHI of 3 days. In a trial in Australia that matched GAP conditions, the concentration of spinosad residues in Chinese cabbage was 0.10 mg/kg.

Spinosad is registered in Japan for use on Chinese cabbage at a spray concentration of 0.01 kg ai/hl with a PHI of 3 days. In trials in Japan that matched GAP conditions, the concentration of spinosad residues in Chinese cabbage was 0.09 (2) mg/kg.

In the USA, spinosad is registered for use on leafy vegetables at 0.18 kg ai/ha with a 1-day PHI. In trials in the USA that matched GAP conditions (0.15 kg ai/ha is sufficiently close to 0.18 kg ai/ha), the

concentrations of spinosad residues were 0.052, 0.11, 0.12, 0.67, 0.73, 0.77, 0.85, 0.93 and 2.0 mg/kg in head lettuce; 1.4, 1.9, 2.0, 4.7, 4.9 and 5.2 mg/kg in leaf lettuce; and 1.5, 1.9, 2.4, 2.8, 2.9, 3.0, 4.0, 4.4 and 4.5 mg/kg in spinach.

The range of residue concentrations was quite wide, but there was overlap among the different crops. The Meeting decided to pool the data to support an MRL for leafy vegetables, as follows (ranked order): 0.040, 0.052, 0.090 (2), 0.10, 0.11, 0.12, 0.21, 0.67, 0.73, 0.77, 0.85, 0.93, 1.0, 1.1, 1.4, 1.5, 1.7, 1.9 (2), 2.0 (2), 2.4, 2.8, 2.9, 3.0, 3.5, 4.0 (2), 4.4, 4.5, 4.7, 4.9, 5.0, 5.2, 5.5, 5.6 and 5.7 mg/kg. The Meeting estimated a maximum residue level of 10 mg/kg and an STMR value of 1.9 mg/kg for spinosad in leafy vegetables.

Celery

In the USA, spinosad is registered for use on leafy vegetables, including celery, at 0.18 kg ai/ha with a 1-day PHI. In trials in the USA that matched GAP (0.15 kg ai/ha is sufficiently close to 0.18 kg ai/ha), the concentrations of spinosad residues in celery were: 0.40, 0.45, 0.84, 1.1, 1.3 and 1.7 mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg and an STMR value of 0.97 mg/kg for spinosad in celery.

Legume vegetables

Spinosad is registered in the USA for use on succulent beans at 0.11 kg ai/ha with harvesting permitted 3 days after the final application. In 11 trials that matched GAP, the concentrations of spinosad residues in snap beans seed and pod, in ranked order, were: < 0.01 (2), 0.02 (3), 0.042, 0.077, 0.085, 0.14, 0.15 and 0.20 mg/kg. In seven trials that matched GAP, the concentrations of spinosad residues in snow peas seed and pod, in ranked order, were: < 0.01, 0.01, 0.03, 0.039, 0.063, 0.20 and 0.21 mg/kg.

The Meeting agreed to pool the data for snap beans and snow peas to estimate an MRL for legume vegetables. The concentrations of residues, in ranked order, were: < 0.01 (3), 0.01, 0.02 (3), 0.03, 0.039, 0.042, 0.063, 0.077, 0.085, 0.14, 0.15, 0.20 (2) and 0.21 mg/kg. The Meeting estimated a maximum residue level of 0.3 mg/kg and an STMR value of 0.041 mg/kg for spinosad in legume vegetables.

Soya bean (dry)

Spinosad is registered in Brazil for use on soya beans with application at 0.024 kg ai/ha and a 9-day PHI. In two trials in Brazil with a 9-day PHI but with application at 0.048 kg ai/ha, the concentration of spinosad residues was below the LOQ (0.01 mg/kg).

Spinosad is registered in the USA for use on soya beans at 0.070 kg ai/ha with harvesting permitted 28 days after the final application. The concentrations of spinosad residues were below the LOQ (0.01 mg/kg) in seven trials in which the application rate was 0.38 kg ai/ha and the PHI was 28 days.

The Meeting agreed that the residue in soya beans is effectively zero because application rates higher than that of GAP did not produce concentrations of residues exceeding the LOQ. The Meeting estimated a maximum residue level of 0.01* mg/kg and an STMR value of 0 mg/kg for spinosad in soya bean (dry).

Potato

In Brazil, spinosad is registered for use on potato at 0.20 kg ai/ha with harvesting permitted 3 days after the final application. In two trials that matched GAP and two trials at 0.40 kg ai/ha, the concentrations of spinosyn A residues were below the LOQ (0.01 mg/kg).

Spinosad is registered in the USA for use on tuber vegetables including potatoes at 0.11 kg ai/ha with harvesting permitted 7 days after the final application. In 14 trials that matched GAP, the concentrations of spinosad residues were below the LOQ (0.005 mg/kg). In two trials with an application rate of 0.62 kg ai/ha and harvesting 7 and 8 days after the third treatment, the concentrations of residues were also below the LOQ (0.005 mg/kg).

The Meeting agreed that, because higher application rates did not result in measurable residues, the concentration in potatoes was effectively zero. The practical LOQ for enforcement purposes is 0.01 mg/kg. The Meeting estimated a maximum residue level of 0.01* mg/kg and an STMR value of 0 mg/kg for spinosad in potato.

Radish, Japanese

GAP in Japan permits three spray applications of spinosad at a concentration of 0.01 kg ai/hl with harvesting 7 days after the final application. In two trials in which the conditions matched GAP, the concentrations of spinosad residues were < 0.01 and 0.01 mg/kg in Japanese radish roots and 0.07 and 0.23 mg/kg in the leaves.

The Meeting noted that the concentrations in the leaves would be included in the recommendations for leafy vegetables. Only two trials were available, and, even though Japanese radish is a minor crop, the Meeting agreed that the number of trials was insufficient to make a recommendation.

Cereals

Spinosad is registered in Brazil for use on maize at an application rate of 0.048 kg ai/ha and a 7-day PHI. In eight trials in Brazil, all with a 7-day PHI but with application rates of 0.048 kg ai/ha (two trials), 0.060 kg ai/ha (two trials), 0.096 kg ai/ha (two trials) and 0.12 kg ai/ha (two trials), the concentrations of spinosad residues were all below the LOQ (0.01 mg/kg).

Spinosad is registered in the USA for use on maize at 0.11 kg ai/ha with harvesting permitted 28 days after the final application. In five trials in which the application rate was 0.50 kg ai/ha and the PHI 27–30 days, the concentrations of residues were all below the LOQ (0.01 mg/kg).

The Meeting agreed that the concentration of residues in maize is effectively zero because rates higher than that in GAP did not produce concentrations exceeding the LOQ. The Meeting estimated a maximum residue level of 0.01* mg/kg and an STMR value of 0 mg/kg for spinosad in maize.

Spinosad is registered in the USA for use on sorghum at 0.11 kg ai/ha with harvesting permitted 7 days after the final application. In eight trials that matched GAP, the concentrations of spinosad residues in sorghum, in ranked order, were: 0.03, 0.088, 0.12, 0.16, 0.17, 0.18, 0.47 and 0.68 mg/kg.

The Meeting estimated a maximum residue level of 1 mg/kg and an STMR value of 0.165 mg/kg for spinosad in sorghum.

Spinosad is registered in the USA for use on wheat at 0.11 kg ai/ha with harvesting permitted 21 days after the final application. The Meeting was unable to evaluate the trials on wheat in the USA, because spinosad was used at 0.50 kg ai/ha.

Almonds

Spinosad is registered in the USA for use on almonds at 0.18 kg ai/ha with harvesting permitted 14 days after the final application. The concentrations of spinosad residues in almond kernels were below the LOQ (0.01 mg/kg) in 12 trials that were in line with GAP conditions.

The Meeting estimated a maximum residue level of 0.01* mg/kg and an STMR value of 0.01 mg/kg for spinosad in almonds.

Cotton seed

In Australia, spinosad is registered for use on cotton at 0.10 kg ai/ha with harvesting permitted 28 days after the final application. In six trials in Australia that matched GAP conditions, the concentrations of spinosad residues in cotton seed were below the LOQ (0.01 mg/kg). In six trials at higher application rates (two trials at 0.15 kg ai/ha and four trials at 0.20 kg ai/ha) with harvesting 28 days after the final application, the concentrations of residues in cotton seed were all below the LOQ (0.01 mg/kg).

Spinosad is registered in Brazil for use on cotton, with application at 0.072 kg ai/ha and a 7-day PHI. In two trials in Brazil with a 7-day PHI and application rates of 0.072 and 0.14 kg ai/ha, the concentrations of spinosad residues in cotton seed were below the LOQ (0.01 mg/kg).

Spinosad is registered in the USA for use on cotton at 0.10 kg ai/ha with harvesting permitted 28 days after the final application. The concentrations of spinosad residues in cotton seed were below the LOQ (0.01 mg/kg) in 19 trials in which the PHI was 28 days but with various application rates (one trial at 0.10 mg/kg, one at 0.12 kg ai/ha, 14 at 0.125 kg ai/ha, one at 0.14 kg ai/ha and two at 0.20 kg ai/ha).

In summary, the concentrations of spinosad residues in cotton seed were below the LOQ (0.01 mg/kg) in 33 trials on cotton The Meeting noted that, as residues did reach cotton seed in a processing trial with an exaggerated application rate, the concentration could not be considered to be effectively zero.

The Meeting estimated a maximum residue level of 0.01* mg/kg and an STMR value of 0.01 mg/kg for spinosad in cotton seed.

Maize forage and fodder

In the USA, a 7-day PHI is required for use of spinosad on maize (field corn) for maize forage. In 12 trials on sweet corn that matched GAP requirements for maize forage, the concentrations of spinosad residues in sweet corn forage, in ranked order, were: 0.12, 0.074, 0.087, 0.098, 0.099, 0.16, 0.17, 0.18, 0.36, 0.44, 0.48 and 0.49 mg/kg (fresh weight) and 0.12, 0.41, 0.49, 0.50, 0.53, 0.67, 0.72, 1.2, 1.3, 2.3, 2.8 and 3.1 mg/kg (dry weight).

The Meeting estimated a maximum residue level of 5 mg/kg and an STMR value of 0.70 mg/kg for spinosad in maize forage.

In the USA, a 28-day PHI is required for use of spinosad on maize (field corn) for maize fodder. In 12 trials on sweet corn that matched GAP requirements for maize fodder, the concentrations of spinosad residues in sweet corn stover, in ranked order, were: 0.03, 0.053, 0.074, 0.097, 0.099, 0.11, 0.12, 0.17 (2), 0.23, 0.46 and 0.68 mg/kg (fresh weight) and 0.13, 0.15, 0.21, 0.29, 0.38, 0.41, 0.52, 0.61 (2), 0.81, 0.92 and 2.1 mg/kg (dry weight).

The Meeting estimated a maximum residue level of 5 mg/kg and an STMR value of 0.46 mg/kg for spinosad in maize fodder.

Sorghum forage

In the USA, a 7-day PHI is required for use of spinosad on sorghum for fodder and a 14-day PHI for forage. The concentrations of spinosad residues in sorghum forage in four trials that matched GAP were: 0.052, 0.078, 0.095 and 0.18 mg/kg (fresh weight) and 0.18, 0.24, 0.28 and 0.47 mg/kg (dry weight).

The Meeting agreed that the number of supervised trials was insufficient to recommend a maximum residue level.

Wheat forage, hay and straw

In the USA, an application rate of 0.11 kg ai/ha is required for use of spinosad on wheat, with a 21-day PHI required for grain and straw and 14 days for forage and hay. The concentrations of spinosad residues in wheat forage in six trials that matched GAP were: < 0.01 (2), 0.01 (2), 0.05 and 0.054 mg/kg (fresh weight) and 0.04, < 0.05 (2), 0.06, 0.22 and 0.23 mg/kg (dry weight). The Meeting noted that the concentration in forage was lower than that in straw and fodder.

The concentrations of spinosad residues in six trials in the USA that matched GAP were: < 0.01, 0.019, 0.05, 0.052, 0.15 and 0.17 mg/kg (fresh weight) and < 0.02, 0.03, 0.06, 0.13, 0.21 and 0.27 mg/kg (dry weight) in wheat hay; and < 0.01, 0.19, 0.37, 0.53, 0.56 and 0.73 (fresh weight) and < 0.02, 0.22, 0.41, 0.59, 0.64 and 0.83 mg/kg (dry weight) in wheat straw. The combined data for wheat straw and hay were: < 0.02 (2), 0.03, 0.06, 0.13, 0.21, 0.22, 0.27, 0.41, 0.59, 0.64 and 0.83 mg/kg (dry weight).

The Meeting estimated a maximum residue level of 1 mg/kg and an STMR value of 0.215 mg/kg for spinosad in wheat straw and fodder.

Almond hulls

Spinosad is registered in the USA for use on almonds at 0.18 kg ai/ha with harvesting permitted 14 days after the final application. In 12 trials in line with GAP conditions, the concentrations of spinosad residues in almond hulls, in ranked order, were: 0.20, 0.27, 0.28, 0.37, 0.45, 0.49, 0.62, 0.67, 0.69, 0.73, 0.82 and 1.1 mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg and an STMR value of 0.56 mg/kg for spinosad in almond hulls.

Fate of residues during processing

The Meeting received information on the fate of incurred residues of spinosad during the processing of apples, oranges, grapes, tomatoes and cotton seed. Processing factors were calculated for commodities derived from these raw agricultural commodities on the basis of the concentrations of residues of spinosyn A or spinosyns A and D measured by HPLC or of spinosad by immunoassay. The results for spinosyn A or the sum of spinosyns A and D were similar, except at low concentrations, where analytical errors and rounding of data influenced the results When the concentration of residues in a processed commodity did not exceed the LOQ, the processing factor was calculated from the LOQ and was prefixed with a 'less than' symbol (<).

The processing factors for apples were 2.1 and 5.2 (mean, 3.9) for processing to wet pomace, < 0.09 and 0.07 (mean, 0.08) to juice and 0.09 to purée. Application of these factors to the STMR value for apples resulted in STMR-P values of 0.064 mg/kg for wet apple pomace, 0.0013 mg/kg for apple juice and 0.0015 mg/kg for apple purée.

The processing factors for oranges were < 0.13 to juice and 2.2 to dried pulp. Application of these factors to the STMR value for citrus whole fruit resulted in STMR-P values of 0.0069 mg/kg for orange juice and 0.12 mg/kg for dried processed citrus pulp.

The processing factors for tomatoes to juice were 0.026 and 0.25; as the two values did not agree, the Meeting agreed to choose the higher value. The processing factors for tomatoes to purée were 0.18 and 0.58, and again the higher value was chosen. The processing factor for tomato to paste was 1.94. Application of these factors to the STMR value for tomatoes resulted in STMR-P values of 0.0075 mg/kg for tomato juice, 0.017 mg/kg for tomato purée and 0.059 mg/kg for tomato paste.

Application of the processing factors for cotton seed to hulls (0.20), meal (< 0.17), crude oil (0.18) and refined oil (0.20) to the STMR value for cotton seed resulted in STMR-P values of 0.0020 mg/kg for hulls, 0.0017 mg/kg for meal, 0.0018 mg/kg for crude oil and 0.0020 mg/kg for refined oil.

The Meeting recommended MRLs of 0.01* mg/kg for crude and edible cotton seed oils on the basis of the LOQ of the available analytical method.

Residues in animal commodities

Direct treatment of farm animals

Spinosad is registered for direct use on sheep in Australia, by jetting and wound dressing. The jetting mixture contains 25 mg ai/l and is applied at a rate of 0.5 l per month of wool growth.

In a trial in Australia that matched label instructions, long-wool sheep were treated with a hand-held jetting applicator delivering 5.1 l in a 21-s application time for each sheep. Five animals were slaughtered 5, 12, 15 and 21 days after treatment, and residues were measured in the tissues. The concentrations of spinosad residues were below the LOQ (0.01 mg/kg) in muscle, kidney, liver, back fat and perirenal fat in all samples.

The Meeting estimated a maximum residue level of 0.01* mg/kg for spinosad residues in sheep meat (fat) and sheep offal.

The STMR concept is designed for use in supervised field trials on crops to obtain the typical residue value when a pesticide is used at maximum GAP. The method is not directly applicable to a trial of single direct treatment of animals. However, the Meeting agreed that a typical residue value for a pesticide used directly on animals (at maximum label conditions) would be useful in estimating long-term dietary intake. The Meeting estimated a typical concentration of spinosad residues (from direct use at maximum label conditions) of 0.01 mg/kg in sheep meat and sheep offal.

In the USA, beef and dairy cattle may be treated directly with spinosad in an aqueous suspension formulation as a pour-on. The permitted application rate is 2 mg ai/kg bw, and no restrictions on milk or slaughter intervals are imposed. Animals may also be sprayed (at a concentration of 400 mg/l) at a rate of 0.76 g ai/animal. Spinosad is also approved for treatment of animal housing.

In trials in the USA, groups of Holstein dairy cows underwent five cycles of each of three treatments: (1) body spray with 2 l at 400 mg ai/l every 7 days; (2) body spray with 5 l at 400 mg ai/l every 21 days; or (3) pour-on at 2 mg ai/kg bw every 14 days. The housing was sprayed every 7 days. Residues were measured in milk throughout the study. The animals were slaughtered for tissue collection at intervals after a cycle of treatments. Muscle, kidney, liver and milk were analysed by immunoassay and fat by HPLC; the values reported are for the sum of spinosyns A, D, B and B of D. The concentrations of residues arising from treatments 1 and 2 were similar, but both were much lower than that from treatment

3. The highest concentrations observed after treatment 3 were: 0.28 mg/kg in muscle, 0.87 mg/kg, in kidney, 1.2 mg/kg in liver, 2.7 mg/kg in renal fat, 2.2 mg/kg in subcutaneous fat and 0.65 mg/kg in milk.

The Meeting estimated maximum residue levels of 3 mg/kg for cattle meat (fat), 1 mg/kg for cattle kidney, 2 mg/kg for cattle liver and 1 mg/kg for cattle milk.

As for the sheep treatments, the Meeting agreed that a typical residue value for a pesticide used directly on animals (at maximum label conditions) would be useful in estimating long-term dietary intake. In this case, the median concentration of residues in the tissues of the three animals slaughtered at the shortest interval after treatment (or later if the values were higher later) was taken to represent that typical value. For milk, the highest average concentration for the group on the day after treatment (or later if the values were higher later) was taken to represent the typical value.

The Meeting estimated typical concentrations of spinosad residues (from direct use at maximum label conditions) of 0.078 mg/kg for cattle meat, 0.31 mg/kg for kidney, 0.66 mg/kg for liver and 0.65 mg/kg for milk. These values can be used in the same way as STMR values for estimating long-term dietary intake.

Dietary burden of farm animals

The Meeting estimated the dietary burden of spinosad residues in farm animal on the basis of the diets listed in Appendix IX of the *FAO Manual*. Calculation from MRLs and STMR-P values provides the levels in feed suitable for estimating MRLs for animal commodities, while calculation from STMR and STMR-P values for feed is suitable for estimating STMR values for animal commodities. The percentage of dry matter is taken as 100% when MRLs and STMR values are already expressed as dry weight.

The concentrations of spinosad residues in milk reached a plateau after about 6 days, i.e. relatively rapidly. The maximum residue levels in animal commodities were derived from the MRLs, as stated by the 1997 JMPR.

Estimated maximum dietary burden of farm animals

Commodity	Group	Residue (mg/kg)	Basis	Dry matter (%)	Residue, dry weight (mg/kg)	Choose diets (%)			Residue contribution (mg/kg)		
						Beef cattle	Dairy cows	Poultry	Beef cattle	Dairy cows	Poultry
Apple pomace wet	AB	0.064	STMR-P	40	0.16	10			0.016		
Citrus pulp	AB	0.12	STMR-P	91	0.13						
Maize forage	AF	5	MRL	100	5.0	40	50		2.0	2.5	
Maize fodder	AS	5	MRL	100	5.0						
Wheat straw and fodder, dry	AS	1	MRL	100	1.0						
Sorghum	GC	1	MRL	86	1.2	40	40	80	0.47	0.47	0.93
Almond hulls	AM	2	MRL	90	2.2	10	10		0.22	0.22	
Cotton seed hulls		0.0020	STMR-P	90	0.0022						
Cotton seed meal		0.0017	STMR-P	88	0.0019			20			0.0004
					Total	100	100	100	2.7	3.2	0.93

Estimated STMR dietary burden of farm animals

Commodity	Group	Residue (mg/kg)	Basis	Dry matter (%)	Residue, dry weight (mg/kg)	Choose diets (%)			Residue contribution (mg/kg)		
						Beef cattle	Dairy cows	Poultry	Beef cattle	Dairy cows	Poultry
Apple pomace wet	AB	0.064	STMR-P	40	0.16	10			0.016		
Citrus pulp	AB	0.12	STMR-P	91	0.13						
Maize forage	AF	0.70	STMR	100	0.70	40	50		0.28	0.35	
Maize fodder	AS	0.46	STMR	100	0.46						
Wheat straw and fodder, dry	AS	0.215	STMR	100	0.22						
Sorghum	GC	0.165	STMR	86	0.19	40	40	80	0.08	0.08	0.15
Almond hulls	AM	0.56	STMR	90	0.62	10	10		0.062	0.062	
Cotton seed hulls	SO	0.0020	STMR-P	90	0.0022						
Cotton seed meal	SO	0.0017	STMR-P	88	0.0019			20			0.00039
					Total	100	100	100	0.43	0.49	0.15

The dietary burdens of spinosad for estimating MRLs and STMR values for animal commodities (residue concentrations in animal feeds expressed as dry weight) are: 2.7 and 0.43 mg/kg for beef cattle, 3.2 and 0.49 mg/kg for dairy cattle and 0.93 and 0.15 mg/kg for poultry.

Feeding studies

The Meeting received information on the concentrations of residues arising in tissues and milk when dairy cows were dosed with spinosad in capsules at the equivalent of 1, 3 or 10 ppm in the diet for 28 days. The concentrations in fat were higher than those in other tissues. The transfer factors (concentration of residue in tissue ÷ concentration in feed) for tissues and milk were reasonably consistent at the three dietary levels: fat, 0.65, 0.37, 0.57, mean 0.53; muscle, 0.026, 0.018, 0.028, mean 0.024; kidney, 0.073, 0.095, 0.087, mean 0.085; liver, 0.16, 0.16, 0.18, mean 0.17, milk 28 days, 0.044, 0.048, 0.049, mean 0.047; cream 28 days, 0.18, 0.20, 0.19, mean 0.19.

The average concentration in milk (day 14, HPLC analysis) from the three animals at 1 ppm was 0.044 mg/kg, and that in milk from cows at 3 ppm was 0.13 mg/kg. The highest individual concentrations (HPLC analysis) at 3 ppm in the diet were: 1.7 mg/kg in fat, 0.069 mg/kg in muscle, 0.44 mg/kg in liver and 0.26 mg/kg. in kidney. The mean concentrations (HPLC analysis) in the three animals at 1 ppm were 0.65 mg/kg in fat, 0.0.020 mg/kg in muscle, 0.13 mg/kg in liver and 0.065 mg/kg in kidney.

The Meeting received information on the concentrations of residues in tissues and eggs after laying hens were dosed with spinosad at the equivalent of 0.1, 0.3, 1 or 5 ppm in the diet for 41 days. At the lower feeding levels, the concentrations of residues were often below the LOQ of the analytical method. The values in fat were substantially higher than those in other tissues and eggs. The concentrations in fat from hens at 5 ppm were 8.7 and 7.0 times higher than those in hens at 1 ppm in abdominal and subcutaneous fat, respectively, slightly more than the five times that expected. The concentrations of residues in eggs from hens at 5 ppm reached a plateau by day 13, but the values in eggs were generally below the LOQ (0.01 mg/kg) at lower dietary concentrations.

Maximum residue levels

As the maximum dietary burdens of beef and dairy cattle were 2.7 and 3.2 mg/kg, respectively, the concentrations of residues in tissues and milk were taken as those seen at the dietary concentration of 3 ppm, without interpolation. As the STMR dietary burdens (0.43 and 0.49 mg/kg) wee lower than the lowest dietary concentration, 1 ppm, the resulting residues in tissues and milk were calculated by applying the transfer factors (concentration of residue in tissue or milk ÷ concentration in feed) found at the lowest dietary concentration to the STMR dietary burdens.

The highest individual tissue concentration of residue at the relevant dietary concentration was used in conjunction with the highest dietary burden of residue to calculate the likely highest residue in animal commodities. The mean concentration of residue in tissues from animals at the relevant dietary concentration was used in conjunction with the STMR dietary burden to estimate the STMR values for animal commodities. For milk, the mean concentration of residue at the plateau for the relevant dietary concentration was used to estimate both thehighest residue and the STMR values. As the STMR burden of dairy cows exceeds that of beef cattle, it was used to estimate the STMR value in fat, muscle, liver and kidney.

Feeding level (ppm) *Interpolated* / actual	Residue concentration (mg/kg)								
	Milk (mean)	Fat		Muscle		Liver		Kidney	
		Highest	Mean	Highest	Mean	Highest	Mean	Highest	Mean
MRL beef cattle *2.7* / 3									
MRL dairy cows *3.2* / 3	*0.13* / 0.13	*1.7* / 1.7		*0.069* / 0.069		*0.44* / 0.44		*0.26* / 0.26	
STMR beef cattle *0.43* / 1									
STMR dairy cows *0.49* / 1	*0.022* / 0.044		*0.32* / 0.65		*0.010* / 0.020		*0.064* / 0.13		*0.032* / 0.065

The maximum concentrations of residues expected in tissues are: 1.7 mg/kg in fat, 0.069 mg/kg in muscle, 0.26 mg/kg in kidney, 0.44 mg/kg in liver and 0.13 mg/kg in milk.

The Meeting estimated maximum residue levels of 2 mg/kg for cattle meat (fat), 0.5 mg/kg for cattle kidney, 0.5 mg/kg for cattle liver and 0.2 mg/kg for milk.

The STMR dietary burden for beef and dairy cattle is 0.5 mg/kg (mean of 0.47 and 0.53 mg/kg). As the transfer factors were reasonably consistent across dietary levels, the Meeting agreed that extrapolation below the lowest concentration (1 ppm) was appropriate. The Meeting estimated STMR values of 0.32 mg/kg for cattle fat, 0.010 mg/kg for cattle meat, 0.032 mg/kg for cattle kidney, 0.064 mg/kg for cattle liver and 0.022 mg/kg for cattle milk.

The concentrations of residues arising from direct treatment of animals were higher than those resulting from feed intake. The recommended MRLs are therefore based on the direct treatments. Similarly, the estimates for typical concentrations of spinosad residues (from direct use at maximum label conditions) should be used for estimating long-term intake in place of STMR values derived from the dietary burden of farm animals and animal feeding studies.

As the maximum dietary burden of poultry was 0.93 mg/kg, the concentrations of residues in tissues and eggs can be taken directly from the study in which hens were fed a diet containing 1 ppm, without interpolation. The highest concentrations of residues expected are: < 0.01 mg/kg in muscle, 0.16 mg/kg in fat, 0.01 mg/kg in liver and 0.01 mg/kg in eggs.

The Meeting estimated maximum residue levels of 0.2 mg/kg for for poultry meat (fat) and 0.01 mg/kg for eggs. As the STMR dietary burden for poultry was 0.24 mg/kg, the concentrations of residues in tissues and eggs can be taken directly from the study in which hens were fed a diet containing 0.3 ppm, without interpolation. The Meeting estimated STMR values of 0.01 mg/kg for poultry meat, 0.05 mg/kg for poultry fat, 0.01 mg/kg for poultry liver and 0.01 mg/kg for eggs.

Dietary risk assessment

Long-term intake

The evaluation of spinosad resulted in recommendations for new MRLs and STMR values for raw and processed commodities. Data on consumption were available for 29 food commodities and were used to calculate dietary intake. The results are shown in Annex 3.

The IEDIs in the five GEMS/Food regional diets, based on estimated STMRs were 2–30% of the ADI (0–0.02 mg/kg bw). The Meeting concluded that long-term intake of residues of spinosad from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The 2001 JMPR concluded that it was unnecessary to establish an acute RfD for spinosad. The Meeting therefore concluded that short-term dietary intake of spinosad residues is unlikely to present a risk to consumers

4.25 TEBUFENOZIDE (196)

Toxicology

The 1999 JMPR recommended that the acute toxicity of tebufenozide be evaluated as soon as possible. An ADI of 0-0.02 mg/kg bw was established in 1996.

Tebufenozide acts as an insecticide by mimicking the action of ecdysome, the insect moulting hormone. Hence, any effects in mammalian species are likely to be distinct from its intended biological target. Tebufenozide has little acute toxicity when given orally (LD_{50} > 5000 mg/kg bw) in mice and rats, dermally (LD_{50} > 5000 mg/kg bw) in mice and rats, or by inhalation (LC_{50} > 4.3 mg/l air) in rats. In short-term studies of toxicity, the main effect in mice, rats, and dogs was haemotoxicity with signs of regenerative haemolytic anaemia and compensatory responses in haematopoietic tissues. The dog was the most sensitive species, the NOAEL being 150 ppm, equal to 5 mg/kg bw per day, in a 2-week feeding study; the LOAEL was 600 ppm, equal to 19 mg/kg bw per day.

In studies of reproductive and developmental toxicity, tebufenozide had only relatively minor effects, and these occurred only at doses above the NOAEL of the 2-week study in dogs.

The Meeting was unable to identify an appropriate study for deriving a definitive acute RfD. However, it considered that the short-term studies of toxicity had clearly identified an effect (haemotoxicity) that could occur after a single exposure to tebufenozide. The Meeting established an acute RfD of 0.05 mg/kg bw based the NOAEL of 5 mg/kg bw per day in the 2-week study in dogs and a safety factor of 100.

The Meeting noted that this is a conservative estimate of the acute RfD. Submission of the results of a study designed specifically to generate data following a single dose, most probably in dogs, would allow refinement of the acute RfD. The need for such a study is described in Annex 5 of the report of the 2000 JMPR.

A toxicological monograph was not prepared.

Residue and analytical aspects

The insecticide tebufenozide was first evaluated by the 1996 JMPR, which recommended MRLs for grapes, pome fruits, husked rice and walnuts. In 1997, an additional MRL for kiwifruit was recommended, and in 1999 data on pome fruits and grapes were re-evaluated. The present Meeting received information requested by the 1996 JMPR, including information about rotational crops, animal feeding studies, storage stability and data on residues on raisins. Furthermore, the results of new supervised trials and analytical methods for new and previously considered commodities were submitted, and information on currently registered GAPs was provided.

The abbreviations used for metabolites are as follows:

RH-9886: *N-tert*-butyl-*N'*-(4-ethylbenzoyl)-3-hydroxymethyl-5-methylbenzohydrazide
RH-1788: *N-tert*-butyl-*N'*-[4-(1-hydroxyethyl)benzoyl]-3,5-dimethylbenzohydrazide
RH-0282: *N-tert*-butyl-*N'*-[4-(1-hydroxyethyl)benzoyl]-3-hydroxymethyl-5-methylbenzohydrazide
RH-0126: *N-tert*-butyl-*N'*-[4-(1-hydroxyethyl)benzoyl]-3-carboxyl-5-methylbenzohydrazide
RH-2703: *N-tert*-butyl-*N'*-(4-carboxymethylbenzoyl)-3,5-dimethylbenzohydrazide
RH-6595: *N-tert*-butyl-*N'*-(4-acetylbenzoyl)-3,5-dimethylbenzohydrazide
RH-9871: *N-tert*-butyl-*N'*-(4-acetylbenzoyl)-3-hydroxymethyl-5-methylbenzohydrazide
RH-2631: *N-tert*-butyl-*N'*-(4-acetylbenzoyl)-3-carboxyl-5-methylbenzohydrazide
RH-0875: *N-tert*-butyl-*N'*-(4-ethylbenzoyl)-3,5-dicarboxylbenzohydrazide
RH-9841: tebufenozide-olefin
RH-9526: stearic acid conjugate of RH-9886

Environmental fate

Soil

In 1996, the Meeting requested a detailed report of a completed study of uptake by rotational crops that the Meeting was informed was available. The current Meeting received the results of both confined and field studies of rotational crops.

In the study of confined rotational crops, tebufenozide labelled with ^{14}C in the ethylbenzoyl ring, the dimethylbenzoyl ring or the central carbon of the *tert*-butyl group was applied in four applications to bare ground, each at the maximum rate of use described on the label for crops in the USA that could be rotated. Rotational crops (wheat, collards and turnips) were planted back 30, 90, 250 and 365 days after last treatment of the initial crop.

High concentrations of residues were found in wheat at 30 days' plant-back: expressed as parent equivalents, 0.4 mg/kg TRR in grain, 7.2 mg/kg in straw and 2.6 mg/kg in forage. At 90 days plant-back, the TRR had fallen to 0.06 mg/kg in grain, 0.4 mg/kg in straw, and 0.3 mg/kg in forage. The concentrations at 250 and 365 days plant-back were comparable. The main component in all wheat samples was RH-1788, either as the free alcohol or conjugated to glucose or malonylglucose. The parent compound was present in only small amounts (1%) in samples of straw and grain at 30 days plant-back and was not detected in any of the wheat samples at longer plant-back intervals.

The concentration of residues in collard at 30 days plant-back was about 0.1 mg/kg. The residues included the glucose conjugates of RH-1788 and small amounts of glucose conjugates of RH-9886 and RH-0282; the conjugates constituted 42% of the TRR. The main individual component (15%) in collards was RH-5992-olefin (RH-9841). The parent compound was not found.

The concentrations of residues were about 0.1 mg/kg in turnip roots and 0.4 mg/kg in turnip tops at 30 days plant-back. The parent compound was the most prevalent component in turnip roots (20% of TRR, 0.02 mg/kg) and accounted for about 7% of the TRR (0.03 mg/kg) in turnip tops. Sugar conjugates of RH-1788 comprised 14% of TRR in both turnip roots and tops.

Thus, the main residues in wheat samples were RH-1788 and its sugar conjugates. Only the turnip root crop had a significant percentage of tebufenozide. The leafy crop collard contained mainly sugar conjugates of RH-1788 and tebufenozide-olefin (RH-9841).

The metabolites found in rotational crops were similar to those identified previously in the studies of crop metabolism, except that the parent compound was either a minor component or undetectable and large amounts of sugar conjugates were formed from the metabolites. All the metabolites found in rotational crops, except the conjugated metabolites, have also been characterized in rats. In soil, the parent compound and RH-6595 were characterized.

In the field study of rotational crops, leaf lettuce was planted as the primary crop and tebufenozide was applied at maximum GAP rate in the USA. The lettuce was removed at maturity, and rotational crops were planted 30 and 120 days after the last application.

The high-moisture crops, including leaf lettuce, radish tops and roots, squash, green and bulb onion and green peppers, were analysed for residues of tebufenozide and its olefin metabolite RH-9841. These compounds were found at concentrations below the LOQ (0.01 mg/kg) in all crops tested.

The low-moisture crop samples (wheat, sorghum and soya beans), planted at 30 days plant-back, were analysed for residues of tebufenozide and its alcohol metabolite RH-1788. No residues of tebufenozide or RH-1788 were found in wheat or sorghum grain or soya bean seed, at concentrations above the LOQ (0.02 mg/kg). In the plant parts used for animal feed, residues of RH-1788 were found in wheat straw (0.28 mg/kg), wheat hay (0.12 mg/kg) and soya bean forage (0.03 mg/kg); no residues of RH-1788 were found in wheat forage, sorghum forage, fodder or stover or soya bean hay. No residues of the parent compound were found at concentrations above the LOQ (0.02 mg/kg) in any of the animal feed commodities from wheat, sorghum and soya bean.

Methods of analysis

Two analytical methods that had been evaluated by the 1996 JMPR were updated with respect to the methods used to measure residues of tebufenozide in six vegetable crops (lettuce, cabbage, spinach, mustard greens, broccoli and celery) and in pecans. The LOQs were unchanged. The GLC method for determining tebufenozide in grapes, evaluated by the 1996 JMPR, was validated for lettuce. The LOQ was 0.02 mg/kg.

An analytical method for determining tebufenozide in citrus fruit and its processed fractions includes the extraction and partitioning of whole citrus fruit, juice and dry pulp samples and direct partitioning of citrus oil samples. The samples are cleaned-up on a carbon and C-18 solid-phase extraction column and analysed by HPLC with UV detection. The LOQ was 0.02 mg/kg. A confirmatory method is based on the same extraction and purification procedure with HPLC–MS for quantification of residues in whole fruit, juice and dry pulp and HPLC–MS/MS for quantification of residues in oil.

A method for measuring residues of tebufenozide in sugar cane and sugar cane processed fractions and one for residues in cotton seed and cotton seed processed fractions were submitted. The method for cotton seed was used in trials on rapeseed. After extraction, partitioning and further purification, HPLC–UV detection was used for quantification. The LOQ was 0.01 mg/kg for all matrices with both methods. The concentrations of residue obtained by HPLC–UV were confirmed by the HPLC–MS method.

A method was reported for the detection and quantification of residues of tebufenozide and its metabolites RH-9841 and RH-1788 in rotational crops. After extraction, partitioning and clean-up, residues were quantified by LC–MS. The LOQ was 0.01 mg/kg for tebufenozide and RH-9841 in high-moisture crops such as root and leafy vegetables, and 0.02 mg/kg for tebufenozide and RH-1788 in low-moisture crops such as grains.

In a method for enforcement of concentrations of residues of tebufenozide and its metabolites in animal commodities, tebufenozide was quantified in all matrices, RH-9886 in muscle and kidney, RH-0282 in milk, muscle and kidney, fatty acid conjugates of RH-9886 in milk and fat and RH-2703 in liver. Residues of fatty acid conjugates of RH-9886 were hydrolysed with hydrochloric acid, and the hydrolysed and normal extracts were partitioned, cleaned-up and then quantified by HPLC–UV detection. The LOQ was 0.01 mg/kg for all three analytes in milk and 0.02 mg/kg for all analytes in animal tissues. The confirmatory HPLC methods for all matrices consisted of use of modified mobile phases with MS detection.

Stability of residues in stored analytical samples

As described by the 1996 JMPR, the stability of tebufenozide at –20 °C has been demonstrated in apples (at least 33 months), apple juice (at least 6 months), grapes and wine (at least 12 months) and walnuts (at least 18 months). The 1996 JMPR requested representative data on the stability of residues on leafy vegetables for the full duration of the storage studies that the Meeting was informed were in progress, and on the stability of residues in analytical samples of rice stored for longer than the 20–21 days already reported. The present Meeting received reports on stability in storage for wheat, rice, green onion, citrus oil, lettuce and animal commodities.

The stability of RH-6595, RH-1788 and the RH-1788-glucose conjugate was tested in wheat straw derived from a study of rotational crops for only the last 2 years of a 4-year storage period. Although little or no degradation was observed, no information was available about a possible change in composition during the first 2 years of storage. Since degradation is usually not a linear process, extrapolation is not possible. The composition of the residue in extracts of wheat forage samples stored for 4 years, which contained mainly the glucose and malonylglucose conjugates of RH-1788, was comparable to that of the remainder of the extracts stored for 4 years and 7 months, but no information was available about stability during the first 4 years of storage.

The stability of tebufenozide and its metabolites RH-1788, RH-6595 and RH-9886 was examined in frozen stored samples of rice straw and grain from a study of metabolism. Samples were first analysed after 2 years and were re-analysed after another 5 years of frozen storage. The proportions of the metabolites remained essentially the same. Although this study did not cover the first 2 years of storage, it satisfied the request of the 1996 JMPR.

In support of the findings on the stability of tebufenozide residues in stored rotational crops, the metabolite RH-9841 was shown to be stable in green onion for at least 24 months at < –10 ºC. The interval between storage and analysis for high-moisture crop samples in the study of rotational crops was ≤ 20 months.

The stability of tebufenozide was demonstrated in orange oil frozen at –20 ºC for at least 15 months, and in head lettuce stored at –15 ± 10 °C for up to 36 months.

In the supervised trials, the stability of tebufenozide was shown to be at least 189 days in blueberries, 322 days in raspberries, 30 days in cranberries, 279 days in turnip roots and foliage, 236 days in rapeseed, 90 days in rapeseed meal, 83 days in rapeseed oil, 279 days in mint and 285 days in mint oil. The periods evaluated covered the interval between storage and analysis for the crops in the supervised trials.

The intervals between storage and analysis for leafy vegetables and tree nuts are covered by the data on the stability of head lettuce and walnuts, respectively. No studies of the stability of tebufenozide in storage were conducted with citrus fruit (interval between storage and analysis in supervised trials, ≤ 2 years), stone fruit (interval, ≤ 4 months), avocado (interval, ≤ 1 year), cabbage and broccoli (interval, ≤ 2.5 years), fruiting vegetables (interval, ≤ 11 months), celery (interval, ≤ 1.5 years) or sugar cane (interval, ≤ 14 months). The stability of tebufenozide in these commodities can be inferred from the stability of its residues in other crop matrices.

In animal commodities, the stability of tebufenozide and the metabolites of possible concern in each matrix during a certain duration at –15 ± 10 °C was tested. In milk (RH-0282 and RH-9526, 192 days), meat (RH-9886 and RH-0282, 203 days), liver (RH-2703, 182 days) and fat (RH-9526, 145 days), no decrease was found in the concentrations of tebufenozide and the metabolites measured. Although these data do not cover the entire interval between storage and analysis of milk and fat samples in the feeding trial in cows (interval, ≤ 250 days for milk and 274 days for fat), as judged from the stability observed, there should be no concern that the measured concentrations of residues were influenced by the storage period.

Definition of the residue

In 1996, the Meeting agreed that the residue for compliance with MRLs and for estimating dietary intake should be defined as tebufenozide. The residue is fat-soluble.

The Meeting agreed that this residue definition would apply to both plant and animal commodities.

Results of supervised trials

Citrus fruit

Five trials in Spain and five trials in Italy on oranges were conducted according to Spanish and Italian GAP for citrus fruit (two applications at 0.018 or 0.019 kg ai/hl; PHI, 14 days). The concentrations of residues of tebufenozide in these trials were: 0.21, 0.25, 0.36, 0.38, 0.39, 0.43, 0.48, 0.56, 0.60 and 0.78 mg/kg in whole fruit and 0.021, 0.03, 0.04 (2), 0.05, 0.053, 0.11, 0.13 (2) and 0.15 mg/kg in pulp.

Five trials with oranges in Australia and nine in the USA, two trials on lemon in Australia and five in the USA, six trials with grapefruit in the USA and two trials with mandarin in Australia were conducted according to the respective pending national GAPs for citrus fruit. Trials based on pending GAP were not taken into consideration by the Meeting.

The concentrations of residues in mandarin in trials in Italy and Spain conducted according to approved GAP for citrus fruit, with a PHI of at least 14 days, were: 0.30 (2), 0.42, 0.59, 0.60 (2), 0.78, 0.84 and 0.95 mg/kg in whole fruit and 0.069, 0.076, 0.082, 0.092, 0.14 and 0.18 mg/kg in pulp.

As the concentrations of residues of tebufenozide were comparable in the whole commodity and in edible portions (pulp) of citrus fruits, the Meeting agreed to evaluate the combined data for oranges and mandarins to apply to citrus fruit. The concentrations of residues in citrus fruit were, in ranked order (median underlined): 0.21, 0.25, 0.30 (2), 0.36, 0.38, 0.39, 0.42, 0.43, 0.48, 0.56, 0.59, 0.60 (3), 0.78 (2),

0.84 and 0.95 mg/kg in whole fruit and 0.021, 0.03, 0.04 (2), 0.05, 0.053, 0.069, 0.076, 0.082, 0.092, 0.11, 0.13 (2), 0.14, 0.15 and 0.18 mg/kg in the edible portion (pulp).

The Meeting estimated a maximum residue level of 2 mg/kg for tebufenozide in citrus fruit, and an STMR value of 0.079 mg/kg and a highest residue of 0.18 mg/kg for tebufenozide in the edible part of citrus fruit (the pulp).

Stone fruit

The values for residues in peaches and nectarines were derived directly from measurements in fruit without stones, whereas the MRL for peaches and nectarines applies to residues measured in fruit without stones but calculated and expressed as the whole fruit. The weight of the stone is set at a default value of 10% of the total weight of the fruit (see table "Unit weigths and edible %" prepared by GEMS/Food for the CCPR and JMPR; nectarines were assumed to resemble peaches). As correction for the weight of the stones resulted in only marginally different figures, the values for residues were used without correction.

Three trials on peach in New Zealand were conducted according to national GAP for stone fruit (four applications at 0.12 kg ai/ha; PHI, 14 days), yielding concentrations of residues of 0.09, 0.10 and 0.14 mg/kg; and three trials on nectarines conducted at GAP yielded concentrations of residues of 0.05, 0.22 and 0.26 mg/kg.

As the concentrations of residues in the trials on peach and nectarine were within the same range, the Meeting agreed to combine the data for mutual support. The concentrations of residues in peach and nectarine were, in ranked order: 0.05, 0.09, 0.10, 0.14, 0.22 and 0.26 mg/kg.

The Meeting estimated a maximum residue level of 0.5 mg/kg, an STMR value of 0.11 mg/kg and a highest residue of 0.23 mg/kg for tebufenozide in peaches and nectarines.

Berries

Eight field trials were conducted in the USA on blueberry according to national GAP (four applications of 0.29 kg ai/ha; PHI, 14 days), resulting in concentrations of residues of 0.30, 0.34, 0.50, 0.56, 0.81, 1.1, 1.2 and 1.7 mg/kg.

The Meeting estimated a maximum residue level of 3 mg/kg, an STMR value of 0.685 mg/kg and a highest residue of 1.7 mg/kg for tebufenozide in blueberries.

Five trials on raspberries conducted in the USA according to GAP resulted in concentrations of residues of 0.36, 0.50, 0.56, 0.82 and 0.86 mg/kg. The Meeting estimated a maximum residue level of 2 mg/kg, an STMR value of 0.56 mg/kg and a highest residue of 0.86 mg/kg for tebufenozide in raspberries.

Five trials on cranberry (one in Canada, four in the USA) were conducted according to GAP in the USA (four applications of 0.29 kg ai/ha; PHI, 30 days). The concentrations of residues were < 0.01, 0.016, 0.042, 0.046 and 0.28 mg/kg. The Meeting estimated a maximum residue level of 0.5 mg/kg, an STMR value of 0.042 mg/kg and a highest residue of 0.28 mg/kg for tebufenozide in cranberries.

Residues of tebufenozide in grapes were evaluated by the 1996 and 1999 JMPR . The ranked order of concentrations of residues from 18 trials in France and Germany was 0.05, 0.06, 0.07, 0.08, 0.12, 0.18, 0.21, 0.22, 0.24, 0.26 (2), 0.27, 0.28 (3), 0.4, 0.42 and 0.5 mg/kg (see Annex 5, reference 87). Re-evaluation of data from four trials in France conducting according to current GAP in Portugal (three applications of 0.144 kg ai/ha; PHI, 14 days; GAP was pending in 1996) resulted in concentrations of residues of 0.16, 0.29, 0.68 and 0.81 mg/kg (Annex 5, reference 78). Trials on grapes conducted in Australia in 1995 and 1998 according to Australian GAP (0.006 kg ai/hl, ≤ 0.030 kg ai/hl for low volume

spraying; PHI, 21 days) resulted in highest residues at least 21 days after the last treatment of 0.22, 0.39, 0.81, 1.1, 1.3 and 1.5 mg/kg. The four re-evaluated French trials and the Australian trials yielded higher concentrations and were considered to represent different data populations from the study in Germany and the previously considered French trials. Therefore the Meeting estimated the maximum residue level, the STMR value and the highest residue on the basis of the four re-evaluated French and six Australian trials.

The concentrations of residues in grapes in trials with Portuguese and Australian GAP were: 0.16, 0.22, 0.29, 0.39, 0.68, 0.81 (2), 1.1, 1.3 and 1.5 and mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg for tebufenozide in grapes to replace the previous recommendation of 1 mg/kg, an STMR value of 0.745 mg/kg and a highest residue of 1.5 mg/kg.

Avocado

Trials were conducted in Australia and New Zealand on avocado according the approved GAP of New Zealand (four applications of 0.006 kg ai/hl; PHI, 21 days). The results of one trial (Walkamin) were not used because there had been heavy rainfall after the last application and the values for residue in this trial were considerably lower than those in other trials. The concentrations of residues measured in stoneless fruit, but calculated for whole fruit, were: 0.08, 0.10, 0.17, 0.18, 0.28, 0.45 and 0.47 mg/kg. The concentrations in the edible portion of advocados (stoneless fruit) were: 0.09, 0.12, 0.19, 0.21, 0.33, 0.52 and 0.53 mg/kg.

The Meeting estimated a maximum residue level of 1.0 mg/kg for tebufenozide in avocados and an STMR value of 0.21 mg/kg and a highest residue of 0.53 mg/kg for tebufenozide in the edible part of avocados (seeded avocados).

Cabbage

Trials on cabbage in the USA were summarized by the 1996 JMPR but, because there were no approved GAPs at that time, no MRLs were proposed.

In 14 trials on cabbage conducted in the USA according to GAP for brassica (seven applications at 0.14 kg ai/ha; PHI, 7 days), the concentrations of residues were 0.004, 0.03, 0.04, 0.09, 0.11, 0.17, 0.30, 0.38, 0.53, 0.78, 1.0, 1.3, 4.3 and 4.6 mg/kg.

The Meeting estimated a maximum residue level of 5.0 mg/kg, an STMR value of 0.34 mg/kg and a highest residue of 4.6 mg/kg for cabbage.

Broccoli

Trials on broccoli in the USA were summarized by the 1996 JMPR but, because there were no approved GAPs at that time, no MRLs were proposed.

Eleven trials on broccoli conducted in compliance with GAP in the USA for brassica resulted in concentrations of residues of 0.01, 0.07, 0.09, 0.1, 0.11 (2), 0.12, 0.24, 0.31, 0.33 and 0.34 mg/kg.

The Meeting estimated a maximum residue level at 0.5 mg/kg, an STMR value of 0.11 mg/kg and a highest residue of 0.34 mg/kg for broccoli.

Tomato

Trials on tomato were performed in both greenhouses and the field. Five trials conducted in greenhouses in southern Europe in 1996 according to Spanish GAP (three applications of 0.018 kg ai/hl; PHI, 3 days) resulted in concentrations of residues of 0.09, 0.19, 0.20, 0.25 and 0.34 mg/kg. Four trials in greenhouses performed in The Netherlands according to Belgian GAP (two applications of 0.18 kg ai/ha; PHI, 3 days) resulted in concentrations of residues in tomatoes of 0.10, 0.11 (2) and 0.16 mg/kg. The concentrations in tomatoes from field trials in the USA that complied with GAP (four applications of 0.28 kg ai/ha; PHI, 7 days) were 0.031, 0.058, 0.085, 0.089, 0.095, 0.11, 0.13, 0.17, 0.25, 0.31, 0.52 and 0.53 mg/kg. As the results for tomatoes grown in the field and in greenhouses are comparable, the data can be combined. The concentrations of residues in trials conducted according to GAP, in ranked order, were: 0.031, 0.058, 0.085, 0.089, 0.09, 0.095, 0.10, 0.11 (3), 0.13, 0.16, 0.17, 0.19, 0.20, 0.25 (2), 0.31, 0.34, 0.52 and 0.53 mg/kg.

The Meeting estimated a maximum residue level of 1 mg/kg, an STMR value of 0.13 mg/kg and a highest residue of 0.53 mg/kg for tomato.

Peppers

Trials on peppers conducted in the USA according to GAP (four applications at 0.29 kg a.i/ha; PHI, 7 days) gave concentrations of residues of 0.048, 0.052, 0.064, 0.16, 0.17 and 0.64 in bell peppers and 0.040, 0.046 and 0.097 in other peppers.

The Meeting agreed to combine the data for the two types of peppers, resulting in concentrations, in ranked order, of: 0.040, 0.046, 0.048, 0.052, 0.064, 0.097, 0.16, 0.17 and 0.64 mg/kg. The Meeting estimated a maximum residue level of 1 mg/kg, an STMR value of 0.064 mg/kg and a highest residue of 0.64 mg/kg for tebufenozide in peppers.

Leafy vegetables

Eight newly submitted trials on lettuce, head were conducted in Europe according to pending GAP and were therefore not considered by the Meeting. Newly submitted trials on turnip greens in the USA were not performed according to GAP (application rate too high) and were also not taken into consideration.

The results of trials on head lettuce, leaf lettuce, spinach and mustard greens were reviewed by the 1996 JMPR, but, as there were no approved GAPs at that time, no MRLs were proposed. As GAP for leafy vegetables is now registered in the USA, these trials can be evaluated.

Trials on leafy vegetables conducted in the USA in complience with current GAP (seven applications at 0.14 kg ai/ha; PHI, 7 days) resulted in concentrations of residues of: 0.092, 0.14, 0.29, 0.83, 0.9, 2.3, 2.7, 3.2 and 6.6 mg/kg in lettuce, head; 0.41, 0.69, 1.1, 1.7, 2.2, 2.5, 2.6 and 3.2 mg/kg in lettuce, leaf; 0.13 (2), 2.7, 3.3, 3.8, 3.9, 4.2, 7.1 and 8.1 mg/kg in spinach and 0.65, 0.93, 1.6, 1.9, 2.4, 2.6, 3.9, 4.4, 5.6 and 6.9 mg/kg in mustard greens.

As the use patterns of tebufenozide in leafy vegetables are similar and the concentrations of residues are in the same range, the Meeting concluded that the data for leafy vegetable crops could be combined. This resulted in concentrations of residues of tebufenozide, in ranked order, of: 0.092, 0.13, 0.14, 0.29, 0.41, 0.65, 0.69, 0.83, 0.9, 0.93, 1.1, 1.3, 1.6, 1.7, 1.9, 2.2, 2.3, 2.4, 2.5, 2.6 (2), 2.7 (2), 3.2 (2), 3.3, 3.8, 3.9 (2), 4.2, 4.4, 5.6, 6.6, 6.9, 7.1 and 8.1 mg/kg.

The Meeting estimated a maximum residue level of 10 mg/kg, an STMR value of 2.45 mg/kg and a highest residue of 8.1 mg/kg for the crop group leafy vegetables.

Turnip roots

Trials on turnip roots in the USA were not conducted according to GAP (0.14 kg ai/ha; PHI, 7 days) and were therefore not considered The Meeting could not estimate a maximum residue level for tebufenozide residues in turnip roots.

Celery

The maximum residue level in celery applies to the whole commodity after removal of adhering soil and clearly decomposed or withered leaves. The data on residues in trials on celery submitted previously, which were conducted in compliance with currently approved GAP in the USA (seven applications at 0.14 kg a.i/ha; PHI, 7 days), pertained mainly to celery stalks *without* foliage. In two samples of celery stalks with foliage, the concentrations of residues were 0.41 and 1.3 mg/kg. The concentrations of residues in the stalk were lower. Insufficient data were available to estimate a maximum residue level in celery.

Sugar cane

The concentrations of tebufenozide residues in sugar cane were derived from 10 trials in the USA that complied with GAP (four applications, 0.28 mg/kg; PHI, 14 days). The values were 0.013, 0.032, 0.035, 0.054, 0.12 (2), 0.16, 0.28, 0.54 and 0.62 mg/kg.

The Meeting estimated a maximum residue level of 1 mg/kg, an STMR value of 0.12 mg/kg and a highest residue of 0.62 mg/kg for tebufenozide in sugar cane stems.

Tree nuts

Four trials on pecan previously submitted to JMPR, which were conducted within currently approved GAP for pecans (0.28 kg ai/ha; PHI, 14 days), resulted in undetectable residues (< 0.01 mg/kg). Further trials on pecans were conducted in the USA in 1997. Although the total amount of tebufenozide applied was equal to the maximum allowed (2.1 kg ai/ha per season), the application rate per treatment was twice as high and the number of applications twice as low as the critical GAP. Residues were undetectable (< 0.01 mg/kg). Since these results confirm those obtained in 1993, the Meeting decided to include them in the evaluation. The concentration of residues in the 12 trials on pecans was < 0.01 mg/kg.

The Meeting estimated a maximum residue level of 0.01* mg/kg as a practical limit of quantification for tebufenozide in pecans. In addition, the Meeting estimated an STMR value of 0.01 mg/kg and a highest residue of 0.01 mg/kg.

Ten trials were conducted on almonds in the USA in 1995–98 in accordance with GAP for tree nuts excluding pecans (0.53 kg ai/ha; PHI, 14 days). The concentrations of residues were < 0.01 (2), 0.010, 0.016, 0.017, 0.024, 0.029, 0.034, 0.042 and 0.045 mg/kg in almond nut kernel.

The Meeting estimated a maximum residue level of 0.05 mg/kg, an STMR value of 0.0205 mg/kg and a highest residue of 0.045 mg/kg for tebufenozide in almond nut kernel.

Information on residues in macadamia nuts was generated in Australia, where the GAP for macadamia nuts (five applications of 0.009 kg ai/hl or concentrate spraying; PHI, 28 days) is still pending. The data were therefore not considered by the Meeting.

Rape seed

One trial on rape seed was performed in Canada and six in the USA. The approved GAP in the USA is four applications of 0.28 kg ai/ha and a PHI of at least 14 days. In one trial in the USA conducted

according to GAP, the concentration of tebufenozide residue was 1.2 mg/kg. Each of the other trials involved either a deviation from the PHI or a special circumstance such as thawing of samples during transport. The residue values that were probably underestimates were 0.31, 0.47 and 0.52 mg/kg; and the values that were probably overestimates were 0.95, 1.1 and 1.6 mg/kg. However, since the values are more or less within the same range, the Meeting agreed to use all of them. In ranked order, the concentrations of tebufenozide residues in rape seed were 0.31, 0.47, 0.52, 0.95, 1.1, 1.2 and 1.6 mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg, an STMR value of 0.95 mg/kg and a highest residue of 1.6 mg/kg for rape seed.

Mint

Five trials on mint were conducted in the USA according to GAP (0.28 kg ai/ha; PHI, 14 days). The concentrations of residues were much lower in mint foliage from one site (2.9 and 2.6 mg/kg) than in that from the other sites, perhaps due to a frost that killed the mint tops on the day of the first application at the former site. The values from that trial were therefore not used to estimate the maximum residue level. The concentrations of residues in mint foliage in the remaining four trials were 7.5, 8.3, 8.4 and 8.6 mg/kg.

The Meeting estimated a maximum residue level of 20 mg/kg, an STMR value of 8.35 mg/kg and a highest residue of 8.6 mg/kg for tebufenozide in mint.

Almond hulls

Ten residue trials were conducted on almonds in the USA in 1995–98 in accordance with approved GAP for tree nuts excluding pecans (0.53 kg ai/ha; PHI, 14 days). The concentrations of residues measured in hulls (used as feed for livestock) in nine of these trials were 8.4, 9.5, 10, 11, 15, 16, 17 (2) and 21 mg/kg.

The Meeting estimated an maximum residue level of 30 mg/kg, an STMR value of 15 mg/kg and a highest residue of 21 mg/kg for tebufenozide in almond hulls.

Fate of residues during processing

The 1996 JMPR requested information on tebufenozide residues in raisins, raisin culls and rice hulls. The present Meeting received a report on two supervised trials with grapes in which raisins were generated. Furthermore, processing studies on citrus fruit, peaches, tomatoes, sugar cane and rape seed were supplied.

Washing, the first step in processing citrus fruit, removed most of the residue in oranges (86%) and grapefruit (74%). The calculated processing factors for industrial processing of citrus fruits were (mean of two trials, one in orange and one in grapefruit) 26.1 for oil, 0.80 for dried pulp and < 0.016 for juice.

On the basis of the STMR value for citrus whole fruit of 0.48 mg/kg, the Meeting estimated STMR-P values of 12.5 mg/kg for citrus oil, 0.38 mg/kg for dried pulp and 0.0077 mg/kg for citrus juice.

During canning of peaches, all the residues of tebufenozide originally present were depleted, and no measurable residues (> 0.01 mg/kg) were found in either the fruit or the syrup of canned peaches. On the basis of the processing factor for canned peaches of < 0.06 (mean of six trials) and the STMR value for peaches of 0.11 mg/kg, the Meeting estimated an STMR-P value of 0.0066 mg/kg for canned peaches.

Processing of grapes yields wine, wet pomace, juice and raisins. Two trials with dried grapes resulted in a processing factor of 0.74 for raisins. Eight trials on grapes that were processed into juice resulted in a processing factor of 0.13 for juice. The 1996 JMPR determined processing factors of 2.7 (mean of 1.6, 2.8 and 3.7) for wet pomace and 0.36 for mature wine (0.07–0.69; n = 14). Additional

data from 26 studies of wine processing conducted in Australia showed that the residues in pomace were concentrated by factors of 1.6–8.7 with an average of 4.1 (n = 18); the concentrations of residues in wine resulted in processing factors of 0.11–0.43 with an average of 0.25 (n = 23). Combining these processing factors with those of the 1996 JMPR resulted in processing factors of 3.9 for wet pomace (n = 21) and 0.29 for wine (n = 37).

On the basis of the highest residue in grapes of 1.5 mg/kg, the Meeting estimated a maximum residue level of 2.0 mg/kg for tebufenozide in raisins and a highest residue of 1.11 mg/kg. On the basis of the STMR value for grapes of 0.745 mg/kg, the Meeting estimated an STMR-P value for tebufenozide of 0.551 mg/kg in raisins, 0.097 mg/kg in grape juice, 2.90 mg/kg in wet pomace to replace the STMR-P value of 0.36 mg/kg, and 0.216 mg/kg in wine to replace the STMR-P value of 0.03 mg/kg.

Tomatoes were processed differently in the four trials conducted in Europe and the one trial in the USA, but, to the extent that the processes yielded the same products, the data were comparable. About two-thirds of the residue in tomatoes was removed by washing in all five trials. The calculated processing factors were 0.31 for purée (n = 1), 0.73 for paste (n = 5), 0.18 for sterilized juice (n = 4) and 0.28 for preserved fruit (n = 4).

On the basis of the STMR value for tomatoes of 0.13 mg/kg, the Meeting estimated STMR-P values of 0.04 mg/kg for purée, 0.095 mg/kg for paste, 0.023 mg/kg for tomato juice and 0.036 mg/kg for preserved tomatoes.

During isolation of refined sugar from sugar cane, all the residues of tebufenozide originally present were depleted; no residues were present at a concentration > 0.01 mg/kg in the resulting refined sugar in four separate studies. The mean processing factor for refined sugar in three trials was < 0.025. Residues of tebufenozide concentrate in molasses; the processing factor for molasses was 5.9 (n = 3).

On the basis of the STMR value for sugar cane stems of 0.12 mg/kg, the Meeting estimated an STMR-P value of 0.003 mg/kg for refined sugar and 0.71 mg/kg for molasses.

Rape seed was processed in two trials into meal, soapstock and refined oil, resulting in processing factors of 0.15 for meal, 1.1 for soapstock and 2.3 for refined oil. On the basis of the STMR value for rape seed of 0.95 mg/kg, the Meeting estimated an STMR-P value of 0.14 mg/kg for meal, 1.0 mg/kg for soapstock and 2.2 mg/kg for rape seed oil.

Two studies on the processing of mint oil from mint resulted in a mean processing factor of 0.03 for mint oil. On the basis of the STMR value for mint foliage of 8.35 mg/kg, the Meeting estimated an STMR-P value of 0.25 mg/kg for mint oil.

Residues in animal commodities

Dietary burden of farm animals

The Meeting estimated the dietary burden of tebufenozide residues for farm animals from the diets listed in Appendix IX of the *FAO Manual*. Calculation from the HR values provides the concentrations in feed suitable for estimating MRLs for animal commodities, while calculation from the STMR values for feed is suitable for estimating STMR values for animal commodities. In the case of processed commodities, the STMR-P value is used for both intake calculations.

Estimated maximum intake

Commodity	Group	Residue (mg/kg)	Basis	Dry matter (%)	Residue, dry weight (mg/kg)	Choose diets (%)			Residue contribution (mg/kg)		
						Beef cattle	Dairy cows	Poultry	Beef cattle	Dairy cows	Poultry
Almond hulls	AM	30	MRL	90	33.3	10	10	–	3.3	3.3	–
Apple wet pomace	AB	0.4	STMR-P	40	1.0	40	20	–	0.4	0.2	–
Citrus dry pulp	AB	0.38	STMR-P	91	0.42	20	20	–	0.08	0.08	–
Rape seed meal	SO	0.14	STMR-P	88	0.16	10	15	15	0.02	0.02	0.02
Rice grain	GC	0.1	MRL	88	0.0114	–	15	60	–	0.02	0.07
Rice straw[a]	AS	7.7	HR	90	8.6	10	10	–	0.86	0.86	–
Sugar cane molasses	DM	0.71	STMR-P	75	0.9	10	10	–	0.09	0.09	–
					Total	100	100	75	4.8	4.6	0.09

[a] 2.9, 3.9, 6.2 and 7.7 mg/kg (1996 JMPR); STMR = 5.05 mg/kg

Estimated mean intake

Commodity	Group	Residue (mg/kg)	Basis	Dry matter (%)	Residue, dry weight (mg/kg)	Choose diets (%)			Residue contribution (mg/kg)		
						Beef cattle	Dairy cows	Poultry	Beef cattle	Dairy cows	Poultry
Almond hulls	AM	15.5	STMR	90	17.2	10	10	–	1.7	1.7	
Apple wet pomace	AB	0.4	STMR-P value	40	1.0	40	20	–	0.4	0.2	
Citrus dry pulp	AB	0.38	STMR-P value	91	0.42	20	20	–	0.08	0.08	
Rape seed meal	SO	0.14	STMR-P value	88	0.16	10	15	15	0.02	0.02	0.02
Rice grain	GC	0.025	STMR	88	0.028	–	15	60	–	0.004	0.02
Rice straw[a]	AS	5.05	STMR	90	5.6	10	10	–	0.56	0.56	
Sugar cane molasses	DM	0.71	STMR-P value	75	0.95	10	10	–	0.10	0.10	
					Total	100	100	75	2.9	2.7	0.04

[a] 2.9, 3.9, 6.2, 7.7 mg/kg (1996 JMPR); STMR = 5.05 mg/kg

Feeding studies

The 1996 JMPR requested the results of a study in which cows were fed diets containing tebufenozide, which the Meeting was informed was in progress. The present Meeting received those results.

Four cows in each group were given a capsule containing tebufenozide at 0, 6, 18 or 60 ppm ai for 28 days. One cow from each group was observed for 3 days while on a normal diet after the end of the dosing period. Whole milk, fat, meat, kidney and liver samples were analysed. The analytes of interest

included parent tebufenozide in all matrices, RH-9886 in muscle and kidney, RH-0282 in milk, muscle and kidney, fatty acid conjugates of RH-9886 in milk and fat and RH-2703 in liver.

In cows at the two lower concentrations, the values for residues were below the LOQ (0.01 mg/kg in milk and 0.02 mg/kg in other matrices) in milk, muscle and kidney, except for a residue at the LOQ in muscle of one cow at 18 ppm. The concentration of residue in milk reached a plateau within about 3 days. The concentration in cream was not reported. In milk, the highest average group concentration of residue was at the LOD of 0.003 mg/kg in cows at 6 ppm, 0.009 mg/kg at 18 ppm and 0.028 mg/kg at 60 ppm. The highest individual concentrations of residues at 6, 18 and 60 ppm were 0.029 mg/kg, 0.11 mg/kg and 0.38 mg/kg in fat, < 0.006 mg/kg, 0.02 mg/kg and 0.06 mg/kg in muscle, < 0.006 mg/kg, 0.007 mg/kg and 0.04 mg/kg in kidney and 0.014 mg/kg, 0.04 mg/kg and 0.10 mg/kg in liver.

No detectable residues of analytes were found in cows observed on an ormal diet for 3 days after treatment, exept in fat in which approximately 30% of the initial residue was still present.

The Meeting considered that a feeding study with poultry was not necessary, as the concentrations of residues in poultry feed do not exceed 0.1 mg/kg and residues are therefore not expected in poultry products.

Maximum residue levels

As the maximum dietary burden of beef and dairy cattle was 4.8 mg/kg, the concentrations of residues in tissues and milk can be taken directly from results of the feeding study with 6 ppm, without interpolation. The maximum concentrations expected in tissues at this level are: 0.029 mg/kg in fat, < 0.006 mg/kg in muscle and kidney, 0.014 mg/kg in liver and 0.003 mg/kg in milk.

The Meeting estimated maximum residue levels of 0.05 mg/kg for cattle meat (fat), 0.02* mg/kg for cattle kidney, 0.02* mg/kg for cattle liver and 0.01* mg/kg for milk.

The STMR dietary burden of beef and dairy cattle was 2.9 mg/kg, which is about one-half the lowest concentration used in the feeding studies. The Meeting estimated STMR and highest residue values of 0.006 mg/kg for cattle meat and kidney and 0.02 mg/kg for liver, and an STMR value of 0.003 mg/kg for cattle milk.

A study of metabolism in poultry treated orally, evaluated by the 1996 JMPR, showed that, when laying hens were treated at a concentration equivalent to 30 ppm in the feed for 7 days, the concentrations of parent compound were 0.005 mg/kg in eggs, 0.18 mg/kg in fat and undetectable in liver and muscle. The maximum dietary burden of poultry was calculated to be 0.09 mg/kg, which is 300 times lower than that used in the study of metabolism. Therefore, the Meeting agreed to recommend MRLs for poultry meat and eggs at the LOQ. The Meeting acknowledged that the analytical method for animal commodities had not been validated for eggs but accepted that the LOQ for cattle tissues could apply to poultry tissues. The Meeting estimated maximum residue levels for poultry meat (fat) and eggs of 0.02* mg/kg, an STMR value and a highest residue for poultry meat (fat) of 0.02 mg/kg and an STMR value and a highest residue for eggs of 0 mg/kg.

The Meeting was informed that a report on validation of the analytical method for residues of tebufenozide in chicken liver, muscle, fat and eggs was available and would be submitted to a future Meeting.

Further work or information

Desirable

- Information on the level of residues in milk cream

- A report on validation of the analytical method for animal commodities with respect to poultry meat and eggs that the meeting was informed was available.

Dietary risk assessment

Long-term intake

STMR or STMR-P values for tebufenozide were estimated by the current Meeting for 43 plant commodities and animal products. STMR values for four additional plant commodities were estimated by the 1996, 1997 and 1999 Meetings. When data on consumption were available, these values were used in the estimates of dietary intake. The results are shown in Annex 3.

The International Estimated Daily Intakes for the five GEMS/Food regional diets, based on the estimated STMRs, were in the range of 1-20% of the ADI. The Meeting concluded that the chronic intake of residues of tebufenozide 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 tebufenozide was calculated for those plant commodities and animal products for which maximum residue levels and STMRs were estimated and for which consumption data were available. The results are shown in Annex 4. The IESTI represented 0-440% of the acute RfD for the general population and 0-1220% of the acute RfD for children. That representing 440% (general population) and 1220% (children) results from the consumption of leafy vegetables (spinach). The short-term intake of cabbage also exceeded the acute RfD in both groups, with 230% (general population) and 410% (children). For children, the estimated short-term intake of pomefruit (apple) and grapes exceeded the acute RfD with 210% and 190% respectively.

4.26 THIODICARB (154)

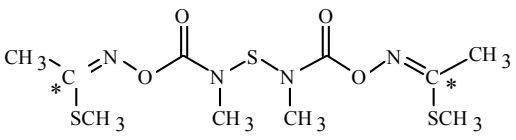
Residue and analytical aspects

Thiodicarb is a carbamate insecticide and molluscicide. It is registered and used in agriculture and horticulture, against lepidoterous insects as a foliar treatment, as a molluscicide in the form of granular bait in various crops and as a seed treatment.

Thiodicarb decomposes in plants and animals and in the environment to the insecticide methomyl. Currently, the MRLs for thiodicarb and methomyl are combined under methomyl.

Thiodicarb was evaluated by the FAO Panel of the JMPR in 1985, 1987 and 1988. The WHO Panel of the JMPR reevaluated its toxicology in 2000.

Metabolism



[acetyl-1-^{14}C]Thiodicarb (designated [acetimide-^{14}C] thiodicarb in 2000 JMPR)

* Denotes ^{14}C carbons

The metabolism of thiodicarb in rats, monkeys, goats and chickens has been reported. Rats were given [acetyl-1-^{14}C]thiodicarb orally at 2 or 16 mg/kg bw in a single dose. More than 70% of the radiolabel was found in urine and respired gases over 7 days. The respired gases contained radiolabelled CO_2 and acetonitrile, and urine contained acetonitrile as a major metabolite and methomyl, methomyl oxime, methomyl sulfoxide and methomyl oxime sulfoxide as minor metabolites.

Cynomolgus monkeys were given a single oral dose of [acetyl-1-^{14}C]thiodicarb at 5 mg/kg bw. About 37% of the administered dose was eliminated in respired air over the first 48 h, consisting of 9% acetonitrile and 28% CO_2. Urine excreted over 168 h contained a combined total of 29% of the administered dose. Thiodicarb, methomyl and methomyl oxime were not detected in urine, blood or liver, while acetic acid was identified in liver.

The metabolic fate of [acetyl-1-^{14}C]thiodicarb in laying hens was studied after administration of a diet containing 15, 29 or 102 ppm for 21 days. The concentrations of residues achieved plateaus in egg white after 2 days and in egg yolk after 10 days. Thiodicarb and the potential metabolites methomyl, methomyl oxime, methomyl oxime sulfoxide and methomyl methylol were not detected in eggs, although low concentrations of acetonitrile (volatile) and acetamide (water-soluble) were found. In addition, considerable radiolabel was present as lipids (70% TRR) and other natural products due to incorporation of $^{14}CO_2$.

The concentrations of radiolabel in tissues of hens given 102 ppm were 4.2 mg/kg in muscle, 6.6 mg/kg in fat, 8.5 mg/kg in kidney and 10 mg/kg in liver. Acetonitrile and acetamide were identified in liver and muscle but not in abdominal fat. About 25% of the TRR in liver, 60% in muscle and 85% in fat was characterized as lipids. Methomyl, methomyl oxime, methomyl oxime sulfoxide and methomyl methylol were not found in any tissue.

The metabolic fate of [acetyl-1-^{14}C]thiodicarb was studied in two lactating goats after administration of 200 and 290 ppm per day for 7 days. The concentration of radiolabel reached maxima of 15 mg/kg and 20 mg/kg in the milk of the two goats on day 3. The goat at the higher dose became ill, and most of the results reported were for tissues from the goat at the lower dose.

After alkaline hydrolysis of water-soluble polar extracts, 32% TRR in liver was identified as acetonitrile, 6% as acetamide and 57% as acetic acid; 23% TRR in kidney was identified as acetonitrile, 10% as acetamide and 43% as acetic acid; and 72% TRR in muscle was acetonitrile, 14% was acetamide and 11% was acetic acid. No thiodicarb, methomyl or methomyl oxime was detected in any tissue.

The metabolites identified in fat were acetonitrile (10% TRR), acetamide (6% TRR) and saponifiable fatty acids and lipids (73% TRR). In milk, acetonitrile (29% TRR), lactose (11% TRR), saponifiable fatty acids and other lipids (32% TRR), palmitic and myristic acids and glycerol were identified. Some of the radiolabel in liver and kidney was also associated with amino acids and proteins.

The metabolism of [acetyl-1-^{14}C]thiodicarb in plants was studied in root crops (potato and carrot), in a fruiting vegetable (tomato), in cereal grain (wheat, maize and sweet corn) and in oilseed crops (cotton, soya bean and peanuts). When the radiolabelled compound was applied to the upper surface of the leaves of potato plants, < 0.2% of the administered dose migrated to the tubers, and 59% was found on the foliage. The constitituents were thiodicarb (main), methomyl and methomyl oxime (trace).

[acetyl-1-^{14}C]Thiodicarb was applied to the upper surface of the leaves of 6-week-old carrot plants, and the carrots were harvested 28 days later. The aerial portions of the plants contained 90% of the applied radiolabel, and 0.06% was found in the roots. The following radiolabelled components were

identified tentatively on the foliage: thiodicarb (79% of applied radiolabel), methomyl (8%), *N*-hydroxymethyl methomyl (0.18%) and methomyl oxime (0.09%).

[acetyl-1-^{14}C]Thiodicarb was also applied to the tops of tomato leaves at the time of flowering. The plants were maintained in a glasshouse, and the fruits were harvested at maturity. About 50% of the radiolabel was lost, perhaps as volatile compounds. About 49% was found on the foliage and about 0.45% on the tomatoes. The constituents on the foliage were identified as thiodicarb (78% TRR), methomyl (6%) and methomyl oxime (0.3%).

[acetyl-1-^{14}C]Thiodicarb was injected into the stems of 3-week-old sweet corn and wheat plants. The plants were maintained for 7 days and then harvested. The following metabolites were identified in both crops: thiodicarb (major), methomyl (major), methomyl oxime (very minor) and methomyl sulfoxide (very minor). About 30–50% of the radiolabel was unaccounted for.

A second study was performed with sweet corn, in which [acetyl-1-^{14}C]thiodicarb was painted onto leaves, ears and silk in one experiment and the leaves only in another. The plants were maintained for 7 days in a glasshouse and then harvested. Almost 70% of the applied radiolabel was unaccounted for. Only minute quantities were found in kernels plus cob. The concentrations on cobs and kernels were similar in the two experiments and were low (0.1–0.15% of the applied dose) in both cases. Over 70% of the radiolabel in the kernels could not be extracted. The metabolites identified on foliage (34% of the applied dose) were thiodicarb (20%), methomyl (6%) and methomyl oxime (trace to 0.3%).

In a study conducted with cotton plants, [^{14}C]thiodicarb was injected into the stem of 4–5-week-old cotton plants, which were maintained in a greenhouse and harvested 7, 14, 21 or 28 days after treatment. In a separate experiment, [^{14}C]thiodicarb was applied by stem injection and topical application to the tops of the leaves of 4-week-old cotton plants maintained in enclosed glass containers. Volatile compounds were collected in a series of traps at intervals of 1, 4 and 7 days after application and were identified as CO_2 and acetonitrile. In the injected plants (with no collection of volatile compounds), the percentage of the total applied radiolabel attributable to compounds soluble in organic solvents decreased from 53% on day 7 to 7% on day 28, whereas the percentage of water-soluble compounds increased from 12% to 21%. Throughout the experiment, 1–2% of the compounds could not be extracted. The compounds soluble in organic solvents were identified as thiodicarb, methomyl and methomyl oxime (trace). Methomyl was the major component on day 28.

The absorption, translocation and metabolism of thiodicarb in and on cotton after application to the leaf surface were investigated in a study in which a solution of [^{14}C]thiodicarb was spread onto the tops of the leaves of cotton plants at the flower bud stage at a rate equivalent to 1.1 kg ai/ha. The plants were maintained in a greenhouse until the bolls were mature, at which time they were harvested and the seeds de-linted. Senescent leaves were also collected for analysis. Lint and seed each contained < 0.1% of the applied dose, which was too little to allow adequate characterization. The senescent leaves were found to contain thiodicarb (22% TRR), methomyl (12% TRR), methomyl oxime (0.14% TRR) and methomyl methylol (0.5% TRR).

A similar experiment was performed with soya bean plants. A solution of [^{14}C]thiodicarb was spread onto the tops of the leaves of soya bean plants at the flower bud stage at a rate approximating 1.12 kg ai/ha. The plants were maintained in a greenhouse until the pods were mature, at which time they were harvested and the seeds separated from the hulls. Senescent leaves were also collected for analysis. Measurements of radiolabel in harvested seed and hull samples indicated activity representing 0.18–0.19% of the applied dose. The organic extract of soya bean leaves contained thiodicarb (85% of the applied radiolabel), methomyl (6%) and methomyl oxime (trace).

In a final study, [acetyl-1-^{14}C]thiodicarb was applied topically to peanut foliage four times at 7-day intervals at a rate of 1.1 kg ai/ha. The plants were harvested 21 days after the last treatment, and foliage, root, nut and shell were analysed separately. Of the applied radiolabel, 22% was in foliage, 0.2% in root, 0.5% in nut and 0.2% in nut shell. Almost 77% was unaccounted for and was presumably volatilized. The foliage contained thiodicarb and methomyl but no methomyl oxime or acetamide. Most (50–70%) of the radiolabelled residues in nut, shell and root could not be extracted. None of the components soluble in organic solvents could be identified.

The Meeting concluded that the metabolism of thiodicarb is adequately understood in both animals and plants. In animals, thiodicarb is converted to methomyl and, presumably via methomyl oxime, to CO_2, acetonitrile and acetamide. These may then be incorporated into natural products. Significantly, thiodicarb, methomyl and methomyl oxime are not found in tissues, eggs or milk. An analogous pathway exists in plants. Thiodicarb and its metabolites showed little tendency to translocate from the point of application. Thiodicarb is converted to methomyl and methomyl is metabolized to CO_2 and acetonitrile. At the point of application, e.g., foliage, the main soluble residue components are thiodicarb and methomyl. Volatile compounds often accounted for 50% or more of the residue. Traces of methomyl oxime, a potential intermediate to CO_2 and acetonitrile, were often found. The volatile compounds may be incorporated into natural products.

Environmental fate

Soil

A study of rotational crops was performed in sandy loam soil under confined conditions after application of [acetyl-1-^{14}C]thiodicarb at a rate of 6.7 kg ai/ha. After the soil had been tilled to a maximum depth of 10 cm, crops of mustard greens, radish and wheat were planted at intervals of 31, 125 and 364 days after treatment. Soil was analysed at the time of treatment and at the first plant-back interval (31 days). At day 0, 82% of the radiolabel was on thiodicarb; by day 31, thiodicarb accounted for 5% and methomyl for 47% of the radiolabel. Residues were found in crops planted 31 and 125 days after treatment but not in those with a 364-day plant-back (< 0.01 mg/kg). The concentrations of residues ranged from 0.11 mg/kg in radish root to 0.81 mg/kg in wheat straw at the 125-day plantback. At the 31-day plantback, the concentrations ranged from 0.48 mg/kg in wheat grain to 2.4 mg/kg in wheat straw.

When the crop matrices were extracted and analysed, the compounds identified included acetic acid released by acid hydrolysis, methomyl (maximum, 15% TRR), and methomyl oxime released by base hydrolysis (2–10% TRR). Most of the radiolabelled residues was not soluble in water or organic solvents and were found to be associated with natural products such as starch, proteins, pectins and lignin. At the 31-day plant-back, methomyl (from thiodicarb plus methomyl) was found at the following concentrations: wheat forage, 0.07 mg/kg; mustard greens, 0.12 mg/kg; radish tops, 0.14 mg/kg; and radish roots, 0.09 mg/kg. At the 125-day plant-back, the concentrations of methomyl were 0.02 mg/k in wheat forage, 0.04 mg/kg in mustard greens and 0.02 mg/kg in radish tops These values represented the LOQ of the analytical methods.

The Meeting concluded that thiodicarb and methomyl degradates persist in soil for at least 4 months and are taken up by plants and ultimately incorporated into natural products. The Meeting further concluded that, under typical GAP, ≥ 15% of the rate used in this study and field conditions, residues of methomyl and thiodicarb would not be quantifiable in rotational crops at intervals > 30 days.

Photolytic degradation of thiodicarb incubated under aerobic conditions at a temperature of 20 °C in a clay loam soil for 21 days was reported. In both irradiated and control soil, 50% of the radiolabelled material was lost as CO_2. Thiodicarb rapidly degraded to methomyl in both soils, the concentration of methomyl reaching a maximum of 80–90% of the applied dose on day 2. The concentration of thiodicarb declined slightly faster in the control than in the irradiated soil.

The Meeting concluded that sunlight has no net effect on the degradation of thiodicarb in soil.

In soil under aerobic conditions, thiodicarb degraded rapidly to methomyl, with a half-time based on first-order kinetics of 0.01–2.0 days, depending of soil type. The half-time of methomyl in sandy loam soil was 27 days. Methomyl oxime was found in the soil, at no more than about 3% of the applied dose. Over 60 days, the amount of radiolabel in sandy loam soil decreased to 42% of the applied dose, and the proportion of volatile compounds, identified as CO_2 and acetonitrile, increased to 53% of the applied dose. After 56 days, the radiolabel associated with volatile compounds represented 61% of the applied dose in clay loam with a high pH, 59% in clay loam at 20 °C and 40% in clay loam incubated at 10 °C. At the same time, the amount of unextractable radiolabel in the soils increased to a maximum of 35% of the applied dose.

The route and rate of degradation of [acetyl-1-^{14}C]thiodicarb under anaerobic conditions was studied in a soil–water mixture. The soil was flooded with deionized water and purged with nitrogen for 42–43 days before treatment to establish anaerobic conditions. A solution of [^{14}C]thiodicarb was applied to the water surface at a nominal application rate equivalent to 1 kg ai/ha. During incubation, the system was purged continuously with nitrogen to maintain anaerobic conditions. Within 16 min, the concentration of thiodicarb was < 1% of the applied dose. The concentration of methomyl was constant, at about 2% of the applied dose. An intermediate compound, *S*-methyl-*N*-[*N*-methyl-*N*-(methylaminothio)-carbamoyloxy] thioacetamidate, was found at ≤ 17% of the applied dose. Acetonitrile was the ultimate degradate, accounting for 88% of the applied radiolabel after 4 h. No more than 16% of the applied radiolabel was associated with the soil at any time.

The adsorption and desorption properties of [acetyl-1-^{14}C]thiodicarb were characterized in four soil types. Thiodicarb had little mobility in clay soil, medium mobility in silt loam and sandy loam and high mobility in sandy soil

The Meeting concluded that thiodicarb degrades within a few days to methomyl in soil under aerobic conditions and that methomyl degrades at a much slower rate. About 50% of methomyl is degraded to volatile compounds over 60 days in various soil types. Under anaerobic conditions in a water–soil mixture, thiodicarb degraded in < 4 h to acetonitrile. The Meeting further concluded that thiodicarb has little mobility in clay but is increasingly mobile in soils containing loam and sand. Some leaching of thiodicarb/methomyl can be expected in soil types other than clay.

Water–sediment systems

The hydrolysis of [acetyl-1-^{14}C]thiodicarb was determined at various pHs in sterile aqueous buffer solutions. After 7 days at pH 7 and pH 5, 92–94% of the applied radiolabel remained as thiodicarb. At pH 9, however, < 1% remained, with 54% methomyl and 32% methomyl oxime. The methomyl underwent degradation at pH 9, resulting in 77% methomyl oxime and 19% methomyl after 30 days.

The photodegradation of [acetyl-1-^{14}C]thiodicarb was tested in a buffered solution at pH 6 under natural sunlight. After 23 days, the solution of a control sample kept in the dark contained 98% of the applied radiolabel, consisting of 67% thiodicarb and 24% methomyl, whereas the irradiated solution contained only 72% of the applied radiolabel, consisting of 12% thiodicarb and 47% methomyl. CO_2 and acetonitrile accounted for 4.4% and 15%, respectively, of the applied radiolabel in the irradiated solution. No volatile compounds arose from the solution maintained in the dark. The time to 50% degradation was calculated to be 8 days in sunlight and 37 days in the dark.

The degradation of thiodicarb, applied at a rate of approximately 0.25 mg/kg of water was investigated in two water–sediment systems under aerobic conditions over 100 days at 20 °C. The

concentration of radiolabel in the water phase of both systems decreased slowly to < 1% of that applied, whereas that in the sediments increased from 10% on day 0 to 30–50% and then decreased to about 15%. Thiodicarb disappeared in both phases within < 1 day. Methomyl accounted for 50% and 17% of the applied dose in the two systems by day 2. Within 100 days, CO_2 accounted for 70% of the applied radiolabel in both systems. The half-time of methomyl was calculated as 20–30 h.

The Meeting concluded that thiodicarb is unstable at alkaline pH, decomposing to methomyl, which is converted to methomyl oxime. The Meeting further concluded that thiodicarb photodegrades in water, with a half-time of 8 days, and that it is rapidly converted to methomyl in water–sediment systems, with ultimate conversion to CO_2.

Methods of analysis

An HPLC method with post-column derivativization and a fluorescence detector has been validated for the determination of thiodicarb and methomyl in milk, muscle, kidney, liver and eggs, with an LOQ of 0.02 mg/kg for both thiodicarb and methomyl. Thiodicarb is unstable in animal matrices and degrades to methomyl.

GC methods exist for the determination of thiodicarb, methomyl and methomyl oxime as methomyl oxime in plant commodities. The commodity is extracted with acetone and water and treated with a coagulation mixture to remove co-extractives. Caustic hydrolysis is used to convert both thiodicarb and methomyl to methomyl oxime, which is quantified by GC with a flame photometric detector in the sulfur mode. Variations have been developed, including the use of GPC for extract clean-up, capillary GC columns and MS detectors. The LOD is either 0.02 or 0.04 mg/kg, depending on the exact procedure.

The Meeting concluded that adequate analytical methods exist for the determination of thiodicarb and methomyl in and on plant and animal commodities for the purposes of data collection and for monitoring and enforcing MRLs.

Stability of residues in stored analytical samples

Data were presented on the stability of thiodicarb and methomyl under frozen storage (–20 °C) in celery, head lettuce, leaf lettuce, spinach, soya bean, soya bean processed commodities (meal, hulls, oil, soapstock), apples, sorghum grain, sorghum forage, sweet corn, cotton seed, cotton seed processed commodities (meal, hulls, oil, soapstock), milk and ruminant muscle, kidney, fat and liver. Thiodicarb plus methomyl was stable in celery, head lettuce and leaf lettuce for at least 7 months, but a significant proportion (30%) was lost in spinach after 5 months. Thiodicarb plus methomyl was stable in soya beans and cotton seed and its processed commodities, except cotton seed soapstock (50% loss) and cotton seed meal (40% loss), for 6 months. Thiodicarb and methomyl were stable in apples for at least 14 months and in sorghum grain for at least 13 months; however, thiodicarb plus methomyl showed a continuous decline on sorghum forage and stover, with a 20% loss over 6 months. Thiodicarb and methomyl were stable on frozen sweet corn (cob plus kernel) for 3 months but showed significant loss thereafter. Thiodicarb and methomyl were each stable in frozen milk, muscle and fat for 2 months but unstable in kidney (50% loss in 2 months, 20% in 1 month), disappearing from liver within 2 days.

The Meeting concluded that the stability of thiodicarb plus methomyl in frozen plant commodities is variable, 6 months generally being the longest desired storage interval. The Meeting further concluded that animal commodities, except liver and kidney, may be stored for 2 months, whereas kidney should be stored no more than 1 month, and liver is not amenable to standard frozen storage (see report item on methomyl).

Definition of the residue

The studies of animal and plant metabolism showed that thiodicarb is converted to methomyl and that methomyl is metabolized primarily to CO_2, acetonitrile and acetamide (animals only). The simpler metabolic products may then be incorporated into natural products, particularly in plants. Thiodicarb/methomyl showed no tendency to bioaccumulate in animal matrices. The P_{ow} of 1.6 indicates no tendency to accumulate in fat. Moreover, the studies of plant metabolism showed that thiodicarb/methomyl has a low tendency to migrate from the point of application, i.e. is not systemic. In both animals and plant, methomyl oxime appeared as a minor metabolite, representing < 1% in most cases, and is probably the intermediate in the metabolism of methomyl.

The analytical method for animal commodities allows determination of both thiodicarb and methomyl but not methomyl oxime. The method for plant commodities does not allow a distinction between thiodicarb and methomyl but reflects the sum of thiodicarb, methomyl and methomyl oxime as methomyl oxime.

The Meeting concluded that the residue definition for both plant and animal commodities is thiodicarb and methomyl, expressed as methomyl. This definition takes into account the fact that methomyl oxime is a very minor metabolite and is not determined in some methods. Expresson of the total residue as methomyl is consistent with the combination of the MRLs for thiodicarb and methomyl and reflects the fact that a significant portion of the residue found after use of thiodicarb is methomyl. The practical effect is small, as the conversion factor from mg/kg thiodicarb to mg/kg methomyl is 0.92.

Results of supervised field trials

The results of supervised field trial studies were presented for apple, grapes, potato, sugar beet roots, head lettuce, spinach, broccoli, Brussels sprouts, cabbage, cauliflower, collards, chick peas, garden (green) peas, pea hay, soya beans, soya bean forage and hay and straw, tomato, barley grain, wheat grain, maize grain, sweet corn, rice grain, sorghum grain, barely forage and straw, wheat forage and straw, rice straw, sorghum forage and straw and stover, sweet corn forage, cotton seed, cotton forage, rape seed grain and rape seed forage (green) and straw.

As relevant GAP was not available for sorghum grain, this commodity was not considered further.

Generally, information on moisture content was not available for the forages, stovers and fodders, and the default values for per cent dry matter presented in Appendix IX of the *FAO Manual* were used.

Supervised trials on <u>apple</u> were conducted in Australia, Italy, Greece, Japan and the USA. The only relevant GAP is that of Japan, in which a wettable powder formulation of 750 g ai/kg may be applied three times at a maximum rate of 0.075 kg ai/hl, with a 21-day PHI, or a suspension concentrate formulation of 320 g/l may be applied three times at a rate of 0.043 kg ai/hl, with a 21-day PHI. In eight trials conducted at GAP with the wettable powder formulation, the ranked order of concentrations of residues was: 0.40, 0.43, 0.48, 0.68, 0.91 (2), 1.5 and 1.6 mg/kg. In four trials conducted at GAP with the suspension concentrate formulation, the ranked order of concentrations of residues was: 0.30, 0.32, 0.61 and 0.68. The data from the 12 trials may be combined, as they appear to represent the same population, as follows (ranked order, median underlined): 0.30, 0.32, 0.40, 0.43, 0.48, <u>0.61</u>, <u>0.68</u> (2), 0.91 (2), 1.5 and 1.6 mg/kg (see report item on methomyl).

Supervised trials on <u>grapes</u> were conducted in France, Italy and Spain. The two trials in Spain were not conducted at the GAP of Spain (0.75 kg ai/ha; PHI, 21 days). The one trial in Italy and two in France were conducted at the GAP of France (0.45 kg ai/ha; PHI, 14 days), as no GAP was available for Italy. The ranked order of concentrations of residues was: 0.59 and 0.7 (2) mg/kg (see report item on methomyl).

Supervised trials on potato were presented from Japan and the United Kingdom. The trials in Japan involved five foliar applications at a GAP rate of 0.075 kg ai/hl and a 7-day PHI. In four trials conducted at GAP, no residues were detected: < 0.007 mg/kg (2) and < 0.008 mg/kg (2). The trials reported from the United Kingdom involved bait application to soil at 0.2 kg ai/ha and a PHI of 21 days. In the 11 trials at GAP, the concentrations of residues were: < 0.04 mg/kg (11) (see report item on methomyl, foliar use).

Four supervised trials on sugar beet were reported from the United Kingdom, where the GAP of Belgium requires application of a bait to soil at 0.2 kg ai/ha with no specified PHI. All the concentrations of residues in or on beet roots were < 0.040 mg/kg. The Meeting concluded that the number of trials was insufficient to permit estimation of a maximum residue level or an STMR value. The Meeting further agreed to withdraw the recommended MRL for sugar beets (0.1 mg/kg).

Supervised trials were conducted on lettuce, head, involving application of a granular bait to soil in Italy (no GAP) and France (0.8 kg ai/ha; PHI, 7 days) and aerial and ground foliar application in Spain (no GAP) and the USA (0.84 kg ai/ha; PHI, 14 days). In two trials in France at GAP, the concentrations of residues were 0.048 and 0.14 mg/kg. In 36 trials in the USA at GAP, the ranked order of concentrations of residues was: < 0.04 (3), 0.07 (2), 0.09 (2), 0.12, 0.14, 0.19, 0.21, 0.25, 0.34, 0.35, 0.36, 0.42, 0.44, 0.48, 0.49, 0.71, 0.96, 1.2, 1.7 (2), 1.8, 1.9, 2.6, 3.0, 3.2, 6.2, 6.3, 7.7, 10, 13, 17 and 18 mg/kg (see report item on methomyl).

Supervised field trials on spinach were conducted in the USA. In the nine trials at GAP (foliar spray at 0.84 kg ai/ha; PHI, 14 days), the ranked order of concentrations of residues was: 0.04 (2), 0.21, 1.0, 3.2, 3.5, 4.1, 12 and 25 mg/kg (see report item on methomyl).

Supervised field trials were conducted on collards in the USA (GAP: suspension concentrate, 0.84 kg ai/ha; PHI, 14 days). In two trials conducted under maximum conditions, the concentrations of residues were 1.5 and 1.8 mg/kg. The Meeting concluded that the number of trials was insufficient to permit estimation of a maximum residue level or STMR value but decided to combine the data with those for leafy vegetables treated with methomyl (see report item on methomyl).

Supervised field trials were conducted on broccoli in the USA. The GAP for foliar application (ground or aerial) is 1.2 kg ai/ha; with a 7-day PHI. The ranked order of concentrations of residues in the seven trials at GAP was: 1.1, 1.3, 1.6, 1.9, 2.6, 5.0 and 5.6 mg/kg. Two trials were reported from Australia, but they were not conducted at GAP (0.75 kg ai/ha; PHI, 7 days) (see report item on methomyl).

Supervised field trials were conducted on Brussels sprouts in The Netherlands and the United Kingdom (GAP of Belgium: bait application, 40 g ai/kg, 0.2 kg ai/ha; PHI, 21 days). In eight trials conducted at maximum GAP, the ranked order of concentrations of residues was < 0.04 (4), ≤ 0.05 (3) and 0.059 mg/kg. The Meeting decided to establish a group maximum residue level for Brassica vegetables based on foliar application, which results in higher concentrations of residues (see report item on methomyl).

Supervised trials were conducted on foliar application to cabbage in Australia (no GAP) and the USA (1.2 kg ai/ha; PHI, 7 days). In 19 trials at GAP, the ranked order of concentrations of residues was: 0.08 (2), 0.12, 0.53, 0.76, 0.97, 1.2, 1.3, 2.1, 2.7, 2.8, 3.0, 3.1, 3.5, 3.8, 4.3, 4.8, 5.0 and 5.3 mg/kg (see report item on methomyl).

Supervised field trials with foliar application to cauliflower were conducted in the USA (GAP: 1.2 kg ai/ha; PHI, 7 days). In eight trials at GAP, the ranked order of concentrations of residues was: 0.09, 0.16, 0.27, 0.45, 0.64, 0.71 and 2.3 (2) mg/kg (see report item on methomyl).

Supervised trials were conducted on garden peas in Australia. None of the trials met GAP (0.28 kg ai/h; PHI, 21 days), and the Meeting agreed to withdraw the recommended MRL for peas, shelled (succulent seeds) (0.5 mg/kg).

Supervised trials of foliar application to chick-pea were conducted in Australia. None of the trials met GAP (0.28 kg ai/ha; PHI, 21 day PHI).

Supervised field trials were conducted on foliar treatment of soya beans in Australia (0.28 kg ai/ha; PHI, 28 day), Brazil (0.06 kg ai/ha; PHI, 14 days) and the USA (0.84 kg ai/ha; PHI, 28 days). None of the trials in Australia and Brazil met GAP. In 19 trials with foliar ground application in the USA that were at GAP, the ranked order of concentrations of residues was: < 0.04 (17), 0.06 and 0.15 mg/kg.

The Meeting estimated a maximum residue level of 0.2 mg/kg, an STMR value of 0.04 mg/kg and a highest residue of 0.15 mg/kg. The Meeting agreed to maintain the current recommended MRL for soya bean (dry) (0.2 mg/kg).

Supervised field trials on tomato were conducted in Australia (0.52 kg ai/ha; PHI, 1 day), Spain (0.94 kg ai/ha; PHI, 7 days) and the USA (no GAP). The trials in Spain were conducted in glasshouses. In two trials in Australia that met GAP, the concentrations of residues were 0.09 and 0.73 mg/kg. In nine trials in Spain at GAP, the ranked order of concentrations was: 0.05, 0.06, 0.08, 0.09, 0.13, 0.16, 0.18, 0.23 (2), 0.33 and 0.73 mg/kg (see report item on methomyl).

Supervised field trials were conducted on sweet corn in the USA (0.84 kg ai/ha; no PHI) and Australia (0.75 kg ai/ha; PHI, 7 days) with foliar application. None of the trials in Australia met GAP. In 22 trials in the USA at GAP, the ranked order of concentrations of residues was: < 0.02, 0.02, < 0.03 (6), < 0.04, 0.04, 0.06, 0.07 (2), 0.08, 0.11, 0.13, 0.22, 0.28, 0.43, 0.54, 0.82 and 1.5 mg/kg. Additional trials of seed treatment were presented, but there is no GAP for this application in the USA. Field trials were also conducted with methomyl, and the Meeting decided to combine the data sets (see report item on methomyl).

Supervised field trials of the application of granular bait to barley were conducted in Germany (0.2 kg ai/ha; PHI not specified) and the United Kingdom (at drilling and before the second node is detectable; 0.2 kg ai/ha; PHI not specified). In two trials in Germany and six in the United Kingdom at GAP, the ranked order of residues was: < 0.02 (2), ≤ 0.04 (5) and 0.06 mg/kg. Trials with foliar application of methomyl resulted in higher concentrations (see report item on methomyl).

Supervised field trials of the application of granular bait to wheat were conducted in Germany (0.2 kg ai/ha; PHI not specified) and the United Kingdom (at drilling and before the second node is detectable; 0.2 kg ai/ha; PHI not specified). In three trials in Germany and six in the United Kingdom at GAP, the ranked order of concentrations of residues was < 0.02 (3), < 0.04 (5) and 0.06 mg/kg. Supervised field trials conducted with methomyl yielded higher values (see report item on methomyl). Supervised field trials with seed treatment were provided from Brazil, but no GAP was reported and the LOQ was unacceptably high, at 0.2 mg/kg.

Supervised field trials on maize were conducted in Brazil with both foliar (0.1 kg ai/ha; PHI, 30 days) and seed treatment (7 kg/t of seeds). The trials with foliar application were conducted at an excessive rate (two to four times GAP), but the concentrations of residues were < 0.1 (6) mg/kg. In four trials of seed treatment at GAP the concentration was < 0.1 mg/kg. The Meeting concluded that data from the two uses could not be combined. The data for foliar treatment were combined with similar data in trials with methomyl (see the report item on methomyl).

Supervised trials on rice were conducted in Japan with foliar application (1.2 kg ai/ha; PHI, 30 days). In four trials at GAP, the ranked order of concentrations of residues was: < 0.25 (2) and < 0.4 (2) mg/kg. Supervised trials were conducted in Brazil with seed treatment of rice (5.3 kg/t of seed). The one

trial at GAP and three trials at exaggerated rates (1.4–2.7 times GAP) yielded no quantifiable residues; the concentrations of residues were < 0.10 (4) mg/kg. The Meeting considered that the data from foliar and seed treatments could not be combined, and that the numbers of trials for the two treatments were insufficient to permit estimation of a maximum residue level or an STMR value. Furthermore, the LOQ of the analytical method for rice grain in Japan was unacceptably high.

Supervised field trials on barley forage were conducted in Germany (0.2 kg ai/ha) and the United Kingdom (early season, bait application; 0.2 kg ai/ha). In seven trials at GAP, the ranked order of concentrations of residues was: < 0.02 (2), ≤ 0.04 (3), 0.04 and 0.25 mg/kg. Barley forage is not a recognized animal feed commodity.

Supervised field trials were conducted on wheat forage in Germany (0.2 kg ai/ha) and the United Kingdom (0.2 kg ai/ha). In 12 trials at GAP, the ranked order of concentrations of residues was: < 0.02 (4), ≤ 0.04 (4), < 0.03 (2), 0.06 and 0.21 mg/kg. Trials conducted with methomyl by foliar application yielded higher concentrations (see report item on methomyl).

Supervised field trials on barley straw were conducted in Germany (0.2 kg ai/ha) and the United Kingdom (0.2 kg ai/ha). In nine trials at GAP, the ranked order of concentrations of residues was: ≤ 0.04 (6), < 0.2 (2) and 0.24 mg/kg (see report item on methomyl).

Supervised field trials on wheat straw were conducted in Germany (0.2 kg ai/ha). In three trials at GAP, the concentration of residues was < 0.2 mg/kg. The Meeting decided that the number of trials was insufficient to permit estimation of a maximum residue level or an STMR value (see report item on methomyl).

Supervised field trials were conducted on rice straw in Japan. In four trials at GAP (1.2 kg ai/ha; PHI, 30 days), the ranked order of concentrations of residues was: < 0.5, 0.62, and ≤ 1 (2) mg/kg. The Meeting decided to combine these data with those for cereal grain straw treated with methomyl (see report item on methomyl).

Supervised trials on sweet corn fodder were conducted in Australia, but none was at GAP (0.75 kg ai/ha; PHI, 7 days).

Supervised trials were conducted on foliar application to sweet corn forage in the USA. In 12 trials at GAP (0.84 kg ai/ha; PHI, 21 days), the ranked order of concentrations of residues was: < 0.02, < 0.05, 0.06, 0.16, 0.21, 0.56, 1.1, 2.3, 5.2, 6.9, 11 and 18 mg/kg. Trials were also conducted with methomyl, and the Meeting decided to combine the results (see report item on methomyl).

Supervised trials on cotton seed were conducted in Australia (GAP: 0.84 kg ai/ha; PHI, 21 days), Brazil (no GAP), Greece (GAP: 0.8 kg ai/ha; PHI, 28 days), Spain (0.94 kg ai/ha; PHI, 21 days), the Sudan (no GAP) and the USA (1 kg ai/ha; PHI, 28 days) by foliar application. None of the trials in Brazil corresponded to the GAP of Argentina (0.38 kg ai/ha; PHI, 20 days), and none of the trials in Spain was at GAP. One trial in Australia, two in Greece and 15 in the USA were at GAP; the ranked order of concentrations of residues was: ≤ 0.04 mg/kg (12), < 0.05, 0.05, 0.09 and 0.10 (3) mg/kg. Supervised trials were also conducted with methomyl, and the Meeting decided to combine the values (see report item on methomyl). Supervised field trials were presented on seed treatment in the USA, but there is no GAP for this application.

Many supervised field trials on cotton forage were conducted in the USA, but none was at GAP (1.0 kg ai/ha; PHI, 28 days), and cotton forage is not a recognized feed item, either in the USA or in the *FAO Manual*.

Supervised field trials on rape seed were conducted in Germany (0.2 kg ai/ha; no PHI) and the United Kingdom (soil broadcast up to and including stem extension stage; 0.2 kg ai/ha; no PHI) with granular bait. In 14 trials at GAP, the ranked order of concentrations of residues in rape seed was: < 0.04 (4), 0.04, ≤ 0.05 (8) and 0.05 mg/kg. The Meeting estimated a maximum residue level of 0.05 mg/kg and an STMR value of 0.05 mg/kg.

Supervised field trials on rape seed forage (green) were conducted in Germany (winter rape, soil broadcast; 0.2 kg ai/ha; no PHI) and the United Kingdom (soil broadcast, up to an including stem extension stage; 0.2 kg ai/ha; no PHI) with granular bait. In 11 trials at GAP, the ranked order of concentrations of residues was: ≤ 0.02 (8) and < 0.04 (3) mg/kg. Applying the default value for dry matter of 30%, the Meeting estimated a maximum residue level of 0.2 mg/kg, an STMR value of 0.07 mg/kg and a highest residue of 0.13 mg/kg. Data were also presented for rape seed straw, but this is not a recognized feed commodity.

Fate of residues during processing

Studies were conducted on the processing of grapes in France and Spain and of soya, tomato, apple, sweet corn and cotton in the USA. The studies were conducted according to standard commercial practices. One study on tomato was rejected because samples in which residues had been incurred in the field were not used.

The processing factors and the maximum residue levels and STMR-P and HR-P values resulting from application of the factor to the estimated maximum residue levels and STMR values presented above and in the report item on methomyl are summarized in the latter.

Residues in animal commodities

No studies were provided on poultry, but the study of the nature of the residue in poultry was conducted after feeding concentrations ≤ 102 ppm for 21 days. The concentrations of residues reached a plateau in eggs within 10 days. Thiodicarb, methomyl and methomyl oxime were not detected in eggs or tissues, at an estimated LOD of about 0.005 mg/kg. As poultry diet contains a maximum of 2 ppm thiodicarb/methomyl (see report item on methomyl), quantifiable amounts of thiodicarb and/or methomyl in poultry commodities are unlikely. For methomyl plus thiodicarb, the Meeting estimated maximum residue levels of 0.02(*) mg/kg in meat, 0.02(*) mg/kg in eggs and 0.02(*) mg/kg in edible offal. Furthermore, the Meeting estimated STMR and highest residue values of 0.00 mg/kg for edible offal, meat and milk (see report item on methomyl).

In a study in lactating dairy cattle in the USA, thiodicarb was administered orally for 28 consecutive days at 350 or 1050 ppm, as measured from actual feed consumption. Milk, liver, kidney, fat and muscle from cows at 1050 ppm contained no thiodicarb (LOD, 0.1 mg/kg) and no methomyl (LOD, 0.1 mg/kg). The vast majority of samples contained no detectable residues. Thiodicarb/methomyl was detected at 0.02 mg/kg in one milk sample on day 1 and at 0.02 mg/kg on day 25, in one muscle sample at about 0.03 mg/kg, in one liver sample at 0.06 mg/kg and in one kidney sample at 0.01 mg/kg from cows at 1050 ppm. A control sample of liver contained 0.09 mg/kg.

The Meeting estimated the dietary burden of thiodicarb for farm animals on the basis of the diets listed in Appendix IX of the *FAO Manual*. As the data for methomyl and thiodicarb were combined for estimating maximum residue levels and STMR values, a single diet applies to both. The dietary calculations are given in the report item on methomyl. The dietary burden of beef and dairy cattle was estimated to be 28 ppm. No residue (< 0.1 mg/kg) was found in meat, milk, fat, kidney or liver from cattle fed at 350 or 1050 ppm. Thiodicarb/methomyl was detected in a few samples at 0.02–0.03 mg/kg from cattle at 1050 ppm. Residues of thiodicarb/methomyl will therefore not be quantifiable in ruminant commodities. For methomyl plus thiodicarb, the Meeting estimated a maximum residue level of 0.02 (*) mg/kg for meat, 0.02 (*) mg/kg for milk and 0.02 (*) mg/kg for edible offal (see the report item on methomyl). These confirm the existing values.

The average daily dietary burden of thiodicarb for ruminants is a fraction of the maximum daily burden. Thus, the STMR values for meat and milk were estimated to be 0.000 mg/kg. The highest residues for meat and milk were estimated to be 0.000 mg/kg, as there is no reasonable expectation of residues (see report item on methomyl).

On the basis of the data from supervised trials and studies of processing, the Meeting concluded that the concentrations of residues listed in the report item on methomyl are suitable for establishing MRLs and for assessing IEDIs and IESTIs.

Dietary risk assessment

See report item on methomyl.

Long-term intake

STMR or STMR-P values were estimated by the present Meeting for 39 commodities. When data on consumption were available, these values were used in the estimates of dietary intake.

The dietary intakes in the five GEMS/Food regional diets, on the basis of the new STMR values, represented 1–20% of the ADI (Annex 3). The Meeting concluded that the intake of residues of thiodicarb and methomyl resulting from the uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The IESTI for thiodicarb plus methomyl was calculated for the commodities for which maximum residue levels, STMR values and highest residues were established and for which data on consumption (of large portions and unit weight) were available. The results are shown in Annex 4.

The acute RfD for methomyl is 0.02 mg/kg bw. The IESTI represented 0–7200% of the acute RfD for children and 0–2800 % of the acute RfD for the general population. For children, the 100% of acute RfD was exceeded in: apples (770%), broccoli (1500%), Brussels sprouts (450%), head cabbage (1200%), cauliflower (1700%), celery (310%), watermelon (140%), grapes (1600%), kale (1100%), head lettuce (3000%), leaf lettuce (3800%), spinach (7200%), sweet corn (420%) and tomato (190%). For the general population, the acute RfD was exceeded in: apples (260%), broccoli (810%), Brussels sprouts (200%), head cabbage (320%), cauliflower (590%), grapes (470%), kale (670%), head lettuce (2000%), leaf lettuce (1500%), spinach (2800%) and sweet corn (140%).

The information provided to the Meeting precluded an estimate that the acute dietary intake of methomyl plus thiodicarb from the consumption of apples, broccoli, Brussels sprouts, head cabbage, cauliflower, celery (children only), watermelon (children only), grapes, kale, head lettuce, leaf lettuce, spinach, sweet corn and tomato (children only) would be below the acute RfD. The Meeting concluded that the short-term intake of residues of methomyl plus thiodicarb from uses other than on the 14 commodities that have been considered by the JMPR is unlikely to present a public health concern.

5. RECOMMENDATIONS

5.1. In the interests of public health and agriculture and in view of the needs of the Codex Committee on Pesticide Residues, the Meeting *recommended* that Joint Meetings on Pesticide Residues should continue to be held annually.

5.2. The Meeting recommended (section 2.1) that WHO establish a working group, consisting of scientists who have developed the concepts of the acute RfD at JMPR, in national governments and in the European Commission. The working group should develop a working paper for consideration by 2002 JMPR.

5.3 The Meeting recommended (section 2.2)

- that FAO and WHO implement the proposed pilot project on work-sharing in the evaluation of pesticides at the international level in close cooperation with OECD, national governments and regional and sub-regional authorities;
- that CCPR examine the implications of work-sharing on the elaboration and adoption of MRLs for pesticide residues;
- that CCPR, when setting priorities for review of pesticides by JMPR, take into account the scheduling of compounds for review at the national and regional level.

5.4 The Meeting recommended (section 2.3) adoption of a standard system for numerical expression of residue limits up to 10 mg/kg, i.e. 0.01, 0.02, 0.03, 0.05, 0.07, 0.1, 0.2, 0.3, 0.5, 0.7, 1, 2, 3, 5, 7 and 10 mg/kg. For higher values, recommended MRLs of 15, 20 and 25 mg/kg have been found useful; above these values, rounding to the next 10, i.e. 30, 40, 50, etc, is preferred. The option of using other values as necessary should be maintained.

5.5 The Meeting agreed (section 2.4) to request data submitters to provide all relevant studies for evaluation of pesticide residues unless they have prior permission from the FAO and WHO Secretaries to withhold specific studies that have been reviewed recently.

5.6 The Meeting recommended (section 2.5) that the part of this report relating to recommended MRLs resulting from studies of direct treatment of animals and residues in animal feed be referred to the Joint FAO/WHO Expert Committee on Food Additives (JECFA) for information and comment if necessary.

5.7 The Meeting reiterated its view (section 2.6) that the evaluation of data on residues from trials with pesticides is a complex task which includes consideration of several factors, such as metabolism and rate of disappearance, and it cannot be based only on calculations; therefore, statistical methods can only support expert judgement.

6. FUTURE WORK

The items listed below should be considered by the Meeting in 2002 and 2003. The compounds listed include those recommended as priorities by the CCPR at its Thirty-third or earlier sessions and compounds scheduled for re-evaluation within the CCPR periodic review programme.

6.1 2002 JMPR

Toxicological evaluations

New compounds
Esfenvalerate (purified isomer of fenvalerate)
Flutolanil

Periodic re-evaluations
Acephate (095)
Metalaxyl-M (purified isomer of metalaxyl)
Methamidophos (100)
Oxamyl (126)

Pirimiphos-methyl (086)
Tolylfluanid (162)
Triazophos (143)

Evaluations
Carbofuran (096) – acute toxicity
Ethephon (106) – acute toxicity
Fenamiphos (085) – acute toxicity
Folpet (041) – acute toxicity
Oxydemeton-methyl (166) – acute toxicity

Residue evaluations

New compounds
Esfenvalerate (purified isomer of fenvalerate)
Flutolanil
Imadocloprid

Periodic re-evaluations
Carbaryl (008)
Deltamethrin (135)
Diflubenzuron (130)
Oxamyl (126)
Pirimiphos Methyl
Propargite (113)
Tolylfluanid (162)

Evaluations
Carbofuran (096)
Cyfluthrin (157)
Myclobutanil (181)
Phosmet (103)

6.2 2003 JMPR

Toxicological evaluations

New compounds
Cyprodinil
Dimethenamid-P
Famoxadone
Methoxyfenozide

Periodic re-evaluations
Bendiocarb (137)
Carbosulfan (145)
Cyhexatin (067)/azocyclotin (129)
Glyphosate (158)
Paraquat (057)
Phorate (112)
Pirimicarb (101)
Terbufos (167)
Triadimefon (133)/triadimenol (168)

Evaluations
Dimethoate (027) – acute toxicity
Malathion (049) – acute toxicity

Residue evaluations

New compounds
Cyprodinil
Dimethenamid-P
Famoxadone
Methoxyfenozide
Pyrochlostrobin

Periodic re-evaluations
Acephate (095)
Ethoprophos (149)
Fenitrothion (037)
Lindane (048)
Metalaxyl-M (purified isomer of metalaxyl)
Methamidophos (100)
Methoprene (147)
Paraquat (057)
Prochloraz (142)
Propineb

Evaluations
Carbendazim (072)
Dicloran (083)
Dithiocarbamates (105)
Dimethoate (027)
Iprodione (111)

ANNEX 1

ACUTE DIETARY INTAKES, ACUTE REFERENCE DOSES, RECOMMENDED MAXIMUM RESIDUE LIMITS AND SUPERVISED TRIALS MEDIAN RESIDUE VALUES RECORDED BY THE 2001 MEETING

The 2001 Joint FAO/WHO Meeting on Pesticide Residues (JMPR) was held in Geneva, Switzerland, from 17 to 26 September 2001. The following information is an extract of the results of the Joint Meeting.

The Meeting evaluated or re-evaluated 26 pesticides.

The Meeting allocated acceptable daily intakes (ADIs) and acute reference doses (acute RfDs), estimated maximum residue levels which it recommended for use as maximum residue limits (MRLs) by the CCPR, and estimated supervised trials median residue (STMR) and highest residue (HR) values as a basis for estimating the dietary intakes of residues of the pesticides reviewed. The STMR is the expected residue concentration (in mg/kg) in the edible portion of a food commodity when a pesticide has been used according to maximum GAP conditions. The STMR is estimated as the median of the residue values (one from each trial) from supervised trials conducted according to maximum GAP conditions. The highest residue (HR) value is the highest concentration of residue found in the edible portion of a commodity in trials in which the maximum residue level was evaluated. The estimates are recorded in the table below.

As in recent years, the Meeting devoted particular attention to estimating the dietary intakes of the pesticides reviewed in relation to their ADIs. Those compounds for which estimated dietary intake might, on the basis of the available information, exceed their ADIs are marked with footnotes. The Meeting also estimated the acute dietary risk of some of the pesticides.

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 Residue Limits for Pesticides (*Codex Alimentarius*, Vol. 2B) and other documents and working documents of the Codex Alimentarius Commission.

The table will be included as Annex 1 in the report of the 2001 JMPR to be published late this year. This report will provide full details of the reasons for the recommendations, of the calculations of dietary intake and of the assessment of dietary risk of the pesticides reviewed. As usual, this table will also become the Annex to the "JMPR—Evaluations 2001 Part I—Residues", to be published in 2002.

The following qualifications are used in the Table.

* following recommended MRL	At or about the limit of determination
* following name of pesticide	New compound
** following name of pesticide	Reviewed within CCPR periodic review programme
Po	Recommendation accommodates post-harvest treatment of the commodity.
PoP	Recommendation accommodates post-harvest treatment of the primary food commodity (classes D and E in CODEX classification).
T	Temporary
W in place of a recommended MRL	Previous recommendation withdrawn, recommended MRL withdrawn, or existing Codex or draft MRL recommended

Pesticide (Codex reference number)	ADI (mg/kg bw)	CCN	Commodity name	Recommended MRL (mg/kg)		STMR, STMR-P (mg/kg)	HR HR-P (mg/kg)
				New	Previous		
Aldicarb (117)	0–0.003	FI 0327	Banana	0.2	W	0.01	0.10
		VR 0589	Potato	0.5	0.5	0.06	0.45
			Potato, microwaved			0.042	0.315
			Potato flakes			0.045	
			Potato chips			0.228	
			Potato frozen fries			0.0174	
			Potato cooked fries			0.0234	
		Residue: for compliance with MRLs and estimation of dietary intake for plant commodities: sum of aldicarb, aldicarb sulfoxide and aldicarb sulfone, expressed as aldicarb. Acute RfD: 0.003 mg/kg bw					
Carbaryl (008)	0–0.008	Acute RfD: 0.2 mg/kg bw					
Chlorpropham (201)	0–0.03	MM 0812	Cattle meat	0.1(fat)	–	0.004	0.004
		ML 0812	Cattle milk	0.0005*F	–	0.0003	
		MO 0812	Cattle, edible offal of	0.01*	–	0.005	0.007
		VR 0589	Potato	30 Po	–	11	23
			Potato chips with skin			4.6	
			Potato chips without skin			1.1	
			Potato dehydrated granules			0.845	
			Potato French fries with skin			1.6	
			Potato French fries without skin			0.2	
			Potato, cooked[1]			3.6	7.6
			Potato, peeled and cooked			0.098	0.2
		Residue: for compliance with MRLs and for estimation of dietary intake: chlorpropham. The residue is fat-soluble. [1]The information provided to the JMPR precludes an estimate that the dietary intake would be below the acute RfD. Acute RfD: 0.03 mg/kg bw					
Chlorpyrifos-methyl (090)	0–0.01	Acute RfD: Unnecessary					
2,4-D (020)	0.01	FC 0001	Citrus fruits	1 Po	–	0.3 [1]	
			Citrus juice			0.03[1]	
			Citrus oil			0.3 [1]	
		FC 0203	Grapefruit	W	0.1		
		FC 0004	Oranges, sweet, sour	W	0.1		
		Residue: for compliance with MRLs and for estimation of dietary intake: 2,4-D. [1]As no data for edible portion were available, STMR values are based on results for whole fruits. Acute RfD: Unnecessary					
Diazinon (022)	0–0.002	Acute RfD: 0.03 mg/kg bw					
Diflubenzuron (130)	0–0.02	Acute RfD: Unnecessary					
Dimethipin** (151)	0–0.02	SO 0691	Cottonseed	1	0.5	0.1	0.7
		OC 0691	Cottonseed oil, crude	0.1	0.1	0.02	
		OR 0691	Cottonseed oil, edible	0.1	0.02*	0.02	
		MO 0105	Edible offal (mammalian)	0.01*	0.02*	0	0

Pesticide (Codex reference number)	ADI (mg/kg bw)	CCN	Commodity name	Recommended MRL (mg/kg)		STMR, STMR-P (mg/kg)	HR HR-P (mg/kg)
				New	Previous		
		PE 0112	Eggs	0.01*	0.02*	0	0
		SO 0693	Linseed	W	0.2		
		MM 0095	Meat (from mammals other than marine mammals)	0.01*	0.02*	0	0
		ML 0106	Milks	0.01*	0.02*	0	
		VR 0589	Potato	0.05*	0.05*	0.02	0.02
		PM 0110	Poultry meat	0.01*	0.02*	0	0
		PO 0111	Poultry, edible offal	0.01*	0.02*	0	0
		SO 0495	Rapeseed	0.2	–	0.1	0.1
		SO 0702	Sunflower seed	1	0.5	0.1	0.77
		OC 0702	Sunflower seed oil, Crude	W	0.1		
		OR 0702	Sunflower seed oil, edible	W	0.02*		
		Residue: for compliance with MRL and for estimation of dietary intake: dimethipin.					
		Acute RfD: 0 .02 mg/kg bw					
Dinocap (087)	0–0.008	FB0269	Grapes	0.5	1	0.05	0.35
		Residue: for compliance with MRL and for estimation of dietary intake: dinocap					
		Acute RfD: 0.03 mg/kg bw (for the general population)					
		0.008 mg/kg bw (for women of childbearing age)					
Diphenylamine** (030)	0–0.08	FP 0226	Apple	10 Po	5 Po	4.45	
		JF 0226	Apple juice	0.5 PoP		0.23	
		AB 0226	Apple pomace (dry)	25 PoP		10.6	
			Apple pomace (wet)			21	
		MO 1280	Cattle, kidney	0.01*		0.0007	
		MO 1281	Cattle, liver	0.05		0.024	
		ML 0812	Cattle milk	0.0004* F[1]		0.00015	
		MM 0812	Cattle meat	0.01* (fat)		0.0005	
		FP 0230	Pear	5 Po		2.2	
		Residue: for compliance with the MRL and for estimation of dietary intake: diphenylamine.					
		The residue is fat-soluble.					
		[1] Equivalent to 0.01* mg/kg in the milk fat					
		Acute RfD: Unnecessary					
Fenpropimorph (188)	0–0.003	Acute RfD: 1 mg/kg bw					
Fipronil (202)	0–0.0002[1]	FI 0327	Banana	0.005	–	0.004	0.005
		GC 0640	Barley	0.002*	–	0.004	0.004
		VB 0041	Cabbages, head	0.02	–	0.005	0.00215
		MO 1280	Cattle, kidney	0.02	–	0.014	0.018
		MO 1281	Cattle, liver	0.1	–	0.064	0.079
		MM 0812	Cattle meat	0.5 (fat)	–	0.015	0.019
		ML 0812	Cattle milk	0.02	–	0.011	
		PE 0112	Eggs	0.02	–	0.006	0.0078
		VB 0042	Flowerhead brassicas	0.02	–	0.005	0.00215
		GC 0645	Maize	0.01	–	0.005	0.02
		AF 0645	Maize forage	0.1[2]	–		
		AS 0645	Maize fodder	0.1[2]	–		
		GC 0647	Oats	0.002*	–	0.004	0.004
		VR 0589	Potato	0.02	–	0.004	0.028
			Potato chips			0.0009	
			Potato flakes			0.0011	
		PO 0110	Poultry, edible offal of	0.02	–	0.008	0.0084
		PM 0110	Poultry meat	0.01*	–	0.006	0.006
		GC 0649	Rice	0.01	–	0.006	0.013
		AS 0649	Rice straw and fodder, dry	0.2[2]	–		
		GC 0650	Rye	0.002*	–	0.004	0.004

Pesticide (Codex reference number)	ADI (mg/kg bw)	CCN	Commodity name	Recommended MRL (mg/kg)		STMR, STMR-P (mg/kg)	HR HR-P (mg/kg)
				New	Previous		
		VR 0596	Sugar beet	0.2	–	0.0125	0.17
			Sugar beet leaves or tops	0.2[2]	–		
		SO 0702	Sunflower seed	0.002*	–	0.004	0.008
		GC 0653	Triticale	0.002*	–	0.004	0.004
		GC 0654	Wheat	0.002*	–	0.004	0.004
		Residues: for compliance with MRLs for plant commodities: fipronil. For compliance with MRLs for animal commodities: sum of fipronil and 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulfonyl pyrazole (MB 46136), expressed as fipronil. For estimation of dietary intake for plant and animal commodities: sum of fipronil, 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulfonyl pyrazole (MB 46136), 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (MB 45950) and 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethyl pyrazole (MB 46513), expressed as fipronil. The residue is fat-soluble. [1]Group ADI for fipronil and fipronil-desulfinyl [5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethyl pyrazole (MB 46513)] [2]Expressed on dry weight basis. Acute RfD: 0.003 mg/kg bw (for fipronil and fipronyl-desulfinyl[5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethyl pyrazole (MB 46513)], alone or in combination)						
Haloxyfop (194)	0–0.0003	AL 1021	Alfalfa forage (green)	5.0[1]	W	2.33	–
		MM 0812	Cattle meat	0.05	W	0.02	0.03
		ML 0812	Cattle milk	0.3	W	0.22	–
		MO 0812	Cattle, edible offal of	–	W	–	–
		MO 1280	Cattle, kidney	1	–	0.73	0.95
		MO 1281	Cattle, liver	0.5	–	0.28	0.33
		PE 0840	Chicken eggs	0.01*	0.01*	0.002	0.003
		PM 0840	Chicken meat	0.01*[2]	0.01*	0.002	0.03
		PO 0840	Chicken, edible offal of	0.05	0.1	0.009	0.003
		AV 1051	Fodder beet leaves or tops	0.3[1]	W	0.03	–
		AV 0596	Sugar beet leaves or tops	0.3[1]	W	0.03	–
		Residue: for compliance with MRLs and for estimation of dietary intake for products of animal origin: haloxyfop ester, haloxyfop and its conjugates expressed as haloxyfop (whole product basis). [1]Fresh weight basis [2]With adhering skin Acute RfD: may be necessary but has not yet been established Note: The information provided to the JMPR precludes an estimate that the dietary intake would be below the ADI.					
Imidacloprid*	0–0.06	Acute RfD: 0.4 mg/kg bw					
Imazalil (110)	0–0.03	Acute RfD: Unnecessary					
Iprodione (111)	0–0.06	VO 0448	Tomato	5	5	1.1	4.2
			Tomato juice			0.55	
			Tomato puree			0.55	
			Tomato ketchup			0.99	
		Residue: for compliance with MRLs and for estimation of the dietary intake: iprodione Acute RfD: may be necessary but has not been established					
Kresoxim-methyl (199)	0–0.4	FC 0203	Grapefruit	0.5	–		
			Grapefruit, edible portion of			0.01	
		FT 0305	Olives	0.2	–	0.05	
		OC 0305	Olive oil, virgin	0.7	–	0.22	
		FC 0004	Oranges, sweet, sour	0.5		0.13	

Pesticide (Codex reference number)	ADI (mg/kg bw)	CCN	Commodity name	Recommended MRL (mg/kg)		STMR, STMR-P (mg/kg)	HR HR-P (mg/kg)
				New	Previous		
			Oranges, edible portion of			0.01	
		Residue: for compliance with MRLs and for estimation of the dietary intake for plant commodities: kresoxim-methyl. For compliance with MRLs and for estimation of the dietary intake for animal commodities: α-(*para*-hydroxy-*ortho*-tolyloxy)-*ortho*-tolyl(methoxyimino) acetic acid, expressed as kresoxim-methyl Acute RfD: Unnecessary							
Methomyl** (094)	0–0.02	AL 1021	Alfalfa forage (green)	25[1]	10 fresh wt		
		AL 1020	Alfalfa fodder (hay)	20[1]	–		
		FP 0226	Apple[4]	2[2]	–	0.41	1.6
		JF 0226	Apple juice	–	–	0.12	
		VS 0621	Asparagus	2[1]	2	0.33	1.1
		GC 0640	Barley	2[1]	0.5	0.14	1.3
		AS 0640	Barley straw and fodder,dry	W	5		
		VD 0071	Beans (dry)	0.05[1]	0.1	0.02	0.023
		AL 0061	Bean fodder (hay)	10[1]	–		
		VP 0061	Beans (except broad and soya	1[1]	–	0.005	0.68
		VB 0040	Brassica (cole or cabbage) vegetables[4]	7[3]	–	1.3	5.6
		VB 0041	Cabbages, head	W	5		
		VB 0404	Cauliflower	W	2		
		VS 0624	Celery[4]	3[1]	2	0.66	2
		AS 0161	Cereal grain, straw, fodder (dry), hay	10[3]	–		
		FC 0001	Citrus fruits	1[1]	1	0.034 flesh	0.18 flesh
		AB 0001	Citrus pulp, dry	3	–		
		JF 0001	Citrus juice	–		0.004	
		VP 0526	Common bean (pods and/or immature seeds)	1[1]	2	0.055	0.68
		SO 0691	Cottonseed	0.2[3]	0.5		
		OR 0691	Cottonseed, edible oil	0.04		0.006	
			Cottonseed, meal	0.05	–		
			Cottonseed, hulls	0.2	–		
		VC 0424	Cucumber	W	0.2		
		VC 0045	Cucurbits, fruiting vegetables[5]	0.1[1]		0.02	0.07
		MO 0105	Edible offal (from mammals other than marine mammals)	0.02*[3]	0.02*	0.00	0.00
		VO 0440	Egg plant	W	0.2		
		PE 0840	Eggs	0.02*[3]	–	0.00	0.00
		FB 0270	Grapes[4]	7[1]	5	0.86	5.2
		DH 1100	Hops, dry	W	10		
		VL 0480	Kale	W	5		
		VL 0482	Lettuce, head	W	5		
		VL 0053	Leafy vegetables[4]	30[3]	–	1.4	25
		GC 0645	Maize	0.02*[1]	0.05*	0.02	0.02
		AS 0645	Maize fodder	W	50 fresh wt		
		AF 0645	Maize forage	50[3]	50 fresh wt		
		OR 0645	Maize, edible oil	0.02*	–	0.004	
		MM 0095	Meat (from mammals other than marine mammals)	0.02*[3]	0.02*	0.000	0.000
		VC 0046	Melons, except watermelon	W	0.2		
		ML 0106	Milks	0.02*[3]	0.02*	0.000	
		AM 0738	Mint hay	W	2		

Pesticide (Codex reference number)	ADI (mg/kg bw)	CCN	Commodity name	Recommended MRL (mg/kg)		STMR, STMR-P (mg/kg)	HR HR-P (mg/kg)
				New	Previous		
		FS 0245	Nectarines	0.2[1]	5	0.05	0.10
		AS 0647	Oat straw and fodder, dry	W	5		
		GC 0647	Oats	0.02*[1]	0.5		
		VA 0385	Onion, bulb	0.2[1]	0.2	0.068	0.14
		VA 0387	Onion, Welsh	W	0.5		
		AL 0528	Pea vines (green)	40[1]	10 fresh wt		
		FS 0247	Peach	0.2[1]	5	0.05	0.10
		SO 0697	Peanut	W	0.1		
		AL1270	Peanut forage (green)	W	5		
		FP 0230	Pear	0.3[1]	–	0.09	0.18
		VP 0063	Peas (pods and succulent; immature seeds)	5[1]	5	0.46	4.0
		VP 0064	Peas, shelled (succulent seeds)	W	0.5		
		VO 0051	Peppers	W	1		
		Fl 0353	Pineapple	W	0.2		
		FS 0014	Plums	1[1]	–	0.08	0.51
		VR 0589	Potato	0.02*[3]	0.1	0.00	0.00
		PO 0110	Poultry meat	0.02*[3]	–	0.00	0.00
		PO 0111	Poultry, edible offal of	0.02*[3]	–	0.00	0.00
		SO 0495	Rapeseed	0.05[2]	–		
			Rapeseed forage	0.2	–		
		GC 0651	Sorghum	W	0.2		
		AF 0651	Sorghum forage (green)	1[1]	1		
		VD 0541	Soya bean (dry)	0.2[2]	0.2		
		VP 0541	Soya bean (immature seed)	W	0.1		
		AL 1265	Soya bean forage (green)	40[1]	10		
		AL 0541	Soya bean hay	0.2[1]	–		
			Soya bean hulls	1	–		
			Soya bean meal	0.2			
		VD 0541	Soya bean oil, crude	0.2	–	0.04	
		OR 0541	Soya bean oil, refined	0.2	–	0.04	
		VL 0502	Spinach	W	5		
		VC 0431	Squash, summer	W	0.2		
		VR 0596	Sugar beet	W	0.1		
		VO 0447	Sweet corn (corn-on-the-cob)[4]	2[2]	2	0.065	1.5
		VO 0448	Tomato[4]	1[2]	1	0.16	0.73
		VJ 0448	Tomato paste	–	–	0.007	
		VC 0432	Watermelon	W	0.2		
		GC 0654	Wheat	2[1]	0.5	0.14	1.3
		CF 01211	Wheat flour	0.03	–	0.003	
		CF 0654	Wheat bran	3	–	0.27	
		CF 1210	Wheat germ	2	–	0.13	
		–	Wine, of grape	–	–	0.26	
		Residue: for compliance with MRLs and for the estimation of dietary intake: sum of thiodicarb and methomyl, expressed as methomyl. [1]Resulting from consideration of methomyl supervised field trial data. [2]Resulting from consideration of thiodicarb supervised field trial data. [3]Resulting from consideration of methomyl + thiodicarb supervised field trial data. [4]The information provided to the JMPR precludes an estimate that the dietary intake would be below the acute RfD. [5]The information provided to the JMPR precludes an estimate that the dietary intake for watermelon would be below the acute RfD. Acute RfD: 0.02 mg/kg bw					
Methoprene** (147)	0–0.09[1] 0–0.05[2]	[1]ADI for the *R,S* racemate [2]ADI for *S*-methoprene Acute RfD: Unnecessary					

Pesticide (Codex reference number)	ADI (mg/kg bw)	CCN	Commodity name	Recommended MRL (mg/kg)		STMR, STMR-P (mg/kg)	HR HR-P (mg/kg)
				New	Previous		
Phosalone (060)	0–0.02	Acute RfD: 0.3 mg/kg bw					
Piperonyl butoxide** (062)	0–0.2	ML 0812	Cattle milk	0.2[1]		0.14[2]	
		MO 1280	Cattle kidney	0.3[1]		0.21[2]	
		MO 1281	Cattle liver	1		0.10	
		MM 0812	Cattle meat	5 (fat)[1]		0.16[2,3]	
		GC 0080	Cereal grains	30 Po		11	
		FC 0001	Citrus fruit	5		1	
		AB 0001	Citrus fruit, dry			5.7	
		JF 0001	Citrus juice	0.05		0.01	
		DM 0001	Citrus molasses			0.53	
		DF 0167	Dried fruits	0.2 Po		0.05	
		PE 0112	Eggs	1[1]		0.36[2]	
		VC 0045	Fruiting vegetables, curcubits	1		0.26	
		VL 0483	Lettuce, leaf	50		38	
		OC 0645	Maize oil, crude	80 PoP		29.7	
		VL 0485	Mustard greens	50		38	
		AL 0072	Pea hay or pea fodder	200		19.9	
		AL 0528	Pea vine (green)	400		108	
		SO 0703	Peanut, whole	1 Po		0.1	
		VO 0051	Peppers	2		0.675	
		PM 0110	Poultry meat	5 (fat)[1]		1.0[2,3]	
		PO 0111	Poultry, Edible offal	10[1]		2.03[2]	
		VD 0070	Pulses	0.2 Po		0.05	
		VL 0494	Radish leaves	50		38	
		VR 0075	Root and tuber vegetables, except carrots	0.5		0.10	
		VL 0502	Spinach	50		38	
		VO 0448	Tomato	2		0.675	
		VJ 0448	Tomato, juice	0.3		0.10	
			Tomato, puree			0.22	
		GC 0654	Wheat	W	10Po		
		CM 0654	Wheat bran, unprocessed	100 PoP		38.5	
		CF 1211	Wheat flour	10 PoP		3.5	
		CF 1211	Wheat germ	100 PoP		30.8	
		CF 1212	Wheat wholemeal	30 PoP		10.8	
		Residue: for compliance with MRLs and for estimation of the dietary intake for plant and animal commodities: piperoyl butoxide [1]The MRL accommodates external animal treatment [2]Not STMR but median residues from animals in a treated group [3]In muscle Acute RfD: Unnecessary					
Prochloraz** (142)	0–0.01	Acute RfD: 0.1 mg/kg bw					
Pyriproxyfen (200)	0–0.1	Safety of addition to drinking-water as a larvicide was evaluated Acute RfD: Unnecessary					
Spinosad* (203)	0–0.02	AM 0660	Almond hulls	2		0.56	
		TN 0660	Almonds	0.01*		0.01	
		JF 0226	Apple juice			0.0013	
			Apple pomace, wet			0.064	
			Apple puree			0.0015	
		FP 0226	Apples	0.1		0.0165	
		VB 0040	Brassica vegetables, Head cabbages, Flowerhead brassicas	2		0.27	
		MO 1280	Cattle kidney	1[1]		0.31[2]	
		MO 1281	Cattle liver	2[1]		0.66[2]	

Pesticide (Codex reference number)	ADI (mg/kg bw)	CCN	Commodity name	Recommended MRL (mg/kg)		STMR, STMR-P (mg/kg)	HR HR-P (mg/kg)
				New	Previous		
		MM 0812	Cattle meat	3 (fat)[1]		0.078[2]	
		ML 0812	Cattle milk	1[1]		0.65	
		VS 0624	Celery	2		0.97	
		FC 0001	Citrus fruits	0.3		0.01	
		AB 0001	Citrus, dried processing pulp			0.12	
		SO 0691	Cotton seed	0.01*		0.01	
			Cotton seed hulls			0.0020	
			Cotton seed meal			0.0017	
		OC 0691	Cotton seed oil, crude	0.01*		0.0018	
		OR 0691	Cotton seed oil, edible	0.01*		0.0020	
		PE 0112	Eggs	0.01		0.01	
		VC 0045	Fruiting vegetables, cucurbits	0.2		0.046	
		FI 0341	Kiwifruit	0.05		0.02	
		VL 0053	Leafy vegetables	10		1.9	
		VP 0060	Legume vegetables	0.3		0.041	
		GC 0645	Maize	0.01*		0	
		AS 0645	Maize fodder (dry)	5		0.46	
		AF 0645	Maize forage (dry)	5		0.70	
		JF 0004	Orange juice			0.0072	
		VO 0051	Peppers	0.3		0.056	
		VR 0589	Potato	0.01*		0	
		PM 0110	Poultry meat	0.2 (fat)		0.01	
		MO 0822	Sheep, edible offal of	0.01*,[1]		0.01	
		MM 0822	Sheep meat	0.01* (fat)[1]		0.01	
		GC 0651	Sorghum	1		0.165	
		VD 0541	Soya bean (dry)	0.01*		0	
		FS 0012	Stone fruits	0.2		0.0265	
		VO 0447	Sweet corn (corn-on-the-cob)	0.01*		0.01	
		VO 0448	Tomato	0.3		0.03	
		JF 0448	Tomato juice			0.0075	
			Tomato paste			0.059	
			Tomato puree			0.017	
		AS 0654	Wheat straw and fodder, dry	1		0.215	
		Residue: for compliance with MRL and for estimation of dietary intake : sum of spinosyn A and spinosyn D. The residue is fat-soluble, but residues in milk should be measured on the whole milk. [1]The MRL accommodates external animal treatment [2]Residues from direct animal treatment – not an STMR, but median of residues from animals in a treatment group Acute RfD: Unnecessary					
Tebufenozide (196)	0–0.02	TN 0660	Almonds	0.05	–	0.0205	0.045
		AM 0660	Almond hulls	30		15.5	
		FI 0326	Avocado	1	–	0.21	0.53
		VB 0400	Broccoli	0.5	–	0.11	0.34
		FB 0020	Blueberries	3	–	0.685	1.7
		VB 0041	Cabbage, head[1]	5	–	0.34	4.6
		MO 1280	Cattle, kidney	0.02*		0.006	0.006
		MO 1281	Cattle, liver	0.02*	–	0.02	0.02
		MM 0812	Cattle meat (F)	0.05		0.006	0.006
		ML 0812	Cattle milk	0.01*	–	0.003	
		FC 0001	Citrus fruit	2	–	0.079	0.18
			Citrus oil			12.5	
			Citrus dried pulp			0.38	
		JF 0001	Citrus juice			0.0077	

Pesticide (Codex reference number)	ADI (mg/kg bw)	CCN	Commodity name	Recommended MRL (mg/kg)		STMR, STMR-P (mg/kg)	HR HR-P (mg/kg)
				New	Previous		
		FB 0265	Cranberries	0.5	–	0.042	0.28
		DF 0269	Dried grapes (currants, raisins and sultanas)	2	–	0.551	1.11
		PE 0112	Eggs	0.02*		0	0
		FB 0269	Grapes[1]	2	1	0.745	1.5
			Grape wet pomace			2.9	
			Wine			0.216	
		JF 0269	Grape juice			0.097	
		VL 0053	Leafy vegetables[1]	10	–	2.45	8.1
		HH 0738	MintM	20	–	8.35	8.6
			int oil			0.25	
		FS 0245	Nectarines	0.5	–	0.11	0.23
		FS 0247	Peaches	0.5	–	0.11	0.23
			Canned peaches			0.0066	
		TN 0672	Pecans	0.01*	–	0.01	0.01
		VO 0051	Peppers	1		0.064	0.64
		PM 0110	Poultry meat	0.02*	–	0.02	0.02
		FB 0272	Raspberries	2		0.56	0.86
		SO 0495	Rapeseed	2	–	0.95	1.6
			Rapeseed mealR			0.14	
			apeseed soapstock			1.0	
		OC 0495	Rapeseed oil			2.2	
		GS 0659	Sugarcane stems	1	–	0.12	0.62
			Refined sugar			0.003	
			Molasses			0.708	
		VO 0448	Tomatoes	1	–	0.13	0.53
			Tomato puree			0.04	
			Tomato paste			0.095	
			Tomatoes (preserved)			0.036	
		JF 0448	Tomato juice			0.023	
		Residue: for compliance with MRL and for estimation of dietary intake for plant and animal products: tebufenozide The residue is fat-soluble [1]The information provided to the JMPR precludes an estimate that the dietary intake would be below the acute RfD.Acute RfD: 0.05 mg/kg bw					
Thiodicarb** (154)	0–0.03	Residue for compliance with MRL and for the estimation of dietary intake: sum of thiodicarb and methomyl, expressed as methomyl Acute RfD: 0.04 mg/kg bw.					

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)
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)
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)
Bromide ion (047)	1968 (R), 1969 (T,R), 1971 (R), 1979 (R), 1981 (R), 1983 (R), 1988 (T,R), 1989 (R), 1992 (R)

Bromomethane (052)	1965 (T,R), 1966 (T,R), 1967 (R), 1968 (T,R), 1971 (R), 1979 (R), 1985 (R), 1992 (R)
Bromophos (004)	1972 (T,R), 1975 (R), 1977 (T,R), 1982 (R), 1984 (R), 1985 (R)
Bromophos-ethyl (005)	1972 (T,R), 1975 (T,R), 1977 (R)
Bromopropylate (070)	1973 (T,R), 1993 (T,R)
Butocarboxim (139)	1983 (R), 1984 (T), 1985 (T), 1986 (R)
Buprofezin (173)	1991 (T,R), 1995 (R), 1996 (corr. to 1995 report.), 1999 (R)
sec-Butylamine (089)	1975 (T,R), 1977 (R), 1978 (T,R), 1979 (R), 1980 (R), 1981 (T), 1984 (T,R: withdrawal of temporary ADI, but no evaluation)
Cadusafos (174)	1991 (T,R), 1992 (R), 1992 (R)
Campheclor (071)	1968 (T,R), 1973 (T,R)
Captafol (006)	1969 (T,R), 1973 (T,R), 1974 (R), 1976 (R), 1977 (T,R), 1982 (T), 1985 (T,R), 1986 (corr. to 1985 report), 1990 (R), 1999 (acute Rf D)
Captan (007)	1965 (T), 1969 (T,R), 1973 (T), 1974 (R), 1977 (T,R), 1978 (T,R), 1980 (R), 1982 (T), 1984 (T,R), 1986 (R), 1987 (R and corr. to 1986 R evaluation), 1990 (T,R), 1991 (corr. to 1990 R evaluation), 1994 (R), 1995 (T), 1997 (R), 2000 (R)
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)
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)
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)
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)
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)
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)
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)
Demeton (092)	1965 (T), 1967 (R), 1975 (R), 1982 (T)
Demeton-*S*-methyl (073)	1973 (T,R), 1979 (R), 1982 (T), 1984 (T,R), 1989 (T,R), 1992 (R), 1998 (R)
Demeton-*S*-methylsulphon (164)	1973 (T,R), 1982 (T), 1984 (T,R), 1989 (T,R), 1992 (R)
Dialifos (098)	1976 (T,R), 1982 (T), 1985 (R)
Diazinon (022)	1965 (T), 1966 (T), 1967 (R), 1968 (T,R), 1970 (T,R), 1975 (R), 1979 (R), 1993 (T,R), 1994 (R), 1996 (R), 1999 (R), 2001 (T)
1,2-Dibromoethane (023)	1965 (T,R), 1966 (T,R), 1967 (R), 1968 (R), 1971 (R),

	1979 (R), 1985 (R)
Dichlorfluanid (082)	1969 (T,R), 1974 (T,R), 1977 (T,R), 1979 (T,R), 1981 (R),1982 (R), 1983 (T,R), 1985 (R)
1,2-Dichloroethane (024)	1965 (T,R), 1967 (R), 1971 (R), 1979 (R), 1985 (R)
Dichlorvos (025)	1965 (T,R), 1966 (T,R), 1967 (T,R), 1969 (R), 1970 (T,R), 1974 (R), 1977 (T), 1993 (T,R)
Dicloran (083)	1974 (T,R), 1977 (T,R), 1998 (T,R)
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)
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)
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)
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-*ortho*-cresol (DNOC)	1965 (T)
Dodine (084)	1974 (T,R), 1976 (T,R), 1977 (R), 2000 (T)
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)
Ethephon (106)	1977 (T,R), 1978 (T,R), 1983 (R), 1985 (R), 1993 (T), 1994 (R), 1995 (T), 1997 (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)
Fenamiphos (085)	1974 (T,R), 1977 (R), 1978 (R), 1980 (R), 1985 (T), 1987 (T), 1997 (T), 1999 (R)
Fenarimol (192)	1995 (T,R,E), 1996 (R and corr. to 1995 report)
Fenbuconazole (197)	1997 (T,R)
Fenbutatin oxide (109)	1977 (T,R), 1979 (R), 1992 (T), 1993 (R)
Fenchlorfos (036)	1968 (T,R), 1972 (R), 1983 (R)
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)
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)
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)
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)
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)
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)
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)
Methacrifos (125)	1980 (T,R), 1982 (T), 1986 (T), 1988 (T), 1990 (T,R), 1992 (R)
Methamidifos (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)
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)
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)
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)
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)
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)
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)
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)
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)
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)
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)
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)
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)
Pyriproxyfen	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),
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)
Thianedazole (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)
Thiphanate-methyl (077)	1973 (T,R), 1975 (T,R), 1977 (T), 1978 (R), 1988 (R), 1990 (R), 1994 (R), 1995 (T,E), 1998 (T,R)
Thiram (105)	See Dithiocarbamates, 1965 (T), 1967 (T,R), 1970 (T,R), 1974 (T), 1977 (T), 1983 (R), 1984 (R), 1985 (T,R), 1987 (T), 1988 (R), 1989 (R), 1992 (T), 1996 (R)
Tolclofos-methyl (191)	1994 (T,R) 1996 (corr. to Annex II of 1995 report)
Tolylfluanid (162)	1988 (T,R), 1990 (R), 1991 (corr. to 1990 report)
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)
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
Vamidothion (078)	1973 (T,R), 1982 (T), 1985 (T,R), 1987 (R), 1988 (T), 1990 (R), 1992 (R)
Vinclozolin (159)	1986 (T,R), 1987 (R and corr. to 1986 report and R evaluation), 1988 (T,R), 1989 (R), 1990 (R), 1992 (R), 1995 (T)
Zineb (105)	See Dithiocarbamates, 1965 (T), 1967 (T,R), 1993 (T)
Ziram (105)	See Dithiocarbamates, 1965 (T), 1967 (T,R), 1996 (T,R)

DIETARY INTAKES OF PESTICIDES IN RELATION TO ADIs

The following Tables give details of the estimated daily intakes of the pesticides evaluated by the Meeting for the five GEMS/Food regional diets, and show the ratios of the estimated intakes to the corresponding ADIs.
(*) at or about the LOD

The ranges of the intake/ADI ratios for all the compounds evaluated are tabulated in Sec 3, page 19.

ALDICARB (117) **Dietary Intake Estimate (DIE)**

ADI = 0.003 mg/kg bodyweight or 0.18 mg for a 60 kg person

Commodity		MRL	STMR	Processing	Notes	Adjusted	Middle Eastern		Far Eastern		African		Latin American		European	
		mg/kg	mg/kg	Factor		STMR	Diet	DIE	Diet	DIE	Diet	DIE	Diet	DIE	Diet	DIE
FI 0327	Banana	0,2	0,01				8,3	0,0000	26,2	0,0000	21,0	0,0000	102,3	0,0000	22,8	0,0000
VD 0071	Beans, dry	0,1					6,8	0,0007	6,8	0,0007	0,0	0,0000	13,5	0,0014	4,3	0,0004
VB 0402	Brussels sprouts	0,1					0,5	0,0001	1,0	0,0001	0,0	0,0000	1,1	0,0001	2,7	0,0003
FC 0001	Citrus fruit	0,2					54,3	0,0109	6,3	0,0013	5,1	0,0010	54,8	0,0110	49,0	0,0098
SB 0716	Coffee beans	0,1					5,3	0,0005	0,4	0,0000	0,0	0,0000	3,6	0,0004	7,9	0,0008
SO 0691	Cotton seed	0,1					0,0	0,0000	2,0	0,0002	1,5	0,0002	4,0	0,0004	1,0	0,0001
OR 0691	Cotton seed oil, edible	0,01*					3,8	0,0000	0,5	0,0000	0,5	0,0000	0,5	0,0000	0,0	0,0000
FB 0269	Grapes	0.2					15.75	0,0032	1,0	0,0002	0,0	0,0000	1,3	0,0003	13,8	0,0028
GC 0645	Maize	0,05					16,5	0,0008	0,0	0,0000	0,0	0,0000	1,5	0,0001	0,0	0,0000
MM 0095	Meat	0,01*					37,0	0,0004	32,8	0,0003	23,8	0,0002	47,0	0,0005	155,5	0,0016
ML 0106	Milks	0,01*					116,8	0,0012	32,0	0,0003	41,8	0,0004	160,0	0,0016	294,0	0,0029
VA 0385	Onion bulb	0,1					23,0	0,0023	11,5	0,0012	7,3	0,0007	13,8	0,0014	27,8	0,0028
SO 0697	Peanut	0,02					0,3	0,0000	0,2	0,0000	2,3	0,0000	0,3	0,0000	3,0	0,0001
OR 0697	Peanut oil, edible	0,01*					0,0	0,0000	1,8	0,0000	3,5	0,0000	0,5	0,0000	1,8	0,0000
TN 0672	Pecan	1					0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000	0,3	0,0003
VR 0589	Potatoes	0,5	0,06	0,75	1/	0,042	59,0	0,0027	19,2	0,0086	20,6	0,0009	40,8	0,0018	240,8	0,0108
GC 0651	Sorghum	0,1					2,0	0,0002	9,7	0,0010	26,6	0,0027	0,0	0,0000	0,0	0,0000
VD 0541	Soya bean, dry	0,02*					4,5	0,0001	2,0	0,0000	0,5	0,0000	0,0	0,0000	0,0	0,0000
VR 0596	Sugar beet	0,05*					0,5	0,0000	0,0	0,0000	0,0	0,0000	0,3	0,0000	2,0	0,0001
GS 0659	Sugar cane	0,1					18,5	0,0019	7,3	0,0007	15,9	0,0016	3,5	0,0004	0,0	0,0000
SO 0702	Sunflower seed	0,05*					1,0	0,0001	0,0	0,0000	0,6	0,0000	0,0	0,0000	0,0	0,0000
VR 0508	Sweet potato	0,1					1,5	0,0002	81,3	0,0081	14,3	0,0014	13,8	0,0014	1,3	0,0001
GC 0654	Wheat	0,02					327,3	0,0065	114,8	0,0023	28,3	0,0006	116,8	0,0023	178,0	0,0036
						Total =		0,0315		0,0175		0,0101		0,0237		0,0359
						% ADI=		17		11		6		13		20
						Rounded % ADI =		20		10		6		10		20

CARBARYL
(8)

ADI = 0.0008 mg/kg bodyweight or 0.048 mg for a 60 kg person

Commodity		MRL	Notes	Middle Eastern		Far Eastern		African		Latin American		European	
		mg/kg		Diet	TMDI	Diet	TMDI	Diet	TMDI	Diet	TMDI	Diet	TMDI
Code	Name			g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day
FP 0226	Apple	5		7,5	0,0375	4,7	0,0233	0,3	0,0013	5,5	0,0275	40,0	0,2000
FS 0240	Apricot	10		3,0	0,0300	0,0	0,0000	0,0	0,0000	0,0	0,0000	3,5	0,0350
VS 0621	Asparagus	10		0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000	1,5	0,0150
FI 0327	Banana	5		8,3	0,0413	26,2	0,1308	21,0	0,1050	102,3	0,5113	22,8	0,1138
GC 0640	Barley	5		1,0	0,0050	3,5	0,0175	1,8	0,0088	6,5	0,0325	19,8	0,0988
VR 0574	Beetroot	2		0,5	0,0010	0,0	0,0000	0,0	0,0000	0,3	0,0005	2,0	0,0040
FB 0264	Blackberries	10		0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000
FB 0020	Blueberries	7		0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000	0,5	0,0035
VB 0041	Cabbages, Head	5		5,0	0,0250	9,7	0,0483	0,0	0,0000	10,5	0,0525	26,8	0,1338
VR 0577	Carrot	2		2,8	0,0055	2,5	0,0050	0,0	0,0000	6,3	0,0125	22,0	0,0440
MM 0812	Cattle meat	0,2		18,5	0,0037	3,5	0,0007	10,4	0,0021	30,0	0,0060	63,3	0,0127
FS 0013	Cherries	10		0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000	3,0	0,0300
FC 0001	Citrus fruits	7		54,3	0,3798	6,3	0,0443	5,1	0,0356	54,8	0,3833	49,0	0,3430
VP 0526	Common bean (pods and/or immature seeds)	5		3,5	0,0175	0,8	0,0042	0,0	0,0000	4,0	0,0200	12,0	0,0600
SO 0691	Cotton seed	1		0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000
VD 0527	Cowpea (dry)	1		0,0	0,0000	0,0	0,0000	5,1	0,0051	0,3	0,0003	0,0	0,0000
FB 0265	Cranberry	7		0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000	0,3	0,0018
VC 0424	Cucumber	3		4,8	0,0143	4,5	0,0135	0,0	0,0000	8,3	0,0248	9,0	0,0270
FB 0266	Dewberries	10		0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000
VO 0440	Egg plant	5		6,3	0,0313	3,0	0,0150	0,7	0,0033	6,0	0,0300	2,3	0,0113
PE 0112	Eggs	0,5		14,6	0,0073	13,1	0,0066	3,7	0,0019	11,9	0,0060	37,6	0,0188
MM 0814	Goat meat	0,2		2,0	0,0004	0,7	0,0001	2,3	0,0005	0,8	0,0002	0,3	0,0001
FB 0269	Grapes	5		15,8	0,0788	1,0	0,0050	0,0	0,0000	1,3	0,0063	13,8	0,0688
FI 0341	Kiwifruit	10		0,0	0,0000	0,0	0,0000	1,9	0,0193	0,1	0,0010	1,5	0,0150
VL 0053	Leafy vegetables	10		2,8	0,0275	0,0	0,0000	0,0	0,0000	6,0	0,0600	24,5	0,2450
VC 0046	Melons, except Watermelon	3		16,0	0,0480	2,0	0,0060	0,0	0,0000	2,8	0,0083	18,3	0,0549
AO3 0001	Milk products	0,1		15,5	0,0016	0,7	0,0001	0,4	0,0000	7,8	0,0008	46,8	0,0047
ML 0106	Milks	0,1		116,8	0,0117	32,0	0,0032	41,8	0,0042	160,0	0,0160	294,0	0,0294
FS 0245	Nectarine	10		1,3	0,0125	0,3	0,0025	0,0	0,0000	0,4	0,0038	6,3	0,0630
AO51900	Nuts (whole in shell)	10		4,3	0,0430	17,7	0,1770	14,8	0,1480	19,9	0,1990	11,8	0,1180
GC 0647	Oats	5		0,0	0,0000	0,0	0,0000	0,2	0,0008	0,8	0,0038	2,0	0,0100
VO 0442	Okra	10		0,8	0,0075	0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000
FT 0305	Olives	10											
DM 0305	Olives, processed	1		1,3	0,0125	0,0	0,0000	0,0	0,0000	0,3	0,0025	2,8	0,0275
VR 0588	Parsnip	2		0,5	0,0010	0,0	0,0000	0,0	0,0000	0,3	0,0005	2,0	0,0040
FS 0247	Peach	10		1,3	0,0125	0,3	0,0025	0,0	0,0000	0,4	0,0038	6,2	0,0620
SO 0703	Peanut, whole	2		0,0	0,0000	4,0	0,0080	5,5	0,0110	1,3	0,0025	0,3	0,0005
FP 0230	Pear	5		3,3	0,0163	2,8	0,0142	0,0	0,0000	1,0	0,0050	11,3	0,0563
VP 0063	Peas	5		5,5	0,0275	0,7	0,0035	0,0	0,0000	0,3	0,0015	14,0	0,0700
VO 0051	Peppers	5		3,4	0,0170	2,1	0,0105	5,4	0,0270	2,4	0,0120	10,4	0,0520
FS 0014	Plums (including Prunes)	10		1,8	0,0175	0,5	0,0050	0,0	0,0000	0,0	0,0000	4,3	0,0430
VR 0589	Potato	0,2		59,0	0,0118	19,2	0,0038	20,6	0,0041	40,8	0,0082	240,8	0,0482
PM 0110	Poultry meat	0,5		31,0	0,0155	13,2	0,0066	5,5	0,0028	25,3	0,0126	53,0	0,0265
PO 0113	Poultry skin	5		0,1	0,0005	0,1	0,0005	0,1	0,0005	0,1	0,0005	0,1	0,0005
VC 0429	Pumpkins	3		10,5	0,0315	2,2	0,0065	0,0	0,0000	14,0	0,0420	3,5	0,0105
VR 0494	Radish	2		0,5	0,0010	0,0	0,0000	0,0	0,0000	0,3	0,0005	2,0	0,0040

FB 0272	Raspberries, Red, Black	10		0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000	0,5	0,0050
GC 0649	Rice	5		48,8	0,2440	279,3	1,3965	103,4	0,5170	86,5	0,4325	11,8	0,0590
CM 0649	Rice, husked	5		0,0	0,0000	1,8	0,0092	34,7	0,1733	21,0	0,1050	2,5	0,0125
GC 0650	Rye	5		0,0	0,0000	1,0	0,0050	0,0	0,0000	0,0	0,0000	1,5	0,0075
MM 0822	Sheep meat	0,2		13,5	0,0027	0,7	0,0001	2,0	0,0004	3,0	0,0006	10,3	0,0021
GC 0651	Sorghum	10		2,0	0,0200	9,7	0,0967	26,6	0,2658	0,0	0,0000	0,0	0,0000
VD 0541	Soya bean (dry)	1		4,5	0,0045	2,0	0,0020	0,5	0,0005	0,0	0,0000	0,0	0,0000
VC 0431	Squash, Summer	3		10,5	0,0315	2,2	0,0065	0,0	0,0000	14,0	0,0420	3,5	0,0105
FB 0275	Strawberry	7		0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000	5,3	0,0368
VR 0596	Sugar beet	0,2		0,5	0,0001	0,0	0,0000	0,0	0,0000	0,3	0,0001	2,0	0,0004
VR 0497	Swede	2		0,5	0,0010	0,0	0,0000	0,0	0,0000	0,3	0,0005	2,0	0,0040
VO 1275	Sweet corn (kernels)	1		0,0	0,0000	0,0	0,0000	3,3	0,0033	0,0	0,0000	6,2	0,0062
VO 0448	Tomato	5		81,5	0,4075	7,0	0,0350	16,5	0,0825	25,5	0,1275	66,0	0,3300
TN 0085	Tree nuts	1		1,0	0,0010	13,5	0,0135	3,4	0,0034	17,5	0,0175	3,8	0,0038
GC 0654	Wheat	5		3,0	0,0150	0,5	0,0025	0,0	0,0000	2,0	0,0100	1,0	0,0050
CM 0654	Wheat bran, unprocessed	20		0,3	0,0050	0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000
CF 1211	Wheat flour	0,2		323,0	0,0646	114,0	0,0228	28,3	0,0057	112,0	0,0224	175,8	0,0352
CF 1212	Wheat wholemeal	2		1,0	0,0020	0,3	0,0007	0,0	0,0000	2,8	0,0055	1,3	0,0025
VC 0433	Winter squash	3		1,5	0,0045	0,3	0,0009	0,0	0,0000	2,0	0,0060	0,5	0,0015
				Total = 1,7978			2,1556		1,4331		2,2670		2,6877
				% ADI = 375%			488%		299%		472%		560%
			Rounded	% ADI = 370			490%		300%		470%		560%

CHLORPROPHAM (201) **International Estimated Daily Intake (IEDI)**

ADI = 0.03 mg/kg bodyweight or 01.8 mg for a 60 kg person

Commodity		MRL	STMR	Processing	Notes	Adjusted	Middle Eastern		Far Eastern		African		Latin American		European	
		mg/kg	mg/kg	Factor		STMR	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI
Code	Name					mg/kg	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	Mg/day
VR 0589	Potato	30	11	0,33	1/, Po	3,6	59	0,2124	9,2	0,0331	20,6	0,0742	40,8	0,1469	240,8	0,8669
MM 0812	Cattle meat	0,1	0,004		2/, fat		18,5	0,0001	3,5	0,0000	10,4	0,0000	30,0	0,0001	63,3	0,0003
MO 0812	Cattle, edible offal of	0,01*	0,005				2,5	0,0000	0,3	0,0000	1,8	0,0000	5,0	0,0000	6,0	0,0000
ML 0812	Cattle milk	0.0005*	0,0002		F		79,5	0,0000	23,3	0,0000	35,8	0,0000	159,3	0,0000	287,0	0,0001
						Total =		0,2125		0,0331		0,0742		0,1470		0,8672
						% ADI =		12		2		4		8		48
						Rounded % ADI =		10		2		4		8		50

1/ Cooked potato, with skin

2/ STMR expressed on muscle basis

CLETHODIM (187) **International Estimated Daily Intake (IEDI)**

ADI = 0.01 mg/kg bodyweight or 0.6 mg for a 60 kg person

Commodity		MRL	STMR	Processing	Notes	Adjusted	Middle Eastern		Far Eastern		African		Latin American		European	
		mg/kg	mg/kg	Factor		STMR	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI
Code	Name					mg/kg	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day
VD 0071	Beans, dry	2	0,81				6,8	0,0055	6,8	0,0055	0	0	13,5	0,0109	4,3	0,0035
VP 0061	Beans, except broad and soya	0,5	0,05				0,1	0	0,1	0	0,1	0	0,1	0	0,1	0
SO 0702	Cotton seed oil, edible		0,5	0,1		0,05	1	0,0001	0	0	0,6	0	0	0	0	0
MO 0105	Edible offal, mammalian	0,2	0				4,2	0	1,4	0	2,4	0	6,1	0	12,4	0
PE 0112	Eggs	0,05	0				14,6	0	13,1	0	3,7	0	11,9	0	37,6	0
OR 0697	Peanut oil, edible	0,12	0,12				0	0	1,8	0,0002	3,5	0,0004	0,5	0,0001	1,8	0,0002
VD 0561	Field pea (dry)	2	0,08				0,5	0	1,7	0,0001	0	0	1,3	0,0001	1,8	0,0001
VA 0381	Garlic	0,5	0,1				2	0,0002	2,2	0,0002	0	0	0,5	0,0001	3	0,0003
VA 0385	Onion, bulb	0,5	0,1				23	0,0023	11,5	0,0012	7,3	0,0007	13,8	0,0014	27,8	0,0028
MM0095	Meat, mammalian except marine	0,05	0				37	0	32,8	0	23,8	0	47	0	155,5	0
ML 0106	Milks	0,05	0				116,8	0	32	0	41,8	0	160	0	294	0
SO 0697	Peanut	5	1,3				0,3	0,0003	0,2	0,0002	2,3	0,003	0,3	0,0004	3	0,0039
OR 0697	Peanut oil, edible		0,09				0	0	1,8	0,0002	3,5	0,0003	0,5	0	1,8	0,0002
VR 0589	Potato	0,5	0,5				59	0,0295	19,2	0,0096	20,6	0,0103	40,8	0,0204	240,8	0,1204
PO 0111	Poultry offal	0,2	0				0,1	0	0,1	0	0,1	0	0,4	0	0,4	0
PM 0110	Poultry meat	0,2	0				31	0	13,2	0	5,5	0	25,3	0	53	0
OR 0495	Rape seed oil, edible	0,5	0,5				4,5	0,0023	2,7	0,0014	0	0	0,3	0,0001	7,3	0,0037
VD 0541	Soya bean, dry	10	1	10		10	4,5	0,045	2	0,02	0,5	0,005	0	0	0	0
OR 0541	Soya bean oil, edible	0,5	0,5	0,002		0,001	1,3	0	1,7	0	3	0	14,5	0	4,3	0
VR 0596	Sugar beet	0,1	0,1				0,5	0,0001	0	0	0	0	0,3	0	2	0,0002
SO 0702	Sunflower seed	0,5	0,06				1	0,0001	0	0	0,6	0	0	0	0	0
OC 0702	Sunflower seed oil, crude	0,1	0,012				9,3	0,0001	0,5	0	0,3	0	0,8	0	8,5	0,0001
VO 0448	Tomato	1	0,35				44,1	0,0154	5,7	0,002	14,6	0,0051	25,5	0,0089	38,2	0,0134
VJ 0448	Tomato juice		0,35	0,77		0,27	0,3	0,0001	0	0	0	0	0	0	2	0,0005
	Tomato paste		0,35	3,43		1,2	5,8	0,0069	0,2	0,0002	0,3	0,0003	0	0	4	0,0048
	Tomato puree		0,35	2,2		0,77	0,3	0,0002	0	0	0	0	0	0	2	0,0015
						Total =		0,10804		0,04075		0,02527		0,04244		0,15555
						% ADI =		18%		7%		4%		7%		26%
						Rounded % ADI =		20%		7%		4%		7%		30%

2,4-D (20) **International Estimated Daily Intake (IEDI)**

ADI = 0.01 mg/kg bodyweight or 0.6 mg for a 60 kg person

Commodity		MRL	STMR	Processing	Notes	Adjusted	Middle Eastern		Far Eastern		African		Latin American		European	
		mg/kg	mg/kg	Factor		STMR	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI
Code	Name					mg/kg	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day
FB 0018	Berries and other small fruits	0,1	0,05				0	0,0000	16	0,0008	1	0,0001	0,0000	0,0000	1,5	0,0001
MO 0105	Edible offal, mammalian	10	2,75				4,2	0,0116	1,4	0,0039	2,4	0,0066	6,1000	0,0168	12,4	0,0341
PE 0112	Eggs	0,01*	0				14,6	0,0000	13,1	0,0000	3,7	0,0000	11,9000	0,0000	37,6	0,0000
FB 0269	Grapes		0				15,8	0,0000	1	0,0000	0	0,0000	1,3000	0,0000	13,8	0,0000
FC 0001	Citrus fruits	1	0,3		Po		54,3	0,0163	6,3	0,0019	5,1	0,0015	54,8000	0,0164	49	0,0147
	Citrus juice			0,1	1/	0,03	7,3	0,0002	0	0,0000	0	0,0000	0,3000	0,0000	4,5	0,0001
	Citrus oil			1		0,3	0	0,0002	0	0,0000	0	0,0000	0,0000	0,0000	0	0,0000
GC 0645	Maize	0,05*	0,01				48,3	0,0005	31,2	0,0003	106,2	0,0011	41,8000	0,0004	8,8	0,0001
CF 1255	Maize flour		0,01				31,8	0,0003	31,2	0,0003	106,2	0,0011	40,3000	0,0004	8,8	0,0001
MM 0095	Meat	0,2*	0,125				37	0,0046	32,8	0,0041	23,8	0,0030	47,0000	0,0059	155,5	0,0194
ML 0106	Milks	0,1*	0,043				116,8	0,0050	32	0,0014	41,8	0,0018	160,0000	0,0069	294	0,0126
FP 0009	Pome fruit	0,01*	0				10,8	0,0000	7,5	0,0000	0,3	0,0000	6,5000	0,0000	51,3	0,0000
VR 0589	Potato	0,2	0,05				59	0,0030	19,2	0,0010	20,6	0,0010	40,8000	0,0020	240,8	0,0120
PM 0110	Poultry meat	0,05*	0				31	0,0000	13,2	0,0000	5,5	0,0000	25,3000	0,0000	53	0,0000
PO 0111	Poutry, edible offal of	0,05*	0				0,1	0,0000	0,1	0,0000	0,1	0,0000	0,4000	0,0000	0,4	0,0000
CM 0649	Rice, husked	0,1	0,01				0	0,0000	1,8	0,0000	34,7	0,0003	21,0000	0,0002	2,5	0,0000
GC 0650	Rye	2	0,22				0	0,0000	1	0,0002	0	0,0000	0,0000	0,0000	1,5	0,0003
GC 0651	Sorghum	0,01*	0,01				2	0,0000	9,7	0,0001	26,6	0,0003	0,0000	0,0000	0	0,0000
VD 0541	Soya bean, dry	0,01*	0				4,5	0,0000	2	0,0000	0,5	0,0000	0,0000	0,0000	0	0,0000
FS 0012	Stone fruit	0,05*	0				7,3	0,0000	1	0,0000	0	0,0000	0,8000	0,0000	22,8	0,0000
GS 0659	Sugar cane	0,02	0,01				18,5	0,0002	7,3	0,0001	15,9	0,0002	3,5000	0,0000	0	0,0000
VO 0447	Sweet corn on the cob	0,05*	0,05				0	0,0000	0	0,0000	4,4	0,0002	0,0000	0,0000	8,3	0,0004
TN 0085	Tree nuts	0,2	0,05				1	0,0001	13,5	0,0007	3,4	0,0002	17,5000	0,0009	3,8	0,0002
GC 0654	Wheat	2	0,22				4,3	0,0009	0,8	0,0002	0	0,0000	4,8000	0,0010	2,3	0,0005
CF 0654	Wheat bran		0,22	3,65		0,803	0,1	0,0001	0,1	0,0001	0,1	0,0001	0,1000	0,0001	0,1	0,0001
CF1211	Wheat flour		0,22	0,11		0,024	323,0	0,0078	114,0	0,0028	28,3	0,0007	112,0	0,0027	175,8	0,0043
	1/ Orange juice only					Total =		0,0505		0,0177		0,0180		0,0538		0,0991
						% ADI =		8%		3%		3%		9%		17%
						Rounded % ADI =		8%		3%		3%		9%		20%

DIMETHIPIN (151) **International Estimated Daily Intake (IEDI)**

ADI = 0.02 mg/kg bodyweight or 1.2 mg for a 60 kg person

Commodity		MRL	STMR	Processing	Notes	Adjusted	Middle Eastern		Far Eastern		African		Latin American		European	
		mg/kg	mg/kg	Factor		STMR mg/kg	Diet g/day	IEDI mg/day	Diet g/day	IEDI mg/day	Diet g/day	IEDI mg/day	Diet g/day	IEDI mg/day	Diet g/day	IEDI mg/day
Code	Name															
OR 0691	Cotton seed oil, edible	0,1	0,02*				3,8	0,0001	0,5	0,0000	0,5	0,0000	0,5000	0,0000	0	0,0000
MO 0105	Edible offal (mammalian)	0,01*	0				4,2	0,0000	1,4	0,0000	2,4	0,0000	6,1000	0,0000	12,4	0,0000
PE 0112	Eggs	0,01*	0				14,6	0,0000	13,1	0,0000	3,7	0,0000	11,9000	0,0000	37,6	0,0000
MM 0095	Meat	0,01*	0				37	0,0000	32,8	0,0000	23,8	0,0000	47,0000	0,0000	155,5	0,0000
ML 0106	Milks	0,01*	0				116,8	0,0000	32	0,0000	41,8	0,0000	160,0000	0,0000	294	0,0000
VR 0589	Potato	0,05*	0,02				59	0,0012	19,2	0,0004	20,6	0,0004	40,8000	0,0008	240,8	0,0048
PM 0110	Poultry meat	0,01*	0				31	0,0000	13,2	0,0000	5,5	0,0000	25,3000	0,0000	53	0,0000
PO 0111	Poultry, Edible offal of	0,01*	0				0,1	0,0000	0,1	0,0000	0,1	0,0000	0,4000	0,0000	0,4	0,0000
SO 0495	Rape seed	0,2	0,1		1/		4,5	0,0005	2,7	0,0003	0,0	0,0000	0,3	0,0000	7,3	0,0007
SO 0702	Sunflower seed	1	0,1				1,0	0,0	0,0	0,0	0,6	0,0	0,0	0,0000	0,0	0,0000
						Total =		0,0505		0,0177		0,0180		0,0538		0,0991
						% ADI =		8%		3%		3%		9%		17%
						Rounded % ADI =		8%		3%		3%		9%		20%

1/ Consumption of edible rape seed oil use

DINOCAP (87 International Estimate Daily Intake (IEDI)

ADI = 0.008 mg/kg bodyweight or 0.48 mg for a 60 kg person

Commodity		MRL	STMR	Processing	Notes	Adjusted	Middle Eastern		Far Eastern		African		Latin American		European	
		mg/kg	mg/kg	Factor		STMR	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI
Code	Name					mg/kg	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day
FP 0226	Apple	0,2	0,05				7,5	0,0004	4,7	0,0002	0,3	0	5,5	0,0003	40,0	0,002
FB 0269	Grape	0,5	0,05				15,8	0,0008	1,0	0,0001	0,0	0	1,3	0,0001	13,8	0,0007
FB 0275	Strawberry	0,5	0,06				0,0	0	0,0	0	0,0	0	0,0	0	5,3	0,0003
FS 0247	Peach	0,1	0,05				2,5	0,0001	0,5	0	0,0	0	0,8	0	12,5	0,0006
VO 0051	Pepper	0,2	0,06				3,4	0,0002	2,1	0,0001	5,4	0,0003	2,4	0,0001	10,4	0,0006
VC 0045	Cucurbits, fruiting vegetables	0,05	0,05				80,5	0,004	18,2	0,0009	0,0	0	30,5	0,0015	38,5	0,0019
VO 0448	Tomato	0,3	0,045				81,5	0,0037	7,0	0,0003	16,5	0,0007	25,5	0,0011	66,0	0,003
						Total =		0,0092		0,0017		0,0011		0,0032		0,0091
						% ADI =		2%		0%		0%		1%		2%

DIPHENYLAMINE(30) **International Estimated Daily Intake (IEDI)**

ADI = 0.08 mg/kg bodyweight or 4.8 mg for a 60 kg person

Commodity		MRL	STMR	Processing	Notes	Adjusted	Middle Eastern		Far Eastern		African		Latin American		European	
		mg/kg	mg/kg	Factor		STMR	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI
Code	Name					mg/kg	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day
FP 0226	Apples	10 Po	4,45				7,5	0,0334	4,7	0,0208	0,3	0,0011	5,5	0,0245	40	0,1780
MO 1280	Cattle kidney	0,01*	0,0007				0,1	0,0000	0	0,0000	0,1	0,0000	0,2	0,0000	0,2	0,0000
MO 1281	Cattle liver	0,05	0,024				0,2	0,0000	0	0,0000	0,1	0,0000	0,3	0,0000	0,4	0,0000
MM 0812	Cattle meat	0,01*	0,0005		1/, fat		18,5	0,0000	3,5	0,0000	10,4	0,0000	30,0	0,0000	63,3	0,0000
ML 0812	Cattle milk	0,0004*	0,00015		F, 2/		79,5	0,0000	23,2	0,0000	35,8	0,0000	159,3	0,0000	287	0,0000
FP 0230	Pear	5	2,2		Po		3,3	0,0072	2,8	0,0062	0	0,0000	1,0	0,0022	11,3	0,0248
						Total =		0,0406		0,0270		0,0011		0,0267		0,2028
						% ADI=		1%		1%		0%		1%		4%

1/ STMR based on residues in muscle

2/ Equivalent to 0.01* mg/kg in the milk fat

FIPRONIL (202) **International Estimated Daily Intake (IEDI)**

ADI = 0.0002 mg/kg bodyweight or 0.012 mg for a 60 kg person

Commodity		MRL	STMR	Processing	Notes	Adjusted	Middle Eastern		Far Eastern		African		Latin American		European	
		mg/kg	mg/kg	Factor		STMR	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI
Code	Name					mg/kg	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day
FI 0327	Banana	0,005	0,004				8,3	0,0000	26,2	0,0001	21	0,0001	102,3	0,0004	22,8	0,0001
GC 0640	Barley	0,002	0,004				1	0,0000	3,5	0,0000	1,8	0,0000	6,5	0,0000	19,8	0,0001
VB 0400	Brocolli	0,02	0,005		1/		0,5	0,0000	1	0,0000	0	0,0000	1,1	0,0000	2,7	0,0000
VB 0041	Cabbages, head	0,02	0,005		1/		5	0,0000	9,7	0,0000	0	0,0000	10,5	0,0001	26,8	0,0001
VB 0404	Cauliflower	0,02	0,005		1/		1,3	0,0000	1,5	0,0000	0	0,0000	0,3	0,0000	13	0,0001
MO1280	Cattle, kidney	0,02	0,014				0,1	0,0000	0	0,0000	0,1	0,0000	0,2	0,0000	0,2	0,0000
MO1281	Cattle, liver	0,1	0,064				0,2	0,0000	0	0,0000	0,1	0,0000	0,3	0,0000	0,4	0,0000
MM 0812	Cattle meat	0,5	0,015		2/		18,5	0,0003	3,5	0,0001	10,4	0,0002	30	0,0005	63,3	0,0009
ML 0812	Cattle milk	0,02	0,011				79,5	0,0009	23,2	0,0003	35,8	0,0004	159,3	0,0018	287	0,0032
PE 0112	Eggs	0,02	0,006				14,6	0,0001	13,1	0,0001	3,7	0,0000	11,9	0,0001	37,6	0,0002
GC 0645	Maize	0,01	0,005				48,3	0,0002	31,2	0,0002	106,2	0,0005	41,8	0,0002	8,8	0,0000
GC 0647	Oats	0,002	0,004				0	0,0000	0	0,0000	0,2	0,0000	0,8	0,0000	2	0,0000
VR 0589	Potato	0,02	0,004				59	0,0002	19,2	0,0001	20,6	0,0001	40,8	0,0002	240,8	0,0010
PM 0110	Poultry meat	0,01	0,006		2/		31	0,0002	13	0,0001	6	0,0000	25	0,0002	53	0,0003
PO 0110	Poultry, Edible offal of	0,02	0,008				0,1	0,0000	0,1	0,0000	0,1	0,0000	0,4	0,0000	0,4	0,0000
GC 0649	Rice	0,01	0,006				48,8	0,0003	279,3	0,0017	103,4	0,0006	86,5	0,0005	11,8	0,0001
GC 0650	Rye	0,002	0,004				0	0,0000	1	0,0000	0	0,0000	0	0,0000	1,5	0,0000
VR 0596	Sugar beet	0,2	0,0125				0,5	0,0000	0	0,0000	0	0,0000	0,3	0,0000	2	0,0000
SO 0702	Sunflower seed	0,002	0,004				1	0,0000	0	0,0000	0,6	0,0000	0	0,0000	0	0,0000
GC 0653	Triticale	0,002	0,004				0	0,0000	1	0,0000	0	0,0000	0	0,0000	0	0,0000
GC 0654	Wheat	0,002	0,004				327,3	0,0013	114,8	0,0	28,3	0,0001	116,8	0,0005	178	0,0007
FP 226	Apples	10	4,45				7,5	0,0334	4,7	0,0208	0,3	0,0011	5,5	0,0245	40	0,1780
	1/ Based on MRL for VB 42 Flowerhead brassicas 1/ STMR based on residues in muscle					Total =		0,0036		0,0030		0,0021		0,0043		0,0069
						% ADI=		30%		27%		17%		36%		58%
						Rounded % ADI=		30%		30%		20%		40%		60%

HALOXYFOP (194) **International Estimated Daily Intake (IEDI)**

ADI = 0.0002 mg/kg bodyweight or 0.012 mg for a 60 kg person

Commodity		MRL	STMR	Processing	Notes	Adjusted	Middle Eastern		Far Eastern		African		Latin American		European	
		mg/kg	mg/kg	Factor		STMR mg/kg	Diet g/day	IEDI mg/day	Diet g/day	IEDI mg/day	Diet g/day	IEDI mg/day	Diet g/day	IEDI mg/day	Diet g/day	IEDI mg/day
Code	Name															
FI 327	Banana	0,05 *	0				8,3	0,0000	26,2	0,0000	21	0,0000	102,3	0,0000	22,8	0,0000
MM 812	Cattle meat	0,05	0,02				18,5	0,0004	3,5	0,0001	10,4	0,0002	30	0,0006	63,3	0,0013
ML 812	Cattle milk	0,3	0,22				79,5	0,0175	23,2	0,0051	35,8	0,0079	159,3	0,0350	287	0,0631
MO 1280	Cattle kidney	1	0,73				0,1	0,0001	0	0,0000	0,1	0,0000	0,2	0,0001	0,2	0,0001
MO 1281	Cattle liver	0,5	0,28				0,2	0,0001	0	0,0000	0,1	0,0000	0,3	0,0001	0,4	0,0001
PE 840	Chicken eggs	0,01 *	0,002				14,5	0,0001	13	0,0001	3,6	0,0000	11,8	0,0001	37,5	0,0004
PM 840	Chicken meat	0,01 *	0,002		1/		30,5	0,0001	11,5	0,0000	5,5	0,0000	25,3	0,0001	44	0,0001
PO 840	Chicken, edible offal of	0,05	0,009				0	0,0000	0	0,0000	0	0,0000	0,3	0,0000	0,3	0,0000
FC 1	Citrus fruits	0,05 *	0				54,3	0,0000	6,3	0,0000	5,1	0,0000	54,8	0,0000	49	0,0000
OC 691	Cotton seed oil, crudue	0,5	0,1				3,8	0,0004	0,5	0,0001	0,5	0,0001	0,5	0,0001	0	0,0000
FB 269	Grapes	0,05 *	0				15,8	0,0000	1	0,0000	0	0,0000	1,3	0,0000	13,8	0,0000
SO 697	Peanut	0,05	0,03				0,3	0,0000	0,2	0,0000	2,3	0,0001	0,3	0,0000	3	0,0001
VP 63	Peas (pods and succulent = immature seeds)	0,2	0,02				5,5	0,0005	0,7	0,0001	0	0,0000	0,3	0,0000	14	0,0013
FP 9	Pome fruits	0,05 *	0				10,8	0,0000	7,5	0,0000	0,3	0,0000	6,5	0,0000	51,3	0,0000
VD 70	Pulses (dry)	0,2	0,03				24,6	0,0007	19,8	0,0006	17,8	0,0005	23,1	0,0007	12,1	0,0004
VR 589	Potato	0,1	0,04				59	0,0024	19,2	0,0008	20,6	0,0008	40,8	0,0016	240,8	0,0096
OC 495	Rape seed oil, edible	5	0,28				4,5	0,0013	2,7	0,0008	0	0,0000	0,3	0,0001	7,3	0,0020
CM 1206	Rice bran, unprocessed	0,02	0,02				0,1	0,0000	0,1	0,0000	0,1	0,0000	0,1	0,0000	0,1	0,0000
CM 649	Rice, husked	0,02 *	0				0	0,0000	1,8	0,0000	34,7	0,0000	21	0,0000	2,5	0,0000
CM 1205	Rice, polished	0,02 *	0				48,8	0,0000	277,5	0,0000	68,8	0,0000	65,5	0,0000	9,3	0,0000
OR 541	Soy bean oil, refined	0,2	0,02				1,3	0,0000	1,7	0,0000	3	0,0001	14,5	0,0003	4,3	0,0001
VR 596	Sugar beet	0,3	0,02				0,5	0,0000	0	0,0000	0	0,0000	0,3	0,0000	2	0,0000
SO 702	Sunflower seed	0,2	0,05				1	0,0001	0	0,0000	0,6	0,0000	0	0,0000	0	0,0000
						Total =		0,0236		0,0076		0,0098		0,0389		0,0787
						% ADI=		131%		46%		54%		216%		437%
						Rounded % ADI=		130%		50%		50%		220%		440%

1/ with adhering skin

IPRODIONE (111) **Dietary Intake Estimate (DIE)**

ADI = 0.06 mg/kg bodyweight or 3.6 mg for a 60 kg person

Commodity		MRL	STMR	Processing	Notes	Adjusted	Middle Eastern		Far Eastern		African		Latin American		European	
		mg/kg	mg/kg	Factor		STMR	Diet	DIE	Diet	DIE	Diet	DIE	Diet	DIE	Diet	DIE
Code	Name					mg/kg	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day
TN 0660	Almond	10	0,2				0,5	0,0001	0,0	0,0000	0,0	0,0000	0,1	0,0000	1,8	0,0004
GC 0640	Barley	2	2				1,0	0,0020	3,5	0,0070	1,8	0,0035	6,5	0,0130	19,8	0,0395
VD 0071	Beans, dry	0,1	0,1				6,8	0,0007	6,8	0,0007	0,0	0,0000	13,5	0,0014	4,3	0,0004
FB 0264	Blackberries	30	30				0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000
VB 0400	Brocolli	25	25				0,5	0,0125	1,0	0,0242	0,0	0,0000	1,1	0,0263	2,7	0,0669
VR 0577	Carrot	10	10				2,8	0,0275	2,5	0,0250	0,0	0,0000	6,3	0,0625	22,0	0,2200
FS 0013	Cherries	10	10				0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000	3,0	0,0300
VP 0526	Common Bean	2	2				3,5	0,0070	0,8	0,0017	0,0	0,0000	4,0	0,0080	12,0	0,0240
VC 0424	Cucumber	2	2				4,8	0,0095	4,5	0,0090	0,0	0,0000	8,3	0,0165	9,0	0,0180
FB 0269	Grapes	10	10				15,8	0,1575	1,0	0,0100	0,0	0,0000	1,3	0,0125	13,8	0,1375
FI 0341	Kiwifruit	5	5				0,0	0,0000	0,0	0,0000	1,9	0,0097	0,1	0,0005	1,5	0,0075
VL 0482	Lettuce, head	10	10				2,3	0,0225	0,0	0,0000	0,0	0,0000	5,8	0,0575	22,5	0,2250
VL 0483	Lettuce, leaf	25	25				2,3	0,0563	0,0	0,0000	0,0	0,0000	5,8	0,1438	22,5	0,5625
VA 0385	Onion, bulb	0,2	0,2				23,0	0,0046	11,5	0,0023	7,3	0,0015	13,8	0,0028	27,8	0,0056
FS 0247	Peach	10	10				2,5	0,0250	0,5	0,0050	0,0	0,0000	0,8	0,0075	12,5	0,1250
SO 0495	Rapeseed	0,5	0,5				0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000
FB 0272	Raspberries	30	30				0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000	0,5	0,0150
CM 0649	Rice, husked	10	10				0,0	0,0000	1,8	0,0183	34,7	0,3467	21,0	0,2100	2,5	0,0250
FB 0275	Strawberry	10	10				0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000	5,3	0,0525
VR 0596	Sugar beet	0,1	0,2				0,5	0,0001	0,0	0,0000	0,0	0,0000	0,3	0,0001	2,0	0,0004
SO 0702	Sunflower seed	0,5	0,5				1,0	0,0005	0,0	0,0000	0,6	0,0003	0,0	0,0000	0,0	0,0000
VO 0448	Tomato	5	1,1				44,1	0,0485	5,7	0,0063	14,6	0,0160	25,5	0,0281	42,2	0,0464
VJ 0448	Tomato juice			0,5		0,55	0,3	0,0001	0,0	0,0000	0,0	0,0000	0,0	0,0000	2,0	0,0011
	Tomato paste			0,5		0,55	5,8	0,0032	0,2	0,0001	0,3	0,0001	0,0	0,0000	4,0	0,0022
VS 0469	Witloof chicory (sprout)	1	1				0,5	0,0005	0,0	0,0000	0,0	0,0000	0,3	0,0003	2,0	0,0020
						Total =		0,3780		0,1095		0,3778		0,5905		1,6046
						% ADI=		11%		3%		10%		16%		45%
						Rounded % ADI=		10%		3%		10%		20%		50%

KRESOXIM-METHYL (199) **International Estimated Daily Intake (IEDI)**

ADI = 0.4 mg/kg bodyweight or 24 mg for a 60 kg person

Commodity		MRL	STMR	Processing	Notes	Adjusted	Middle Eastern		Far Eastern		African		Latin American		European	
		mg/kg	mg/kg	Factor		STMR	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI
Code	Name					mg/kg	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day
GC 0640	Barley	0,1	0,05				1	0,0001	3,5	0,0002	1,8	0,0001	6,5	0,0003	19,8	0,0010
VC 0424	Cucumber	0,05 *	0,05				4,8	0,0002	4,5	0,0002	0	0,0000	8,3	0,0004	9	0,0005
MO 0105	Offal, edible mammalian	0,05 *	0,01				4,2	0,0000	1,4	0,0000	2,4	0,0000	6,1	0,0001	12,4	0,0001
MF 0095	Fat, mammalian	0,05 *	0,01				0,7	0,0000	1,7	0,0000	0,7	0,0000	4,4	0,0000	7,7	0,0001
FC 0203	Grapfruit	0,5	0,01		1/		1,1	0,0000	0,6	0,0000	0,1	0,0000	2,3	0,0000	1,4	0,0000
FB 0269	Grapes	1	0,2				15,8	0,0032	1	0,0002	0	0,0000	1,3	0,0003	13,8	0,0028
DF 0269	Grapes, dried (raisins)	2	0,32				0,3	0,0001	0	0,0000	0	0,0000	0,3	0,0001	2,3	0,0007
MM 0095	Meat, mammalian exc. marine	0,05 *	0,01				37	0,0004	32,8	0,0003	23,8	0,0002	47	0,0005	155,5	0,0016
ML 0106	Milks	0,01	0,002				116,8	0,0002	32	0,0001	41,8	0,0001	160	0,0003	294	0,0006
FT 0305	Olives	0,2	0,05				1,3	0,0001	0	0,0000	0	0,0000	0,3	0,0000	2,8	0,0001
OC 0305	Olive oil, Virgin	0,7	0,22	0,2			1,5	0,0000	0	0,0000	0	0,0000	0	0,0000	7,8	0,0001
FC 0004	Oranges, Sweet, Sour	0,5	0,01		1/		22	0,0002	2,8	0,0000	3,4	0,0000	21,7	0,0002	20,9	0,0002
FP 0009	Pome fruits	0,2	0,05				10,8	0,0005	7,5	0,0004	0,3	0,0000	6,5	0,0003	51,3	0,0026
PM 0110	Poultry meat	0,05 *	0,01				31	0,0003	13,2	0,0001	5,5	0,0001	25,3	0,0003	53	0,0005
GC 0650	Rye	0,05 *	0,05				0	0,0000	1	0,0001	0	0,0000	0	0,0000	1,5	0,0001
GC 0654	Wheat	0,05 *	0,05				327,3	0,0164	114,8	0,0057	28,3	0,0014	116,8	0,0058	178	0,0089
							Total =	0,0218		0,0074		0,0020		0,0086		0,0214
							% ADI=	0%		0%		0%		0%		0%

1/ STMR based on edible por

METHOMYL
(94)

International Estimated Daily Intake (IEDI)

ADI = 0.02 mg/kg bodyweight or 1.2 mg for a 60 kg person

Commodity		MRL 1/	STMR	Processing	Notes	Adjusted	Middle Eastern		Far Eastern		African		Latin American		European	
Code	Name	mg/kg	mg/kg	Factor		STMR mg/kg	Diet g/day	IEDI mg/day	Diet g/day	IEDI mg/day	Diet g/day	IEDI mg/day	Diet g/day	IEDI mg/day	Diet g/day	IEDI mg/day
FP 0226	Apple	2	0,41				7,5	0,0031	4,7	0,0019	0,3	0,0001	5,5	0,0023	40,0	0,0164
VS 0621	Asparagus	2	0,33				0,0	0	0,0	0	0,0	0	0,0	0	1,5	0,0005
GC 0640	Barley	2					1,0	0,002	3,5	0,007	1,8	0,0035	6,5	0,013	19,8	0,0395
VP 0061	Beans	1	0,005				0,1	0	0,1	0	0,1	0	0,1	0	0,1	0
VD 0071	Beans(dry)	0,05	0,02				6,8	0,0001	6,8	0,0001	0,0	0	13,5	0,0003	4,3	0,0001
VB 0040	Brassica vegetables	7	1,3				6,3	0,0081	11,2	0,0145	0,0	0	10,8	0,014	39,8	0,0517
VS 0624	Celery	3	0,66				0,5	0,0003	0,0	0	0,0	0	0,3	0,0002	2,0	0,0013
FC 0001	Citrus fruit	1	0,034		2/		38,0	0,0013	4,4	0,0001	3,6	0,0001	38,4	0,0013	49,0	0,0017
	Citrus juice		0,004		3/		7,3	0	0,0	0	0,0	0	0,3	0	4,5	0
VP 0526	Common bean	1	0,055				3,5	0,0002	0,8	0	0,0	0	4,0	0,0002	12,0	0,0007
OR 0691	Cottonseed, edible oil	0,04	0,006				3,8	0	0,5	0	0,5	0	0,5	0	0,0	0
VC 0424	Cucumber	0,1	0,02				4,8	0,0001	4,5	0,0001	0,0	0	8,3	0,0002	9,0	0,0002
VC 0045	Cucurbits, fruiting vegetables	0,1	0,02				80,5	0,0016	18,2	0,0004	0,0	0	30,5	0,0006	38,5	0,0008
MO 0105	Edible offal of mammals ex. marine mammals	0,02*	0				4,2	0	1,4	0	2,4	0	6,1	0	12,4	0
PE 0840	Eggs	0,02*	0				14,5	0	13,0	0	3,6	0	11,8	0	37,5	0
FB 0270	Grapes	7	0,86				15,8	0,0136	1,0	0,0009	0,0	0	1,3	0,0011	13,8	0,0119
	Grape wine		0,26				0,5	0,0001	0,0	0	0,8	0,0002	19,8	0,0051	97,8	0,0254
VL 0053	Leafy vegetables	30	1,4				7,8	0,0109	9,7	0,0135	0,0	0	16,5	0,0231	51,3	0,0718
GC 0645	Maize	0,02*	0,02				48,3	0,001	31,2	0,0006	106,2	0,0021	41,8	0,0008	8,8	0,0002
OR 0645	Maize, edible oil	0,02*	0,004				1,8	0	0,0	0	0,3	0	0,5	0	1,3	0
MM 0095	Meat from mammals ex. marine mammals	0,02*	0				37,0	0	32,8	0	23,8	0	47,0	0	155,5	0
VC 0046	Melons, except watermelons	0,1	0,02				16,0	0,0003	2,0	0	0,0	0	2,8	0,0001	18,3	0,0004
ML 0106	Milk	0,02*	0				116,8	0	32,0	0	41,8	0	160,0	0	294,0	0
FS 0245	Nectarine	0,2	0,05				1,3	0,0001	0,3	0	0,0	0	0,4	0	6,3	0,0003
GC 0647	Oats	0,02*					0,0	0	0,0	0	0,2	0	0,8	0	2,0	0
VA 0385	Onion, bulb	0,2	0,068				23,0	0,0016	11,5	0,0008	7,3	0,0005	13,8	0,0009	27,8	0,0019
FS 0247	Peach	0,2	0,05				1,3	0,0001	0,3	0	0,0	0	0,4	0	6,3	0,0003
FP 0230	Pear	0,3	0,09				3,3	0,0003	2,8	0,0003	0,0	0	1,0	0,0001	11,3	0,001
VP 0063	Peas	5	0,46				5,5	0,0025	0,7	0,0003	0,0	0	0,3	0,0001	14,0	0,0064
FS 0014	Plum	1	0,08				1,8	0,0001	0,5	0	0,0	0	0,0	0	4,3	0,0003
VR 0589	Potato	0,02*	0				59,0	0	19,2	0	20,6	0	40,8	0	240,8	0
PO 0110	Poultry meat	0,02*	0				31,0	0	13,2	0	5,5	0	25,3	0	53,0	0
PO 0111	Poultry, edible offal	0,02*	0				0,1	0	0,1	0	0,1	0	0,4	0	0,4	0
OR 0541	Soya bean oil, edible	0,2	0,04				1,3	0,0001	1,7	0,0001	3,0	0,0001	14,5	0,0006	4,3	0,0002
VC 0431	Summer squash	0,1	0,02				10,5	0,0002	2,2	0	0,0	0	14,0	0,0003	3,5	0,0001
VO 0447	Sweet corn	2	0,065				0,0	0	0,0	0	4,4	0,0003	0,0	0	8,3	0,0005
VO 0448	Tomato	1	0,16				44,4	0,0071	5,7	0,0009	14,6	0,0023	25,5	0,0041	44,2	0,0071
	Tomato paste		0,007				5,8	0,0000	0,2	0,0000	0,3	0,0000	0	0,0000	4	0,0000
VC 0432	Watermelon	0,1	0,02				49,3	0,001	9,5	0,0002	0,0	0	5,5	0,0001	7,8	0,0002
GC 0654	Wheat	2	0,14				3,9	0,0005	0,6	0,0001	0,2	0,0000	4,6	0,0006	2	0,0003
CM 0654	Wheat bran	3	0,27				0,1	0,0000	0,1	0,0000	0,1	0,0000	0,1	0,0000	0,1	0,0000
CF 1211	Wheat flour	0,03	0,003				323	0,0010	114	0,0003	28,3	0,0001	112	0,0003	176	0,0005
CF 1210	Wheat germ	2	0,13				0,1	0,0000	0,1	0,0000	0	0,0000	0,1	0,0000	0,1	0,0000

Total =	0,0574	0,0424	0,0094	0,0695	0,2416
% ADI=	3%	2%	1%	4%	13%
Rounded % ADI=	3%	2%	1%	4%	10%

1/ Includes residues arising from the use of thiodicarb (154)
2/ STMR based on edible portion

METHOPRENE (147) 1/ **International Estimated Daily Intake (IEDI)**

ADI = 0.05 mg/kg bodyweight or 3.0 mg for a 60 kg person

Commodity		MRL	STMR	Processing	Notes	Adjusted	Middle Eastern		Far Eastern		African		Latin American		European	
		mg/kg	mg/kg	Factor		STMR	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI
Code	Name					mg/kg	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day
ML 0812	Cattle milk	0,05	0,05				79,5	0,0040	23,2	0,0012	35,8	0,0018	159,3	0,0080	287	0,0144
GC 0080	Cereal grains	5	5				106,6	0,5327	338	1,6898	290,1	1,4505	137,7	0,6885	49,3	0,2465
MO 0105	Edible offal (mammalian)	0,1	0,1				4,2	0,0004	1,4	0,0001	2,4	0,0002	6,1	0,0006	12,4	0,0012
PE 0112	Eggs	0,05	0,05				14,6	0,0007	13,1	0,0007	3,7	0,0002	11,9	0,0006	37,6	0,0019
OR 0645	Maize oil, edible	0,2	0,2				1,8	0,0004	0	0,0000	0,3	0,0001	0,5	0,0001	1,3	0,0003
MM 0095	Meat	0,2	0,2				7,4	0,0015	6,3	0,0013	4,8	0,0010	9,4	0,0019	31,1	0,0062
VO 0450	Mushrooms	0,2	0,2				0,3	0,0001	0,5	0,0001	0	0,0000	0	0,0000	4	0,0008
SO 0697	Peanut	2	2				0,3	0,0005	0,2	0,0003	2,3	0,0047	0,3	0,0006	3	0,0060
CM 0654	Wheat bran, unprocessed	10	10				0,3	0,0025	0	0,0000	0	0,0000	0	0,0000	0	0,0000
CF 1211	Wheat flour	2	2				323	0,6460	114	0,2280	28,3	0,0567	112	0,2240	175,8	0,3515
CF 1212	Wheat wholemeal	5	5				1	0,0050	0,3	0,0017	0	0,0000	2,8	0,0138	1,3	0,0063
	1/ S-methoprene					Total =		1,1938		1,9231		1,5151		0,9380		0,6350
						% ADI =		40%		70%		51%		31%		21%
						Rounded % ADI =		40%		70%		50%		30%		20%

METHOPRENE (147) 1/

International Estimated Daily Intake (IEDI)

ADI = 0.09 mg/kg bodyweight or 35.4 mg for a 60 kg person

Commodity		MRL	STMR	Processing	Notes	Adjusted	Middle Eastern		Far Eastern		African		Latin American		European	
		mg/kg	mg/kg	Factor		STMR	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI
Code	Name					mg/kg	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day
ML 812	Cattle milk	0,05	0,05				79,5	0,0040	23,2	0,0012	35,8	0,0018	159,3	0,0080	287	0,0144
GC 80	Cereal grains	5	5				106,6	0,5327	338	1,6898	290,1	1,4505	137,7	0,6885	49,3	0,2465
MO 105	Edible offal (mammalian)	0,1	0,1				4,2	0,0004	1,4	0,0001	2,4	0,0002	6,1	0,0006	12,4	0,0012
PE 112	Eggs	0,05	0,05				14,6	0,0007	13,1	0,0007	3,7	0,0002	11,9	0,0006	37,6	0,0019
OR 645	Maize oil, edible	0,2	0,2				1,8	0,0004	0	0,0000	0,3	0,0001	0,5	0,0001	1,3	0,0003
MM 95	Meat	0,2	0,2				7,4	0,0015	6,3	0,0013	4,8	0,0010	9,4	0,0019	31,1	0,0062
VO 450	Mushrooms	0,2	0,2				0,3	0,0001	0,5	0,0001	0	0,0000	0	0,0000	4	0,0008
SO 697	Peanut	2	2				0,3	0,0005	0,2	0,0003	2,3	0,0047	0,3	0,0006	3	0,0060
CM 654	Wheat bran, unprocessed	10	10				0,3	0,0025	0	0,0000	0	0,0000	0	0,0000	0	0,0000
CF 1211	Wheat flour	2	2				323	0,6460	114	0,2280	28,3	0,0567	112	0,2240	175,8	0,3515
CF 1212	Wheat wholemeal	5	5				1	0,0050	0,3	0,0017	0	0,0000	2,8	0,0138	1,3	0,0063
	1/ R,S racemate					Total =		1,1938		1,9231		1,5151		0,9380		0,6350
						% ADI =		22%		42%		28%		17%		12%
						Rounded % ADI =		20%		40%		30%		20%		10%

MEVINPHOS (53)
ADI = 0.0008 mg/kg bodyweight or 0.048 mg for a 60 kg person

Commodity		MRL	Notes	Middle Eastern		Far Eastern		African		Latin American		European	
		mg/kg		Diet	TMDI	Diet	TMDI	Diet	TMDI	Diet	TMDI	Diet	TMDI
Code	Name			g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day
VB 0041	Cabbages, Head	0,05		5	0,0003	9,7	0,0005	0	0	10,5	0,0005	26,8	0,0013
VP 0526	Common bean (pods and/or immature seeds)	0,05		3,5	0,0002	0,8	0	0	0	4	0,0002	12	0,0006
VA 0384	Leek	0,02		0,5	0	0	0	0	0	0,3	0	2	0
			Total =		0,0004		0,0005		0,0000		0,0007		0,0020
			% ADI =		1%		1%		0%		2%		4%

Piperonyl Butoxide (62) **International Estimated Daily Intake (IEDI)**

ADI = 0.2 mg/kg bodyweight or 12.0 mg for a 60 kg person; 11.0 mg for a 55 kg person in Far Eastern diet

Commodity		MRL	STMR	Processing	Notes	Adjusted	Middle Eastern		Far Eastern		African		Latin American		European	
		mg/kg	mg/kg	Factor		STMR	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI
Code	Name					mg/kg	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day
ML 0812	Cattle milk	0,2	0,14		1/		79,5	0,000	23,2	0,000	35,8	0,000	159,3	0,000	287,0	0,000
MO 1280	Cattle kidney	0,3	0,21		1/		0,1	0,000	0,0	0,000	0,1	0,000	0,2	0,000	0,2	0,000
MO 1281	Cattle liver	1	0,1				0,2	0,000	0,0	0,000	0,1	0,000	0,3	0,000	0,4	0,000
MM 0812	Cattle meat	5	0,16		fat, 1/		18,5	0,000	3,5	0,000	10,4	0,000	30,0	0,000	63,3	0,000
GC 0080	Cereal grains	30 Po	11				106,6	1,172	338,0	3,718	290,1	3,191	137,7	1,515	49,3	0,542
FC 0001	Citrus fruit	5	1				54,3	0,054	6,3	0,006	5,1	0,005	54,8	0,055	49,0	0,049
JF 0001	Citrus juice	0,05	0,01				7,3	0,000	0,0	0,000	0,0	0,000	0,3	0,000	4,5	0,000
DF 0167	Dried fruits	0,2	0,05				0,3	0,000	0,0	0,000	0,0	0,000	0,3	0,000	2,3	0,000
PE 0112	Eggs	1	0,36		1/		14,6	0,005	13,1	0,005	3,7	0,001	11,9	0,004	37,6	0,014
VC 0045	Fruiting vetetables, curcubits	1	0,26				80,5	0,021	18,2	0,005	0,0	0,000	30,5	0,008	38,5	0,010
VL 0483	Lettuce, leaf	50					2,3	0,086	0,0	0,000	0,0	0,000	5,8	0,219	22,5	0,855
OC 0645	Maize oil, crude	80 PoP	29,7				1,8	0,052	0,0	0,000	0,3	0,007	0,5	0,015	1,3	0,037
VL 0485	Mustard greens	50	38				0,1	0,004	0,1	0,004	0,1	0,004	0,1	0,004	0,1	0,004
SO 0703	Peanut, whole	1 Po	0,1				0,0	0,000	4,0	0,000	5,5	0,001	1,3	0,000	0,3	0,000
VO 0051	Pepper	2	0,675				3,4	0,002	2,1	0,001	5,4	0,004	2,4	0,002	10,4	0,007
PM 0110	Poultry meat	5	1		fat, 1/		31,0	0,031	13,2	0,013	5,5	0,006	25,3	0,025	53,0	0,053
PO 0111	Poultry, edible offal	10	2,03		1/		0,1	0,000	0,1	0,000	0,1	0,000	0,4	0,001	0,4	0,001
VD 0070	Pulses	0,2	0,05				24,6	0,001	19,8	0,001	17,8	0,001	23,1	0,001	12,1	0,001
VR 0075	Root and tuber vegetables, except carrots	0,5	0,1				61,8	0,006	108,5	0,011	321,3	0,032	159,3	0,016	242,0	0,024
VL 0502	Spinach	50	38				0,5	0,019	0,0	0,000	0,0	0,000	0,3	0,010	2,0	0,076
VO 0448	Tomato	2	0,675				81,5	0,055	7,0	0,005	16,5	0,011	25,5	0,017	66,0	0,045
VJ 0448	Tomato, juice	0,3	0,1				0,3	0,000	0,0	0,000	0,0	0,000	0,0	0,000	2,0	0,000
CM 0654	Wheat bran, unprocessed	100 PoP	38,5				0,3	0,010	0,0	0,000	0,0	0,000	0,0	0,000	0,0	0,000
CF 1211	Wheat flour	10 PoP	3,5				323,0	1,131	114,0	0,399	28,3	0,099	112,0	0,392	175,8	0,615
CF 1210	Wheat germ	100 PoP	30,8				0,1	0,003	0,1	0,003	0,0	0,000	0,1	0,003	0,1	0,003
CF 1212	Wheat wholemeal	30 PoP	10,8				1,0	0,011	0,3	0,004	0,0	0,000	2,8	0,030	1,3	0,014
						Total	= 2,663		4,175		3,362		2,315		2,349	
						% ADI	= 22%		38%		28%		19%		20%	
					Rounded %	ADI	= 20%		40%		30%		20%		20%	

1/ The MRL accommodate external animal treatment

PROCHLORAZ (142) **Theoretical Maximum Daily Intake (TMDI)**

ADI = 0.01 mg/kg bodyweight or 0.6 mg for a 60 kg person

Commodity		MRL	Notes	Middle Eastern		Far Eastern		African		Latin American		European	
		mg/kg		Diet	TMDI	Diet	TMDI	Diet	TMDI	Diet	TMDI	Diet	TMDI
Code	Name			g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day
FI 326	Avocado	5		0,0	0,0000	0,0	0,0000	0,2	0,0008	3,3	0,0163	1,0	0,0050
FI 327	Banana	5		8,3	0,0413	26,2	0,1308	21,0	0,1050	102,3	0,5113	22,8	0,1138
GC 640	Barley	0,5		1,0	0,0005	3,5	0,0018	1,8	0,0009	6,5	0,0033	19,8	0,0099
MF 812	Cattle fat	0,5		0,3	0,0001	0,3	0,0002	0,3	0,0001	1,5	0,0008	0,0	0,0000
MM 812	Cattle meat	0,1		18,5	0,0019	3,5	0,0004	10,4	0,0010	30,0	0,0030	63,3	0,0063
MO 812	Cattle, Edible offal of	5		2,5	0,0125	0,3	0,0017	1,8	0,0092	5,0	0,0250	6,0	0,0300
SB 716	Coffee beans	0,2		5,3	0,0011	0,4	0,0001	0,0	0,0000	3,6	0,0007	7,9	0,0016
FI 345	Mango	2		2,3	0,0045	5,3	0,0107	3,4	0,0068	6,3	0,0125	0,0	0,0000
ML 106	Milks	0,1		116,8	0,0117	32,0	0,0032	41,8	0,0042	160,0	0,0160	294,0	0,0294
VO 450	Mushrooms	2		0,3	0,0005	0,5	0,0010	0,0	0,0000	0,0	0,0000	4,0	0,0080
GC 647	Oats	0,5		0,0	0,0000	0,0	0,0000	0,2	0,0001	0,8	0,0004	2,0	0,0010
FC 4	Oranges, Sweet, Sour	5		31,5	0,1575	4,0	0,0200	4,8	0,0242	31,0	0,1550	29,8	0,1488
FI 350	Papaya	1		0,0	0,0000	0,2	0,0002	0,0	0,0000	5,3	0,0053	0,0	0,0000
SO 495	Rape seed	0,5		0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000	0,0	0,0000
GC 650	Rye	0,5		0,0	0,0000	1,0	0,0005	0,0	0,0000	0,0	0,0000	1,5	0,0008
FS 12	Stone fruits	0,05		7,3	0,0004	1,0	0,0001	0,0	0,0000	0,8	0,0000	22,8	0,0011
GC 654	Wheat	0,5		327,3	0,1636	114,8	0,0574	28,3	0,0142	116,8	0,0584	178,0	0,0890
			Total =		0,3955		0,2278		0,1665		0,8078		0,4446
			% ADI =		66%		41%		28%		135%		74%
			Rounded % ADI =		70%		40%		30%		140%		70%

SPINOSAD (203)

International Estimated Daily Intake (IEDI)

ADI = 0.02 mg/kg bodyweight or 1.2 mg for a 60 kg person

Commodity		MRL	STMR	Processing	Notes	Adjusted	Middle Eastern		Far Eastern		African		Latin American		European	
		mg/kg	mg/kg	Factor		STMR	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI
Code	Name					mg/kg	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day
TN 0660	Almonds	0,01	0,01				0,5	0	0,0	0	0,0	0	0,1	0	1,8	0
FP 0226	Apples	0,1	0,0165				7,5	0,0001	4,7	0,0001	0,3	0	5,5	0,0001	40,0	0,0007
VB 0040	Brassica vegetables, Head cabbages, Flowerhead brassicas	2	0,27				6,3	0,0017	11,2	0,003	0,0	0	10,8	0,0029	39,8	0,0107
MO 1280	Cattle kidney	1	0,31		1/, 2/		0,1	0	0,0	0	0,1	0	0,2	0	0,2	0,0001
MO 1281	Cattle liver	2	0,66		1/,2/		0,2	0,0001	0,0	0	0,1	1E-04	0,3	0,0002	0,4	0,0003
MM 0812	Cattle meat	3*	0,078		1/, 2/		18,5	0,0014	3,5	0,0003	10,4	8E-04	30,0	0,0023	63,3	0,0049
ML 0812	Cattle milk	1	0,65		1/		79,5	0,0517	23,2	0,0151	35,8	0,023	159,3	0,1035	287,0	0,1866
VS 0624	Celery	2	0,97				0,5	0,0005	0,0	0	0,0	0	0,3	0,0002	2,0	0,0019
FC 0001	Citrus fruits	0,3	0,01				38,0	0,0004	4,4	0	3,6	0	40,9	0,0004	34,3	0,0003
OR 0691	Cotton seed oil, edible	0,01	0,002				3,8	0	0,5	0	0,5	0	0,5	0	0,0	0
PE 0112	Eggs	0,01	0,01				14,6	0,0001	13,1	0,0001	3,7	0	11,9	0,0001	37,6	0,0004
VC 0045	Fruiting vegetables, Cucurbits	0,2	0,046				80,5	0,0037	18,2	0,0008	0,0	0	30,5	0,0014	38,5	0,0018
FI 0341	Kiwifruit	0,05	0,02				0,0	0	0,0	0	1,9	0	0,1	0	1,5	0
VL 0053	Leafy vegetables	10	1,9				7,8	0,0147	9,7	0,0184	0,0	0	16,5	0,0314	51,3	0,0974
VP 0060	Legume vegetables	0,3	0,041				9,5	0,0004	1,5	0,0001	0,0	0	4,3	0,0002	26,0	0,0011
GC 0645	Maize	0,01	0				48,3	0	31,2	0	106,2	0	41,8	0	8,8	0
JF 0004	Orange juice		0,0072				7,3	0,0001	0,0	0	0,0	0	0,3	0	4,5	0
VO 0051	Peppers	0,3	0,056				3,4	0,0002	2,1	0,0001	5,4	3E-04	2,4	0,0001	10,4	0,0006
VR 0589	Potato	0,01	0				59,0	0	19,2	0	20,6	0	40,8	0	240,8	0
PM 0110	Poultry meat	0,2*	0,01				31,0	0,0003	13,2	0,0001	5,5	1E-04	25,3	0,0003	53,0	0,0005
MO 0822	Sheep, Edible offal of	0,01	0,01		1/		1,3	0	0,0	0	0,5	0	0,0	0	1,3	0
MM 0822	Sheep meat	0,01	0,01		1/		13,5	0,0001	0,7	0	2,0	0	3,0	0	10,3	0,0001
GC 0651	Sorghum	1	0,165				2,0	0,0003	9,7	0,0016	26,6	0,004	0,0	0	0,0	0
VD 0541	Soya bean (dry)	0,01	0				4,5	0	2,0	0	0,5	0	0,0	0	0,0	0
FS 0012	Stone fruits	0,2	0,0265				7,3	0,0002	1,0	0	0,0	0	0,8	0	22,8	0,0006
VO 0447	Sweet corn (corn-on-the-cob)	0,01	0,01				0,0	0	0,0	0	4,4	0	0,0	0	8,3	0,0001
VO 0448	Tomato	0,3	0,03				44,1	0,0013	5,7	0,0002	14,6	4E-04	25,5	0,0008	38,2	0,0011
	Tomato juice		0,0075	0,25			0,3	0	0,0	0	0,0	0	0,0	0	2,0	0
	Tomato paste		0,059	1,94			5,8	0,0003	0,2	0	0,3	0	0,0	0	4,0	0,0002
						Total =		0,0778		0,0399		0,0295		0,1440		0,3095
						% ADI=		6%		3%		2%		12%		26%
						Rounded % ADI=		6%		3%		2%		10%		30%

1/ The MRL accommodates external animal treatment

2/ Residues from direct animal treatment-not an STMR but median of residues from animals in atreatment group

TEBUFENOZIDE (196) International Estimated Daily Intake (IEDI)

ADI = 0.02 mg/kg bodyweight or 1.2 mg for a 60 kg person

Commodity		MRL	STMR	Processing	Notes	Adjusted	Middle Eastern		Far Eastern		African		Latin American		European	
		mg/kg	mg/kg	Factor		STMR	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI	Diet	IEDI
Code	Name					mg/kg	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day	g/day	mg/day
TN 0660	Almonds	0,05	0,0205				0,5	0	0	0	0	0	0,1	0	1,8	0
FI 0326	Avocado	1	0,21				0	0	0	0	0,2	0	3,3	0,0007	1	0,0002
VB 0400	Broccoli	0,5	0,11				0,5	0,0001	1	0,0001	0	0	1,1	0,0001	2,7	0,0003
FB 0020	Blueberries	3	0,685				0	0	0	0	0	0	0	0	0,5	0,0003
VB 0041	Cabbage	5	0,34				5	0,0017	9,7	0,0033	0	0	10,5	0,0036	26,8	0,0091
MO 1280	Cattle, kidn	0,02*	0,006				0,1	0	0	0	0,1	0	0,2	0	0,2	0
MO 1281	Cattle, liver	0,02*	0,02				0,2	0	0	0	0,1	0	0,3	0	0,4	0
MM 0812	Cattle meat	0,05	0,006		1/, F		18,5	0,0001	3,5	0	10,4	0,0001	30	0,0002	63,3	0,0004
ML 0812	Cattle milk	0,01*	0,003				79,5	0,0002	23,2	0,0001	35,8	0,0001	159,3	0,0005	287	0,0009
FC 0001	Citrus fruit	2	0,079				54,3	0,0043	6,3	0,0005	5,1	0,0004	54,8	0,0043	49	0,0039
JF 0001	Citrus juice	2	0,0077		2/		7,3	0,0001	0	0	0	0	0,3	0	4,5	0
FB 0265	Cranberries	0,5	0,042				0	0	0	0	0	0	0	0	0,3	0
DF 0269	Dried grape	2	0,551				0,3	0,0001	0	0	0	0	0,3	0,0001	2,3	0,0012
PE 0112	Eggs	0,02*	0				14,6	0	13,1	0	3,7	0	11,9	0	37,6	0
FB 0269	Grapes	2	0,745				15,5	0,0115	1	0,0007	0	0	1,3	0,001	13,8	0,0103
	Wine		0,081				0,5	0	0	0	0,8	0,0001	19,8	0,0016	97,8	0,0079
FI 0341	Kiwifruit	0,5	0,14				0	0	0	0	1,9	0,0003	0,1	0	1,5	0,0002
VL 0053	Leafy vege	10	2,45				7,8	0,0191	9,7	0,0238	0	0	16,5	0,0404	51,3	0,1257
HH 0738	Mint	20	8,35				0,1	0,0008	0,1	0,0008	0,1	0,0008	0,1	0,0008	0,1	0,0008
FS 0245	Nectarines	0,5	0,11				1,3	0,0001	0,3	0	0	0	0,4	0	6,3	0,0007
FS 0247	Peaches	0,5	0,11				1,3	0,0001	0,3	0	0	0	0,4	0	6,3	0,0007
TN 0672	Pecans	0,01*	0,01				0	0	0	0	0	0	0	0	0,3	0
VO 0051	Peppers	1	0,064				3,4	0,0002	2,1	0,0001	5,4	0,0003	2,4	0,0002	10,4	0,0007
FP 0009	Pome fruits	1	0,17				10,8	0,0018	7,5	0,0013	0,3	0	6,5	0,0011	51,3	0,0087
PM 0110	Poultry mea	0,02*	0,02				31	0,0006	13,2	0,0003	5,5	0,0001	25,3	0,0005	53	0,0011
FB 0272	Raspberries	2	0,56				0	0	0	0	0	0	0	0	0,5	0,0003
SO 0495	Rapeseed	2	0,95				0	0	0	0	0	0	0	0	0	0
OR 0495	Rapeseed oil		2,2				4,5	0,0099	2,7	0,0059	0	0	0,3	0,0006	7,3	0,0161
GS 0659	Sugarcane	1	0,12				18,5	0,0022	7,3	0,0009	15,9	0,0019	3,5	0,0004	0	0
	Refined sugar			0		0	73	0	43	0	25,5	0	97,3	0	96,8	0
CM 0649	Rice, husk	0,1	0,03				0	0	1,8	0,0001	34,7	0,001	21	0,0006	2,5	0,0001
VO 0448	Tomatoes	1	0,13				44,1	0,0057	5,7	0,0007	14,6	0,0019	25,5	0,0033	42,2	0,0055
	Tomato paste			0,731		0,095	5,8	0,0005	0,2	0	0,3	0	0	0	4	0,0004
VJ 0448	Tomato juice			0,177		0,023	0,3	0	0	0	0	0	0	0	2	0
TN 0678	Walnut	0,05	0,003				0	0	0	0	0	0	0	0	0,5	0
	Total =							0,05892		0,03867		0,00712		0,060107		0,195053
	% ADI =							5%		3%		1%		5%		16%
	Rounded % ADI =							5%		3%		1%		5%		20%

1/ STMR based on muscle

2/ Consumption for JF 4 Orange juice used

ANNEX 4

ACUTE DIETARY RISK ASSESSMENT

The following Tables give details of the estimated acute dietary intakes of the pesticides for general population and children up to six years old evaluated by the Meeting and show the ratios of the estimated intakes to the corresponding acute reference dose (RfD).

In the case of compounds for which an acute RfD might be necessary but has not yet been established IESTIs were calculated, but the acute risk assessments could not be finalized. Depending on the commodity consumption data, the IESTI for each commodity is calculated for the relevant case described below:

Case 1. Composite sampling data reflect the residue level in the food (unit weight of the whole portion is < 25 g).
Case 2. Composite residue data do not reflect the residue level in individual food commodity units (unit weight of the whole portion is > 25 g).
Case 2a. Unit weight is less than large portion weight.
Case 2b. Unit weight exceeds large portion weight.
Case 3. Processed commodity, where bulking or blending means that the STMR-P represents the likely highest residue.

The percentages of the acute RfD are rounded to one significant figure for values up to and including 100% and to two significant figures for values above 100%.

Annex 4

ALDICARB (117) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**
GENERAL POPULATION (EXCLUDING WOMEN OF CHILD-BEARING AGE)

Acute RfD: 0.003 mg/kg body weight

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
FI 0327	Banana	0,2	0,01		0,10	8,56	USA	65	556	900	FRA	68	612	5	2b	0,00428	140
VR 0589	Potatoes 1/	0,5	0,06		0,45	10,9	NLD	63	687	200	FRA	80	160		2a	0,00681	230
	Potatoes, microwaved 2/		0,04	0,7	0,315	10,9	NLD	63	687	200	FRA	80	160		2a	0,00481	160
	1/A highest residue of 1,2 mg/kg was used in the first term of the equation														Maximum IESTI = 230		
	2/A highest residue of 0.84 mg/kg was used in the first term of the equation																

ALDICARB (117) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**
CHILDREN

Acute RfD: 0.003 mg/kg body weight

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
FI 0327	Banana	0,2	0,01		0,10	19,61	JPN	15,9	312	900	FRA	68	612	5	2b	0,00981	330
VR 0589	Potatoes 1/	0,5	0,06		0,45	19,23	UNK	14,5	279	200	FRA	80	160		2a	0,01693	560
	Potatoes, microwaved 2/		0,04	0,7	0,315	19,23	UNK	14,5	279	200	FRA	80	160		2a	0,01189	400
	1/ A high residue of 1,2 mg/kg was used in the first term of the equation														Maximum IESTI = 560		
	2/A highest residue of 0.84 mg/kg was used in the first term of the equation																

Annex 4

CHLORPROPHAM (201) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**
GENERAL POPULATION

Acute RfD: 0.03 mg/kg body weight

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
VR 0589	Potato	30	11		23,0	10,9	NLD	63	686,7	122	USA	81	99	7	2a	0,46716	1600
	Potato, cooked		3,6	0,33	7,6	10,9	NLD	63	686,7	122	USA	81	99	7	2a	0,15437	510
	Potato peeled and cooked		0,098		0,2	10,9	NLD	63	686,7	122	USA	81	99	7	2a	0,00406	10
	Chips with skin		4,6														
	Chips without skin		1,1														
	French fries with skin		1,6														
	French fries without skin		0,2														
	Dehydrated granules		0,8														
ML 0812	Cattle milk	0,0005	0,0002			39,92	NLD	63	2515,0						3	0,00001	0
MO 0812	Cattle, edible offal of	0,01	0,005		0,007	6,85	AUS	67	459,0						1	0,00005	0
MM 0812	Cattle meat	0,1	0,004		0,004	6,97	AUS	67,0	467,0						1	0,00003	0
															Maximum IESTI = 1600		

CHLORPROPHAM (201) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**
CHILDREN

Acute RfD: 0.03 mg/kg body weight

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
VR 0589	Potato	30	11		23,0	19,23	UNK	14,5	279	122	USA	81	99	7	2a	1,38305	4600
	Potato, cooked		3,6	0,33	7,6	19,23	UNK	14,5	279	122	USA	81	99	7	2a	0,45692	1500
	Potato, peeled and cooked		0,098		0,2	19,23	UNK	14,5	279	122	USA	81	99	7	2a	0,01202	40
	Chips with skin		4,6														
	Chips without skin		1,1														
	French fries with skin		1,6														
	French fries without skin		0,2														
	Dehydrated granules		0,845														
ML 0812	Cattle milk	0,0005	0,0002			76,33	AUS	19	1450						3	0,00002	0
MO 0812	Cattle, edible offal of	0,01	0,005		0,007	11,39	FRA	17,8	203						1	0,00008	0
MM 0812	Cattle meat	0,1	0,004		0,004	12,52	AUS	19	238						1	0,00005	0
															Maximum IESTI = 4600		

Annex 4

DIAZINON (22) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**
CHILDREN

Acute RfD: 0.03 mg/kg body weight

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor		IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g		Case	mg/kg bw	%
FP 0009	**Pome fruit 1/**	0,3	0,04		0,24												
FP 0226	Apple	0,3	0,04		0,24	45,25	USA	15	679	138	USA	92	127	7	2a	0,01569	50
JF 0226	Apple juice		0,0004	0,01											3		
	Apple sauce		0,0004	0,01											3		
	Apple slices, canned		0,0004	0,01											3		
FP 0230	Pear	0,3	0,04		0,24	19,24	USA	15	289	166	USA	91	151	7	2a	0,01729	60
VB 0041	Cabbages, head	0,5	0,01		0,35	8,92	JPN	15,9	142	908	USA	79	717	5	2b	0,01561	50
MM 0814	Goat meat	2	0,02		2/	5,08	USA	15	76								
MO 0098	Kidney of cattle, etc.	0,03	0,01		2/	12,44	USA	15	187								
MO 0099	Liver of cattle, etc.	0,03	0,01		2/	11,39	FRA	17,8	203								
MM 0097	Meat of cattle, etc.	2	0,02		2/	13,72	AUS	19	261								
ML 0106	Milks	0,02	0,02			85,71	USA	15	1286						3	0,00171	6
VO 0448	Tomato	0,5	0,12		0,48	10,6	USA	15	159	123	USA	100	123	7	2a	0,02784	90
	1/ Intake calculated for individual commodities in group 2/ HR not determined														Maximum IESTI = 90		

Annex 4

DIAZINON (22) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**
GENERAL POPULATION

Acute RfD: 0.03 mg/kg body weight

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
FP 0009	**Pome fruit 1/**	0,3	0,04		0,24												
FP 0226	Apple	0,3	0,04		0,24	20,74	USA	65	1348	138	USA	92	127	7	2a	0,0040	10
JF 0226	Apple juice		0,0004	0,01											3		
	Apple sauce		0,0004	0,01											3		
	Apple slices, canned		0,0004	0,01											3		
FP 0230	Pear	0,3	0,04		0,24	10,66	USA	65	693	166	USA	91	151	7	2a	0,0042	10
VB 0041	Cabbages, head	0,5	0,01		0,35	5	FRA	62,3	312	908	USA	79	717	5	2b	0,0088	30
MM 0814	Goat meat	2	0,02		2/	7,34	USA	65	477								
MO 0098	Kidney of cattle, etc.	0,03	0,01		2/	12,12	USA	65	788								
MO 0099	Liver of cattle, etc.	0,03	0,01		2/	5,84	USA	65	380								
MM 0097	Meat of cattle, etc.	2	0,02		2/	7,5	AUS	70	525								
ML 0106	Milks	0,02	0,02			37,94	USA	65	2466						3	0,0008	3
VO 0448	Tomato	0,5	0,12		0,48	6,01	USA	65	391	123	USA	100	123	7	2a	0,0069	20
	1/ Intake calculated for individual commodities in group 2/ HR not determined														Maximum IESTI = 30		

Annex 4

DIMETHIPIN (151) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**
CHILDREN

Acute RfD: 0.02 mg/kg body weight

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
OR0645	Cotton seed oil	0,1	0,04	0,2		0,41	USA	15	6								0
MO 0105	Edible offal mammalian 1/	0,01	0,01		0,00	12,44	USA	15	187								0
PE0112	Eggs	0,01	0,01		0,00	7,5	FR	17,8	134								0
MM0095	Meat	0,01	0,01		0,00	13,71	AUS	19	260								0
ML0106	Milk	0,01	0,01		0,00	85,71	USA	15	1286								0
VR0589	Potato	0,05	0,02		0,02	19,23	UK	14,5	279	122	USA	81	99	7	2a	0,0012	1
PM0110	Poultry meat	0,01	0,01		0,00	11,78	AUS	19	224								0
PO0111	Poultry edible offal	0,01	0,01		0,00	2,47	USA	15	37								0
OC0495	Rapeseed 2/	0,2	0,1		0,1	0,97	AUS	19	18				0		1	0,0001	0
SO0702	Sunflower seed	1	0,01		0,77	1,59	USA	15	24				0		1	0,0012	6
	1/ Consumption of kidney of cattle, goats, pigs and sheep used 2/ Consumption of edible rapeseed oil used														Maximum IESTI = 6		

Annex 4

DIMETHIPIN(151) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**
GENERAL POPULATION

Acute RfD: 0.02 mg/kg body weight

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
OR0645	Cotton seed oil	0,1	0,02	0,2		0,14	USA	65	9				0		3	0,00000	0
MO 0105	Edible offal mammalian 1/	0,01	0		0,00	12,12	USA	65	788								0
PE0112	Eggs	0,01	0		0,00	3,51	FR	62,3	219								0
MM0095	Meat	0,01	0		0,00	7,78	AUS	67	521								0
ML0106	Milk	0,01	0		0,00	37,94	USA	65	2466								0
VR0589	Potato	0,05	0,02		0,02	10,9	NL	63	687	122	USA	81	99	7	1	0,00041	1
PM0110	Poultry meat	0,01	0		0,00	6,44	AUS	67	431								0
PO0111	Poultry edible offal	0,01	0		0,00	3,81	USA	65	248								0
OC0495	Rapeseed 2/	0,2	0,1		0,1	0,97	AUS	67	65				0		1	0,00010	0
SO0702	Sunflower seed	1	0,01		0,77	2,97	USA	65	193				0		1	0,00229	11
	1/ Consumption of kidney of cattle, goats, pigs and sheep used 2/ Consumption of edible rapesee oil used														Maximum IESTI = 11		

Annex 4

DINOCAP (87) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**

WOMEN OF CHILD-BEARING AGE

Acute RfD: 0.008 mg/kg body weight

Commodity Code	Commodity Name	MRL mg/kg	STMR or STMR-P mg/kg	Processing factor	HR or HR-P mg/kg	GEMS/Food large portion g/kg bw	Country of large portion consumption	Body weight kg	Per capita large portion g/person	Unit weight g	Country of unit weight	Percent edible portion %	Unit weight, edible portion g	Variability factor	Case	IESTI mg/kg bw	Percent acute RfD %
FB 0269	Grapes	0.5	0.05		0.35	7.66	AUS	67	513	125	FRA	94	118	7	2a	0.00636	80
	Wine		0.0035	0.07		16.88	AUS	67	1131						3	0.00006	1

Maximum IESTI = 80

Annex 4

DINOCAP (87) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**

CHILDREN

Acute RfD: 0.030 mg/kg body weight

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
FB 0269	Grapes	0,5	0,05		0,35	18	AUS	19	342	125	FRA	94	118	7	2a	0,01929	60
	Wine		0,0035	0,07		0,21	AUS	19	4						3	0,00000	0
															Maximum IESTI = 60		

Annex 4

DINOCAP (87) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**
GENERAL POPULATION (EXCLUDING WOMEN OF CHILD-BEARING AGE)

Acute RfD: 0.030 mg/kg body weight

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
FB 0269	Grapes	1	0,050		0,35	7,66	AUS	67	513	125	FRA	94	118	7	2a	0,00636	20
	Wine		0,0035	0,07		16,88	AUS	67	1131						3	0,00006	0
															Maximum IESTI = 20		

Annex 4

FENPROPIMORPH (188) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**
GENERAL POPULATION

Acute RfD: 1.0 mg/kg body weight

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
FI 0327	Banana	2	0,11		0,43	8,56	USA	65	556	708	USA	68	481	5	2b	0,0161	2
PE 0840	Chicken eggs	0,01	0		1/	3,51	FRA	62,3	219								
MO 0098	Kidney of cattle, goats, pigs and sh	0,05	0,026		1/	12,12	USA	65	788								
MO 0099	Liver of cattle, goats, pigs and she	0,3	0,22		1/	5,84	USA	65	380								
MF 0100	Mammalian fats (except milk fats)	0,01	0,006		1/	1,16	AUS	70	81								
MM 0095	Meat (from mammals other than m	0,02	0,009		1/	7,52	AUS	70	526								
ML 0106	Milks	0,01	0,004			37,94	USA	65	2466								
PF 0111	Poultry fats	0,01	0		1/	0,74	FRA	62,3	46						3	0,0002	0
PM 0111	Poultry meat	0,01	0		1/	6,21	AUS	70	435								
PO 0111	Poultry, Edible offal of	0,01	0		1/	3,81	USA	65	248								
	1/ HR not determined														Maximum IESTI = 2		

FENPROPIMORPH (188) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**
CHILDREN

Acute RfD: 1.0 mg/kg body weight

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
FI 0327	Banana	2	0,11		0,43	19,61	JPN	15,9	312	708	USA	68	481	5	2b	0,0422	4
PE 0840	Chicken eggs	0,01	0		1/	7,5	FRA	17,8	134								
MO 0098	Kidney of cattle, goats,pigs and sh	0,05	0,026		1/	12,44	USA	15	187								
MO 0099	Liver of cattle, goats, pigs and she	0,3	0,22		1/	11,39	FRA	17,8	203								
MF 0100	Mammalian fats (except milk fats)	0,01	0,006		1/	2,98	AUS	19	57								
MM 0095	Meat (from mammals other than m	0,02	0,009		1/	13,71	AUS	19	260								
ML 0106	Milks	0,01	0,004			85,71	USA	15	1286						3	0,0003	0
PF 0111	Poultry fats	0,01	0		1/	1,11	FRA	17,8	20								
PM 0111	Poultry meat	0,01	0		1/	11,78	AUS	19	224								
PO 0111	Poultry, Edible offal of	0,01	0		1/	2,47	USA	15	37								
	1/ HR not determined														Maximum IESTI = 4		

Annex 4

FIPRONIL (202) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**

CHILDREN

Acute RfD: 0.003 mg/kg body weight

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
FI 0327	Banana	0,005	0,004		0,005	19,61	JPN	15,9	311,8	900	FRA	68	612	5	2b	0,00049	20
GC 0640	Barley	0,002	0,004		0,004	0,73	AUS	19	13,9						1	0,00000	0
VB 0400	Broccoli	0,02	0,005		0,0022	10,95	USA	15	164,3	608	USA	78	474,24	5	2b	0,00012	4
VB 0041	Cabbages, head	0,02	0,005		0,00215	8,92	JPN	15,9	141,8	908	USA	79	717,32	5	2b	0,00010	3
PE 0840	Chicken eggs	0,02	0,006		0,0078	7,5	FRA	17,8	133,5						1	0,00006	2
VB 0404	Cauliflower	0,02	0,005		0,00215	12,31	NLD	17	209,3	575	USA	39	224,25	5	2b	0,00013	4
MO 1280	Cattle, kidney	0,02	0,014		0,018	12,44	USA	15	186,6						1	0,00022	7
MO 1281	Cattle, liver	0,1	0,064		0,079	11,39	FRA	17,8	202,7						1	0,00090	30
MM 0812	Cattle meat	0,5	0,015		0,019	12,52	AUS	19	237,9						1	0,00024	8
ML 0812	Cattle milk	0,02	0,011			76,33	AUS	19	1450,3						3	0,00084	30
GC 0645	Maize	0,01	0,005		0,02	8,33	FRA	17,8	148,3						1	0,00017	6
GC 0647	Oats	0,002	0,004		0,004	4,15	USA	15	62,3						1	0,00002	1
VR 0589	Potato	0,02	0,004		0,028	19,23	UNK	14,5	278,8	200	FRA	80	160	7	2a	0,00239	80
	Potato chips		0,0009														
	Potato flakes		0,0011														
PO 0110	Poultry, Edible offal of	0,02	0,008		0,0084	2,47	USA	15	37,1						1	0,00002	1
PM 0110	Poultry meat	0,01	0,006		0,006	11,78	AUS	19	223,8						1	0,00007	2
GC 0649	Rice	0,01	0,006		0,013	12,5	FRA	17,8	222,5						1	0,00016	5
GC 0650	Rye	0,002	0,004		0,004	2,17	NLD	17	36,9						1	0,00001	0
VR 0596	Sugar beet	0,2	0,0125		0,17												
SO 0702	Sunflower seed	0,002	0,004		0,008	1,59	USA	15	23,9						1	0,00001	0
GC 0653	Triticale	0,002	0,004		0,004												
GC 0654	Wheat	0,002	0,004		0,004	10,07	USA	15	151,1						1	0,00004	1
															Maximum IESTI = 80		

Annex 4

FIPRONIL(202) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**

GENERAL POPULATION

Acute RfD: 0.003 mg/kg body weight

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
FI 0327	Banana	0,005	0,004		0,005	8,56	USA	65	556,4	900	FRA	68	612	5	2b	0,00021	7
GC 0640	Barley	0,002	0,004		0,004	6,00	NLD	63	378,0						1	0,00002	1
VB 0400	Broccoli	0,02	0,005		0,00215	5,79	USA	65	376,4	680	USA	78	530	5	2b	0,00006	2
VB 0041	Cabbages, head	0,02	0,005		0,00215	5,00	FRA	62,3	311,5	908	USA	79	717	5	2b	0,00005	2
PE 0840	Chicken eggs	0,02	0,006		0,0078	3,51	FRA	62,3	218,7						1	0,00003	1
VB 0404	Cauliflower	0,02	0,005		0,00215	8,26	UNK	70,1	579,0	575	USA	39	224	5	2b	0,00005	2
MO 1280	Cattle, kidney	0,02	0,014		0,018	12,12	USA	65	787,8						1	0,00022	7
MO 1281	Cattle, liver	0,1	0,064		0,079	7,16	USA	65	465,4						1	0,00057	20
MM 0812	Cattle meat	0,5	0,015		0,019	6,97	AUS	67	467,0						1	0,00013	4
ML 0812	Cattle milk	0,02	0,011			39,92	AUS	67	2674,6						3	0,00044	10
GC 0645	Maize	0,01	0,005		0,02	4,17	FRA	62,3	259,8						1	0,00008	3
GC 0647	Oats	0,002	0,004		0,004	4,9	FRA	62,3	305,3						1	0,00002	1
VR 0589	Potato	0,02	0,004		0,028	10,9	NLD	63	686,7	200	FRA	80	160	7	2a	0,00073	20
	Potato chips		0,0009														
	Potato flakes		0,0011														
PO 0110	Poultry, Edible offal of	0,02	0,008		0,0084	3,81	USA	65	247,7						1	0,00003	1
PM 0110	Poultry meat	0,01	0,006		0,006	6,44	AUS	67	431,5						1	0,00004	1
GC 0649	Rice	0,01	0,006		0,013	5	FRA	62,3	311,5						1	0,00007	2
GC 0650	Rye	0,002	0,004		0,004	1,22	NLD	63	76,9						1	0,00000	0
VR 0596	Sugar beet	0,2	0,0125		0,17												
SO 0702	Sunflower seed	0,002	0,004		0,008	2,97	USA	65	193,1						1	0,00002	1
GC 0653	Triticale	0,002	0,004		0,004												
GC 0654	Wheat	0,002	0,004		0,004	5,89	USA	65	382,9						1	0,00002	1
															Maximum IESTI = 20		

Annex 4

HALOXYFOP (194) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**

GENERAL POPULATION

Acute RfD: may be necessary but has not been established

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
MO 1280	Cattle, kidney	3			0,95	12,12	USA	65	787,8						1	0,01151	-
MO 1281	Cattle, liver	1			0,33	7,16	USA	65	465,4						1	0,00236	-
MM 0812	Cattle meat	0,05			0,03	6,97	AUS	67	467,0						1	0,00021	-
ML 0812	Cattle milk	0,3	0,22			39,92	AUS	67	2674,6						3	0,00878	-
PE 0840	Chicken eggs	0,01 *			0,003	3,51	FRA	62,3	218,7						1	0,00001	-
PM 0840	Chicken meat 1/	0,01 *			0,003	6,44	AUS	67	431,5						1	0,00002	-
PO 0840	Chicken, edible offal of	0,05			0,03	5,53	NLD	63	348,0						1	0,00017	-

1/ with adhering skin

HALOXYFOP (194) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**

CHILDREN

Acute RfD: may be necessary but has not been established

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
MO 1280	Cattle, kidney	3			0,95	12,44	USA	15	186,6						1	0,01182	-
MO 1281	Cattle, liver	1			0,33	11,39	FRA	17,8	202,7						1	0,00376	-
MM 0812	Cattle meat	0,05			0,03	12,52	AUS	19	237,9						1	0,00038	-
ML 0812	Cattle milk	0,3	0,22			76,33	AUS	19	1450,3						3	0,01679	-
PE 0840	Chicken eggs	0,01 *			0,003	7,5	FRA	17,8	133,5						1	0,00002	-
PM 0840	Chicken meat 1/	0,01 *			0,003	11,78	AUS	19	223,8						1	0,00004	-
PO 0840	Chicken, edible offal of	0,05			0,03	2,47	USA	15	37,1						1	0,00007	-
	1/ with adhering skin																

Annex 4

IPRODIONE (111) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**
GENERAL POPULATION

Acute RfD: Maybe necessary but has not yet been established

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
VO 0448	Tomato	5	1,10		4,2	6,01	USA	65	391	123	USA	100	123	7	2a	0,060	-
VJ 0448	Tomato juice		0,55	0,5													
	Tomato paste		0,55	0,5													

IPRODIONE (111) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**

Acute RfD: Maybe necessary but has not yet been established **CHILDREN**

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
VO 0448	Tomato	5	1,10		4,2	10,6	USA	15	159	123	USA	100	123	7	2a	0,244	-
VJ 0448	Tomato juice		0,55	0,5													
	Tomato paste		0,55	0,5													

Annex 4

METHOMYL (94) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**

259 **GENERAL POPULATION**

Acute RfD: 0.02 mg/kg body weight

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
FP 0226	Apple	2	0,41		1,60	20,74	USA	65	1348	138	USA	92	127	7	2a	0,05194	260
	Apple juice		0,12	0,29											3		
VS 0621	Asparagus	2	0,33		1,10	6,32	NLD	63	398	25	FRA	50	13	7	2a	0,00826	40
VD 0071	Beans(dry)	0,05	0,02		0,02	4,1	FRA	62,3	255						1	0,00009	0
VP 0061	Beans	1	0,005		0,68	5	FRA	62,3	312						1	0,00340	20
VB 0040	**Brassica vegetables 1/**	7	1,3		5,60												
VB 0400	Broccoli	7	1,3		5,60	5,79	USA	65	376	608	USA	78	474	5	2b	0,16212	810
VB 0402	Brussels sprouts	7	1,3		5,60	6,25	NLD	63	394	14	UNK	69	10	7	2a	0,04015	200
VB 0041	Cabbages,h	7	1,3		5,60	5	FRA	62,3	142	908	USA	79	717	5	2b	0,06382	320
VB 0404	Cauliflower	7	1,3		5,60	8,26	UNK	70,1	579	575	USA	39	224	5	2a	0,11791	590
VS 0624	Celery	2	0,66		2,00	3,61	FRA	62,3	225								
FC 0001	**Citrus fruit 1/**	1	0,034		0,18												
FC 0005	Grapefruit	1	0,034		0,18	18	JPN	52,6	947	302	UNK	100	302	5	1	0,00737384	40
FC 0204	Lemon/lime	1	0,034		0,18	1,85	FRA	62,3	115	100	FRA	100	100	7	2a	0,00206655	10
FC 0206	Mandarin	1	0,034		0,18	7,77	JPN	52,6	409	100	FRA	100	100	7	2a	0,00345183	20
FC 0004	Orange	1	0,034		0,18	14,81	USA	65	963	190	FRA	100	190	7	2a	0,00582272	30
FF 0001	Citrus juice		0,004	0,12											3		
VP 0526	Common bean	1	0,055		0,68	6,84	NLD	63	431						3	0,0046512	20
OR 0691	Cottonseed, edible oil	0,04	0,006		0,01	0,14	USA	65	9						3	0,00000	0
VC 0045	**Cucurbits, fr. veg. 1/**	0,1	0,02		0,07												
VC 0046	Melons	0,1	0,02		0,07	10,08	USA	65	655	700	FRA	60	420	5	2a	0,00251483	10
VC 0424	Cucumber	0,1	0,02		0,07	4,97	NLD	63	313	400	FRA	90	360	5	2b	0,0017395	10
VC 0431	Summer squash	0,1	0,02		0,07	5,5	FRA	62,3	343	300	FRA	90	270	5	2a	0,00159848	10
VC 0432	Watermelon	0,1	0,02		0,07	29,83	USA	65	1939	4518	USA	46	2078	5	2b	0,0104405	50
PE 0840	Eggs	0,02	0		0,00	3,51	FRA	62,3	219				0		1	0	0
FB 0269	Grapes	7	0,86		5,20	7,66	AUS	67	513	125	FRA	94	118	7	2a	0,09454842	470
	Wine		0,3			16,88	AUS	67	1131						3	0,0043888	20
VL 0053	**Leafy vegetables 1/**	30	1,4		25												
VL 0480	Kale	30	1,4		25	5,35	NLD	63	337						1	0,13375	670
VL 0482	Lettuce, head	30	1,4		25	3,27	USA	65	213	539	USA	95	512	5	2b	0,40875	2000
VL 0483	Lettuce, leaf	30	1,4		25	2,41	NLD	63	152	539	USA	95	512	7	2b	0,30125	1500
VL 0502	Spinach	30	1,4		25	13,01	NLD	63	820	111	UNK	90	100	7	2a	0,56310714	2800

Maize, edible oil	0,02	0,004		25	0,68	NLD	63	43						3	0,00000	0
Meat	0,02	0			7,78	AUS	67	521						1	0	0
Edible offal of mammals, ex.	0,02	0		0										1	0	0
Milk	0,02	0		0	37,94	USA	65	2466						3	0	0
Nectarine	0,2	0,05		0	9,08	USA	65	590	110	FRA	90	99	7	2a	0,00182185	10
Onion	0,2	0,068		0,10	4,91	FRA	62,3	306	110	USA	91	100	7	2a	0,00203706	10
Peach	0,2	0,05		0,14	11,9	JPN	52,6	626	110	FRA	90	99	7	2a	0,00231928	10
Pear	0,3	0,098		0,10	10,66	USA	19,24	205	100	FRA	89	89	7	2a	0,00691464	30
Peas	5	0,46		0,18	1,19	JPN	52,6	63				0		1	0,00476	20
Plum	1	0,08		4	6,35	USA	65	413	6	FRA	83	5	7	2a	0,00347294	20
Potato	0,02	0		0,51	10,9	NLD	63	687	122	USA	81	99	7	2a	0	0
Poultry meat	0,02	0		0	6,44	AUS	67	431						1	0	0
Poultry, edible offal	0,02	0		0	3,81	USA	65	248						1	0	0
Soya bean (dry)	0,2	0,04		0	3,03	JPN	52,6	159						3	0,0001212	1
Soya bean oil	0,2	0,04		0,04	1,51	USA	65	98						2	0,00006	0
Sweet corn 2/	2	0,065		1,5	5,65	USA	65	367	371	UNK	58	215	5	2a	0,02833777	140
Tomato	1	0,16		0,73	6,01	USA	65	391	105	FRA	97	102	7	2a	0,01125042	60
Tomato paste		0,007												3		
Wheat	2	0,14		1,3	5,89	USA	65	383						1	0,007657	40
Wheat flour	0,03	0,003	0,021		5,62	USA	65	365						3	0,00002	0
Wheat bran	3	0,27			1,23	USA	65	80						3	0,0003321	2
Wheat germ	2	0,13	0,93		3,33	FRA	62,3	207						3	0,0004329	2
1/ Short-term intake calculated for individual commodities in group														Maximum IESTI = 2800		
2/ UK typical unit weight used in absence of USA data																

Annex 4

METHOMYL (94) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**
CHILDREN

Acute RfD: 0.02 mg/kg body weight

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
FP 0226	Apple	2	0,41		1,60	45,25	USA	15	679	138	USA	92	127	7	2a	0,15365	770
	Apple juice		0,12	0,29					0						3		
VS 0621	Asparagus	2	0,33		1,10	11,88	USA	15	178	25	FRA	50	13	7	2a	0,01857	90
VD 0071	Beans(dry)	0,05	0,02		0,02	11,76	FRA	17,8	209						1	0,00027	1
VP 0061	Beans	1	0,005		0,68	11,39	FRA	17,8	203						1	0,00775	40
VB 0040	**Brassica vegetables 1/**	7	1,3		5,60												
VB 0400	Broccoli	7	1,3		5,60	10,95	USA	15	164	608	USA	78	474	5	2b	0,30660	1500
VB 0402	Brussels sprouts	7	1,3		5,60	12,5	NLD	17	213	14	UK	69	10	7	2a	0,08909	450
VB 0041	Cabbages,h	7	1,3		5,60	8,92	JPN	15,9	142	908	USA	79	717	5	2b	0,24976	1200
VB 0404	Cauliflower	7	1,3		5,60	12,31	NLD	17	209	575	USA	39	224	5	2b	0,34468	1700
VS 0624	Celery	2	0,66		2,00	6,25	FRA	17,8	111								
FC 0001	**Citrus fruit 1/**	1	0,034		0,18												
FC 0005	Grapefruit	1	0,034		0,18	21,43	FRA	17,8	381	302	UNK	100	302	5	2a	0,01607	80
FC 0204	Lemon/lime	1	0,034		0,18	5,56	JPN	15,9	88	100	FRA	100	100	7	2b	0,00701	40
FC 0206	Mandarin	1	0,034		0,18	22,22	JPN	15,9	353	100	FRA	100	100	7	2a	0,01079	50
FC 0004	Orange	1	0,034		0,18	34,14	UNK	14,5	495	190	FRA	100	190	7	2a	0,02030	100
FF 0001	Citrus juice		0,004	0,12											3		
VP 0526	Common bean	1	0,055		0,68	10,83	NLD	17	184						1	0,00736	40
OR 0691	Cottonseed, edible oil	0,04	0,006		0,01	0,41	USA	15	6						1	0,00000	0
VC 0045	**Cucurbits, fr. veg. 1/**	0,1	0,02		0,07												
VC 0046	Melons	0,1	0,02		0,07	21,74	AUS	19	413	700	FRA	60	420	5	2b	0,00761	40
VC 0424	Cucumber	0,1	0,02		0,07	9,53	NLD	17	162	400	FRA	90	360	5	2b	0,00334	20
VC 0431	Summer squash	0,1	0,02		0,07	11,52	AUS	19	219	300	FRA	90	270	5	2b	0,00403	20
VC 0432	Watermelon	0,1	0,02		0,07	77,51	AUS	19	1473	4518	USA	46	2078	5	2b	0,02713	140
PE 0840	Eggs	0,02	0		0,00	7,5	FRA	17,8	134						1	0,00000	0
FB 0269	Grapes	7	0,86		5,20	18	JPN	15,9	286	125	FRA	94	118	7	2a	0,32417	1600

	Wine		0,3			0,21	AUS	19	4						3	0,00005	0
VL 0053	**Leafy vegetables 1/**	30	1,4		25												
VL 0480	Kale	30	1,4		25	8,74	NLD	17	149						1	0,21850	1100
VL 0482	Lettuce, head	30	1,4		25	4,92	NLD	17	84	539	USA	95	512	5	2b	0,61500	3000
VL 0483	Lettuce, leaf	30	1,4		25	6	NLD	17	102	539	USA	95	512	7	2b	0,75000	3800
VL 0502	Spinach	30	1,4		25	22,2	NLD	17	377	111	UNK	90	100	7	2a	1,43647	7200
OR 0645	Maize, edible oil	0,02	0,004			1,18	FRA	17,8	21						3	0,00000	0
MM 0095	Meat	0,02	0		0	13,71	AUS	19	260						1		0
MO 0105	Edible offal of mammals, ex.	0,02	0		0										1		0
ML 0106	Milk	0,02	0		0	85,71	USA	15	1286						3	0,00000	0
FS 0245	Nectarine	0,2	0,05		0,10	15,9	AUS	19	302	110	FRA	90	99	7	2a	0,00472	20
VA 0385	Onion	0,2	0,068		0,14	7,14	FRA	17,8	127	110	USA	91	100	7	2a	0,00572	30
FS 0247	Peach	0,2	0,05		0,10	16,61	AUS	19	316	110	FRA	90	99	7	2a	0,00479	20
FP 0230	Pear	0,3	0,098		0,18	19,24	UNK	14,5	279	100	FRA	89	89	7	2a	0,01009	50
VP 0063	Peas	5	0,46		4	3	JPN	17,9	54				0		1	0,01200	60
FS 0014	Plum	1	0,08		0,51	14,29	FRA	17,8	254	6	FRA	83	5	7	2a	0,00814	40
VR 0589	Potato	0,02	0		0	19,23	UNK	14,5	279	122	USA	81	99	7	2a	0,00000	0
PO 0110	Poultry meat	0,02	0		0										1		0
PO 0111	Poultry, edible offal	0,02	0		0										1		0
VD 0541	Soya bean (dry)	0,2	0,04			5,55	JPN	15,9	88						3	0,00022	1
OR 0541	Soya bean oil	0,2	0,04			2,36	USA	15	35						3	0,00009	0
VO 0447	Sweet corn 2/	2	0,065		1,5	11,09	UNK	14,5	161	371	UNK	58	215	5	2b	0,08318	420
VO 0448	Tomato	1	0,16		0,73	10,6	USA	15	159	105	FRA	97	102	7	2a	0,03748	190
	Tomato paste		0,007												3		
GC 0654	Wheat	2	0,14		1,3	10,07	USA	15	151						1	0,01309	70
CF 1211	Wheat flour	0,03	0,003	0,02		10,23	AUS	19	194						3	0,00003	0
CM 0654	Wheat bran	3	0,27			1,98	USA	15	30						3	0,00053	3
CF 1210	Wheat germ	2	0,13	0,93		0,53	USA	15	8						3	0,00007	0
	1/ Short-term intake calculated for individual commodities in group														Maximum IESTI = 7200		
	2/ UK typical unit weight used in absence of USA data																

Annex 4

PHOSALONE (60) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**
GENERAL POPULATION

Acute RfD: 0.3 mg/kg body weight

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
FP 0009	Pome fruit	2	0,8		1,5												
FP 0226	Apples	2	0,8		1,5	20,74	USA	65	1348	138	USA	92	127	7	2a	0,0355	10
	Apple compote		0,1	0,14											3		
FP 0230	Pears	2	0,8		1,5	10,66	USA	65	693	166	USA	91	151	7	2a	0,0311	10
FS 0012	Stone fruits	2	0,45		1,6												
FS 0013	Cherries	2	0,45		1,6	6,02	FRA	62,3	375						1	0,0096	3
FS 0240	Apricot	2	0,45		1,6	5,55	JPN	52,6	292	40	FRA	93	37	7	2a	0,0101	3
FS 0245	Nectarine	2	0,45		1,6	9,08	USA	65	590	136	USA	92	125	7	2a	0,0248	8
FS 0247	Peaches	2	0,45		1,6	11,9	JPN	52,6	626	110	FRA	90	99	7	2a	0,0256	9
TN 0660	Almonds	0,1	0,05		0,074	1,4	JPN	52,6	74						1	0,0001	0
TN 0666	Hazelnuts	0,05	0,05		0,05	1,00	AUS	70	70						1	0,0001	0
TN 0678	Walnuts	0,05	0,05		0,05	2,18	FRA	62,3	136						1	0,0001	0
															Maximum IESTI = 10		

Annex 4

PHOSALONE (60) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**

CHILDREN

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
FP 0009	Pome fruit	2	0,8		1,50												
FP 0226	Apples	2	0,8		1,50	45,25	USA	15	679	138	USA	92	127	7	2a	0,11830	40
	Apple compote		0,1	0,14											3		
FP 0230	Pears	2	0,8		1,50	19,24	UNK	14,5	279	166	USA	91	151	7	2a	0,11645	40
FS 0012	Stone fruits	2	0,45		1,60												
FS 0013	Cherries	2	0,45		1,60	16,67	FRA	17,8	297						1	0,02667	9
FS 0240	Apricot	2	0,45		1,60	21,81	AUS	19	414	40	FRA	93	37	7	2a	0,03086	10
FS 0245	Nectarine	2	0,45		1,60	15,89	AUS	19	302	136	USA	92	125	7	2a	0,07794	30
FS 0247	Peaches	2	0,45		1,60	16,61	AUS	19	316	110	FRA	90	99	7	2a	0,06349	20
TN 0660	Almonds	0,1	0,05		0,07	1,76	FRA	17,8	31						1	0,00013	0
TN 0666	Hazelnuts	0,05	0,05		0,05	0,65	NLD	17	11						1	0,00003	0
TN 0678	Walnuts	0,05	0,05		0,05	0,37	USA	15	6						1	0,00002	0
															Maximum IESTI = 40		

Annex 4

TEBUFENOZIDE (196) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**
CHILDREN

Acute RfD: 0.05 mg/kg body weight

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
TN 0660	Almonds	0,05	0,02		0,045	1,76	FRA	17,8	31				0		1	0,00000	0
FI 0 0326	Avocado	1	0,21		0,300	8,70	USA	15	131	201	USA	75	151	7	2b	0,03230	60
VB 0400	Broccoli	0,5	0,11		0,34	10,95	USA	15	164	608	USA	78	474	5	2b	0,01862	40
FB 0020	Blueberries	3	0,685		1,7	7,77	FRA	17,8	138				0		1	0,01321	30
VB 0041	Cabbage	5	0,34		4,60	8,92	JPN	15,9	142	908	USA	79	717	5	2b	0,20516	410
MO 1280	Cattle, kidney	0,02	0,006		0,006	12,44	USA	15	186,6				0		1	0,00025	0
MO 1281	Cattle, liver	0,02	0,02		0,02	11,39	FRA	17,8	202,7				0		1	0,00023	0
MM 0812	Cattle meat	0,05	0,006		0,006	12,52	AUS	19	237,9				0		1	0,00063	1
ML 0812	Cattle milk	0,01	0,003			76,33	AUS	19	1450,3				0		3	0,00076	2
FC 0001	Citrus fruit 1/	2	0,079		0,18												
FC 0005	Grapefruit	2	0,079		0,18	21,43	FRA	17,8	381	302	UNK	53	160	5	2a	0,01033	20
FC 0204	Lemon and lime	2	0,079		0,18	5,56	JPN	15,9	88	100	FRA	64	64	7	2a	0,00535	10
FC 0206	Mandarin	2	0,079		0,18	22,22	JPN	15,9	353	100	FRA	72	72	7	2a	0,00889	20
FC 0004	Orange	2	0,079		0,18	34,14	UNK	14,5	495	190	FRA	72	137	7	2a	0,01633	30
FB 0265	Cranberries	0,5	0,042		0,28	6,87	USA	15	103				0		1	0,00192	4
DF 269	Dried grapes (I	2	0,551		1,11	3,95	USA	15	59				0		1	0,00435	9
PE 0112	Eggs	0,02	0		0,00	7,50	FRA	17,8	134				0		1	0,00015	0
FB 0269	Grapes	2	0,745		1,50	18,00	JPN	15,9	286	125	FRA	94	118	7	2a	0,09351	190
	Wine		0,216	0,29	0,44	0,21	AUS	19	4				0		1	0,00009	0
VL 0053	Leafy vegetables 1/	10	2,45		8,1												
VL 0480	Kale	10	2,45		8,1	8,74	NLD	17	149				0		1	0,07079	140
VL 0482	Lettuce, head	10	2,45		8,1	4,92	NLD	17	84	539	USA	95	512	5	2b	0,19926	400
VL 0483	Lettuce, leaf	10	2,45		8,1	6,00	NLD	17	102	10	USA	100	10	10	2a	0,09150	180
VL 0502	Spinach	10	2,45		8,1	22,20	NLD	17	377	111	UNK	90	100	10	2a	0,60820	1220
FI 0341	Kiwi	0,5	0,14		0,22	10,20	JPN	15,9	162	75	FRA	86	65	7	2a	0,00760	15
HH 0738	Mint	20	8,35		8,6	1,78	AUS	19					0		1	0,01531	30
FS 0245	Nectarine	0,5	0,11		0,23	15,90	AUS	19	302	110	FRA	90	99	7	2a	0,01085	20

FS 0247	Peach	0,5	0,11		0,23	16,61	AUS	19	316	110	FRA	90	99	7	2a	0,01101	20
TN 0672	Pecans	0,01	0,01		0,01	1,17	AUS	19	22				0		1	0,00001	0
VO 0051	Peppers	1	0,064		0,64	3,16	AUS	19	60	172	UNK	93	160	7	2b	0,01416	30
FP 0009	**Pome fruit 1/**	1	0,17		1,1												
FP 0226	Apples	1	0,17		1,1	45,25	USA	15	679	138	USA	92	127	7	2a	0,10564	210
	Apple juice		0,02	0,12													
	Apple puree		0,04	0,23													
FP 0230	Pears	1	0,2		1,1	19,24	UNK	14,5	279	166	USA	91	151	7	2a	0,08992	180
PM 0110	Poultry meat	0,02	0,02		0,02	11,78	AUS	19	224						1	0,00024	0
FB 0272	Raspberries	2	0,56		0,86	4,28	FRA	17,8	76				0		1	0,00368	7
OC 0495	Rapeseed oil		2,2			0,97	AUS	19	18				0		3	0,00213	4
CM 0649	Rice, husked	0,1	0,03		0,07	12,50	FRA	17,8	223				0		1	0,00088	2
GS 0659	Sugarcane stems	1	0,12		0,62												
	Sugar, refined		0,003	0,025		3,14	JPN	15,9	50				0		3	0,00195	4
VO 0448	Tomato	1	0,13		0,53	10,60	USA	15	159	123	USA	100	123	7	2a	0,03170	60
	Tomato puree		0,04	0,31													
	Tomato paste		0,095	0,73													
	Tomatoes (preserved)		0,036	0,28													
JF 0448	Tomato juice		0,023	0,18													
TN 0678	Walnuts	0,05	0,003	0,021	0,02	0,37	USA	15	6						1	0,00001	0
	1/ Short-term intake calculated for individual commodities in group														Maximum IESTI = 1220		

Annex 4

TEBUFENOZIDE (196) **INTERNATIONAL ESTIMATE OF SHORT TERM INTAKE (IESTI)**

GENERAL POPULATION

Acute RfD: 0.0267 mg/kg body weight

Commodity		MRL	STMR or STMR-P	Processing factor	HR or HR-P	GEMS/ Food large portion	Country of high consumption	Body weight	Per capita large portion	Unit weight	Country of unit weight	Percent edible portion	Unit weight, edible portion	Variability factor	Case	IESTI	Percent acute RfD
Code	Name	mg/kg	mg/kg		mg/kg	g/kg bw		kg	g/person	g		%	g			mg/kg bw	%
TN 0660	Almonds	0,05	0,02		0,000	1,40	JPN	52,6	74				0		1	0,00000	0
FI 0 0326	Avocado	1	0,21		0,500	4,17	FRA	62,3	260	300	FRA	60	180	7	2a	0,01075	20
VB 0400	Broccoli	0,5	0,11		0,34	5,79	USA	65	376	608	USA	78	474	5	2b	0,00984	20
FB 0020	Blueberries	3	0,685		1,7	2,36	AUS	67	158				0		1	0,00401	8
VB 0041	Cabbage	5	0,34		4,60	5,00	FRA	62,3	142	908	USA	79	717	5	2b	0,05242	230
MO 1280	Cattle, kidney	0,02	0,02		0,02	12,12	USA	65	788				0		1	0,00024	0
MO 1281	Cattle, liver	0,02	0,02		0,02	7,16	USA	65	465				0		1	0,00014	0
MM 0812	Cattle meat	0,05	0,02		0,05	6,97	AUS	67	467				0		1	0,00035	1
ML 0812	Cattle milk	0,01	0,01			39,92	AUS	67	2675				0		3	0,00040	1
FC 0001	**Citrus fruit 1/**	2	0,079		0,18												
FC 0005	Grapefruit	2	0,079		0,18	18,00	JPN	52,6	947	302	UNK	53	160	5	2b	0,00543	10
FC 0204	Lemon and lime	2	0,079		0,18	1,85	FRA	62,3	115	100	FRA	64	64	7	2a	0,00144	3
FC 0206	Mandarin	2	0,079		0,18	7,77	JPN	52,6	409	100	FRA	72	72	7	2a	0,00288	6
FC 0004	Orange	2	0,079		0,18	14,81	USA	65	963	190	FRA	72	137	7	2a	0,00494	10
FB 0265	Cranberries	0,5	0,042		0,28	6,32	NLD	63	398				0		1	0,00177	4
DF 269	Dried grapes (raisins)	2	0,21		1,10	2,17	FRA	62,3	135				0		1	0,00239	5
PE 0112	Eggs	0,02	0,02		0,02	3,51	FRA	62,3	219				0		1	0,00007	0
FB 0269	Grapes	2	0,28		1,50	7,66	AUS	67	513	125	FRA	94	118	7	2a	0,02727	50
	Wine		0,081	0,27	0,44	16,88	AUS	67	1131				0		1	0,00743	10
VL 0053	**Leafy vegetables 1/**	10	2,45		8,1												
VL 0480	Kale	10	2,45		8,1	5,35	NLD	63	337				0		1	0,04334	90
VL 0482	Lettuce, head	10	2,45		8,1	3,27	USA	65	213	539	USA	95	512	5	2b	0,13244	260
VL 0483	Lettuce, leaf	10	2,45		8,1	2,41	NLD	63	152	10	USA	100	10	10	2a	0,03110	60
VL 0502	Spinach	10	2,45		8,1	13,01	NLD	63	820	111	UNK	90	100	10	2a	0,22100	440
FI 0341	Kiwi	0,5	0,14		0,22	5,63	NLD	63	8	75	FRA	86	65	7	2b	0,00020	0
HH 0738	Mint	20	8,35		8,6	0,12	AUS	67					0		1	0,00103	2
FS 0245	Nectarine	0,5	0,11		0,23	9,08	USA	65	590	110	FRA	90	99	7	2a	0,00419	8
FS 0247	Peach	0,5	0,11		0,23	11,90	JPN	52,6	626	110	FRA	90	99	7	2a	0,00533	10
TN 0672	Pecans	0,01	0,01		0,01	0,35	AUS	67	23				0		1	0,00000	0
VO 0051	Peppers	1	0,064		0,64	3,33	FRA	62,3	207	172	UNK	93	160	7	2a	0,01199	20
FP 0009	**Pome fruit 1/**	1	0,17		1,1												
FP 0226	Apples	1	0,17		1,1	20,74	USA	65	1348	138	USA	92	127	7	2a	0,03571	70

	Apple juice		0,02	0,12													
	Apple puree		0,04	0,23													
FP 0230	Pears	1	0,2		1,1	10,66	USA	65	693	166	USA	91	151	7	2a	0,02706	50
PM 0110	Poultry meat	0,02	0,02		0,02	6,44	AUS	67	431						1	0,00013	0
FB 0272	Raspberries	2	0,56		0,86	5,20	FRA	62,3	324				0		1	0,00447	9
OC0495	Rapeseed oil		2,2	0,39		0,97	AUS	67	65				0		3	0,00213	4
CM 0649	Rice, husked	0,1	0,03		0,07	6,07	JPN	52,6	319				0		1	0,00042	1
GS 0659	Sugarcane stems	1	0,12		0,62												
	Sugar, refined		0,003	0,025		1,40	USA	65	91				0		1	0,00087	2
VO 0448	Tomato	1	0,13		0,53	6,01	USA	65	391	123	USA	100	123	7	2a	0,00920	20
	Tomato puree		0,04	0,31													
	Tomato paste		0,007	0,054											3		
	Tomatoes preserved		0,036	0,277													
JF 0448	Tomato juice		0,023	0,177													
TN 0678	Walnuts	0,05	0,003	0,021	0,02	2,18	FRA	62,3	136						1	0,00004	0
	1/ Short-term intake calculated for individual commodities in group														Maximum IESTI = 360		

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.
57. Pesticide residues in food—1989 evaluations. Part I. Residues. FAO Plant Production and Protection Paper 100, 1990.
58. Pesticide residues in food—1989 evaluations. Part II. Toxicology. FAO Plant Production and Protection Paper 100/2, 1990.
59. Pesticide residues in food—1990. 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 102, Rome, 1990.
60. Pesticide residues in food—1990 evaluations. Part I. Residues. FAO Plant Production and Protection Paper 103/1, Rome, 1990.

61. Pesticide residues in food—1990 evaluations. Part II. Toxicology. World Health Organization, WHO/PCS/91.47, Geneva, 1991.
62. Pesticide residues in food—1991. 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 111, Rome, 1991.
63. Pesticide residues in food—1991 evaluations. Part I. Residues. FAO Plant Production and Protection Paper 113/1, Rome, 1991.
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.
66. Pesticide residues in food—1992 evaluations. Part I. Residues. FAO Plant Production and Protection Paper 118, Rome, 1993.
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.
73. Pesticide residues in food—1994 evaluations. Part II. Toxicology. World Health Organization, WHO/PCS/95.2, Geneva, 1995.
74. Pesticide residues in food—1995. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the Core Assessment Group. FAO Plant Production and Protection Paper 133, Rome, 1996.
75. Pesticide residues in food—1995 evaluations. Part I. Residues. FAO Plant Production and Protection Paper 137, 1996.
76. Pesticide residues in food—1995 evaluations. Part II. Toxicological and Environmental. World Health Organization, WHO/PCS/96.48, Geneva, 1996.
77. Pesticide residues in food—1996. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group. FAO Plant Production and Protection Paper, 140, 1997.
78. Pesticide residues in food—1996 evaluations. Part I. Residues. FAO Plant Production and Protection Paper, 142, 1997.
79. Pesticide residues in food—1996 evaluations. Part II. Toxicological. World Health Organization, WHO/PCS/97.1, Geneva, 1997.
80. Pesticide residues in food—1997. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group. FAO Plant Production and Protection Paper, 145, 1998.
81. Pesticide residues in food—1997 evaluations. Part I. Residues. FAO Plant Production and Protection Paper, 146, 1998.
82. Pesticide residues in food—1997 evaluations. Part II. Toxicological and Environmental. World Health Organization, WHO/PCS/98.6, Geneva, 1998.

83. Pesticide residues in food—1998. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group. FAO Plant Production and Protection Paper, 148, 1999.
84. Pesticide residues in food—1998 evaluations. Part I. Residues. FAO Plant Production and Protection Paper, 152/1 and 152/2 (two volumes).
85. Pesticide residues in food—1998 evaluations. Part II. Toxicological and Environmental. World Health Organization, WHO/PCS/99.18, Geneva, 1999.
86. Pesticide residues in food—1999. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group. FAO Plant Production and Protection Paper, 153, 1999.
87. Pesticide residues in food—1999 evaluations. Part I. Residues. FAO Plant Production and Protection Paper, 157, 2000.
88. Pesticide residues in food—1999 evaluations. Part II. Toxicological. World Health Organization, WHO/PCS/00.4, Geneva, 2000.
89. Pesticide residues in food—2000. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group. FAO Plant Production and Protection Paper, 163, 2001.
90. Pesticide residues in food—2000 evaluations. Part I. Residues. FAO Plant Production and Protection Paper, 165, 2001.
91. Pesticide residues in food—2000 evaluations. Part II. Toxicological. World Health Organization, WHO/PCS/01.3, 2001.

ANNEX 6

CORRECTIONS TO PREVIOUS REPORTS OF THE JMPR

Changes are shown in bold. Minor typographical errors are not included.

Report of the 1999 JMPR

p. 190, Toxicological evaluation, Levels that cause no toxic effect, Rat, first line:

Change "600 ppm, equal to 35 mg/kg bw per day . . . ." to "600 ppm, equal to 27 mg/kg bw per day . . . ."

Report of the 2000 JMPR

Abbreviations, p. x
Change LOD limit of determination to
LOQ limit of **quantification**
This term replaces the formerly used "limit of determination"

Section 4

4.1 Abamectin
p.18 **Change** Table heading "Residue definition" to "Residue **and commodity"**
Recommendations, line 8: **delete "avermectin B_{1b}"**

4.2 Captan
p. 19 *Metabolism, line 2 and p. 20, Plants, last para., line 3:* **change** "tetrachloromethylthio side-chain" to "**tri**chloromethylthio side-chain"
Change throughout:
"*cis* or *trans*-3-hydroxy-1,2,6-trihydrophthalimide" to "*cis* or *trans*-3-hydroxy-1,2,**3**,6-**tetra**hydrophthalimide"
"*cis* or *trans*-5-hydroxy-1,2,6-trihydrophthalimide" to "*cis* or *trans*-5-hydroxy-1,2,**5**,6-**tetra**hydrophthalimide"
p. 20 *para 3, line 2:* **change** "10 ppm for 10," to "10 ppm for 10 **days,"**
Environmental fate, line 4: **delete** "the leaves of"
p. 21 *Last line*: **change** "3-hydroxy-" to 3-hydroxy-**1,2,3,6-tetrahydrophthalimide**" and "5-hydroxy-1,2,6-tri …" to "5-hydroxy-1,2,**5**,6-**tetra** …"

4.4 Chlormequat
p. 37 *First line:* **change** "on residues or GAP were submitted" to "on residues or GAP **for maize** were submitted"
Cows, para. 1, last line: **change** "as least twice as high in liver" to "at least twice as high **as** in liver"
p. 38 *Cows, para. 2:* **delete** "but they were … the compound in water"
p. 39 *Chickens, para. below Table:* **change** first line to "recommended an MRL of 0.1 mg/kg for eggs and **offal**" and last line **change** "liver" to "**offal**"

4.6 Chlorpyrifos
p. 46 *Maize, para. 1, line 7 and para., 3 line 9:* **change** "except that methoxy pyridine" to "except that **trichloro**methoxypyridine"
p. 48 *Results of supervised trials, Apple, line 6:* **change** "but were conducted" to "but were **not** conducted"
p. 55 *Last para., first line:* **change** to "wheat **fodder** and straw"
p. 56 *Fate of residues, Oranges, first para., line 5:* **delete** "and to the maximum residue on whole citrus (1.2 mg/kg)"

Fate of residues, Oranges, second para., line 4: **change** "with an average of 9" to "with an average of **11**" and *line 6*: **change** "citrus oil is 2.2 mg/kg and the HR value is 11 mg/kg" to "citrus oil is 2.**6** mg/kg and the HR value is **13** mg/kg"

4.7 DDT

p. 62 *Residues in animal commodities, last para., line 4 :* **change** "weighing each data set" to "**weighting** each data set"

4.11 Fenitrthion

p. 73 *Paragraph 5, last line:* **change** ". . . 0.2 µg/m^3 per day." to ". . . 0.2 µg/**l** per day."

p. 76 *Second column, line 9:* **change** "2.2 mg/l" to "2.2 µg/**l**".

4.15 Malathion

p. 86 *Residue and analytical aspects, line 3:* **change** "No recommendation was made for wheat grain …" to "No recommendation was made for wheat **bran** …"

4.17 Parathion

p. 88 *Metabolism, first para., lines 1-3:* **delete** "After oral administration of paraoxon … were identified in urine."

Third para., line 4: **change** "(< 0.01 mg/kg)" to "(< 0.01**% of the dose**)"

p. 93 *Second main para., line 4:* **delete** "[1.4. l/ha]" and "[1.3 l/ha]"

4.18 Parathion-methyl

p. 97 *Residue and analytical aspects, line 2:* **change** "listed parathion" to "listed **parathion-methyl**"

Plants, penultimate line: **change** "P-O" to "P = O"

p. 101 *Sugar beet, penultimate line*: **change** "for parathion-methyl in potatoes" to "for parathion-methyl in **sugar beet**"

4.19 Pyrethrins

p. 107 *Residue and analytical aspects, line 5*: **change** "in 1972" to "in **1974**"

p. 109 *Line 8*: **change** "In egg white to "In **hens**"

Plants, line 9: **change** "low lipophilicity" to "**high** lipophilicity"

Line 13: **change** "14.7 mg/kg" to "**14** mg/kg"

Last two lines: **change** "*trans*-chrysanthemic acid-hydroxide-cycle" to "**cyclopropyl-substituted hydroxychrysanthemic** acid"

Degradationn in soil, line 6: **change** "a half-life of about 3.2 days" to " a half-life of about **2.2** days"

Third para., last line: **change** "< 15 cm" to "> 15 cm"

p. 110 *Line 8*: **change** "10^6 mg/cm^2 per h" to "10^{-6} **µ**g/cm^2 per h"

Fate in water and sediment systems, para. 3, line 4: change "Cyclopropane acid" to "Cyclopropane **diacid**"

p. 113 *Fifth para., lines 5-6:* **delete** "bean hay and"

p. 114 *Oranges, line 4*: **change** "factor of 8.55" to "factor of **7.51**"

*Lines 6-7***: change** "0.342 for dry citrus fruit" to "**0.300** for dry citrus **pulp**"

Tomatoes. line 4: **change** 20.2 to "**29.0**"

Lactating dairy cows, line 5: **delete** "(at 0.43 mg/kg)"

p. 115 *Hens, line 1:* **change** "for 35–37 days" to "for **25–27** days"

2.21 Thiabendazole

p. 118 *Apple and pear, third para., lines 4-5:* **change** "the Meeting agreed to withdraw the recommendation of" to "the Meeting **confirmed the 1997 decision to recommend withdrawal of the CXLs of** "

Third para., line 5: **delete** "for these uses"

ANNEX 1

The relevant sections are shown below with corrections in bold. A number of minor errors in commodity names are not listed. These have been corrected in Annex 1 to the 2000 Evaluations.

Pesticide (Codex reference no.)	ADI, (mg/kg bw)	Commodity		Recommended MRL, mg/kg		STMR, (mg/kg)	HR (mg/kg)
		CCN	Name	New	Previous		
Abamectin (177)	0.002	**MO 1280**	Cattle kidney	0.1	0.1		
Chlormequat (015)	0.05	**AS 0650**	Rye straw and fodder, dry	W	20		
		AS 0081	Straw and fodder (dry) of cereal grains	**30**[1]	–	**4.2**[1]	
[1] Expressed on dry weight basis							
Chlorpyrifos (07)	0.01	AL 1020	**Alfalfa fodder**	5 **(dry wt)**	–	0.81 **(dry wt)**	
		AL 1021	Alfalfa forage (green)	20 **(dry wt)**	–	1.2 **(dry wt)**	
			Citrus oil		–	**2.6**	**13**
		AF 0645	Maize forage	20 **(dry wt)**	–	8.2 **(dry wt)**	
		AF 0645	Maize fodder	10 **(dry wt)**	–	2.8 **(dry wt)**	
		AL 0528	Pea vines **(**green**)**	1 **(dry wt)**		0.10 **(dry wt)**	
		AS 0651	Sorghum straw and fodder, dry	2 **(dry wt)**	–	0.29 **(dry wt)**	
		AV 0596	Sugar beet **leaves or tops**	40 **(dry wt)**	–	3.0 **(dry wt)**	
		AS 0654	Wheat straw and fodder, dry	5 **(dry wt)**	–	0.54 **(dry wt)**	
Parathion (58)	0.004	GC **0651**	Sorghum	5	5	1.06	4.2
Pyrethrins (063)	0.04	DM **0001**	Citrus molasses			0.0276	**0.0276**
		AB 0001	Citrus **pulp**, dry			**0.300**	**0.300**
		JF 0448	Tomato juice			0.018	
Thiabendazole (065)	0.1	**MM** 0812	Cattle meat	0.1	0.05	0.02	0.02
		JF 0004	Orange juice			0.11	

ANNEX 2

p. 150 **Change** "Thianedazole" to "**Thiabendazole**" and "Thiphanate-methyl" to "**Thiophanate-methyl**"

ANNEX 6

p. 202 Last reference, **change** to number "**87**"

2000 Evaluations: Part II— Toxicological (WHO/PCS/01.3)

Page 175 Second column in table, line 15: Replace "2.2 mg/l" by 2.2 **µ**g/l".