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[1] T = toxicology; R = residue and analytical aspects
* evaluation in the periodic review programme
** new compound

1994 JOINT MEETING OF THE FAO PANEL OF EXPERTS ON PESTICIDE RESIDUES IN FOOD AND THE ENVIRONMENT AND THE WHO EXPERT GROUP ON PESTICIDE RESIDUES

Rome, 19-28 September 1994

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ABBREVIATIONS WHICH MAY BE USED

(Well-known abbreviations in common scientific use are not included)

Ache	acetylcholinesterase
ADI	acceptable daily intake
AFI(D)	alkali flame-ionization (detector)
ai	active ingredient
ALAT	alanine aminotransferase approx. approximate
ASAT	aspartate aminotransferase
BBA	Biologische Bundesanstalt für Land- und Forstwirtschaft
bw (not b.w.)	body weight
c	centi- (x 10^{-2})
C.A.	Chemical Abstracts
CCPR	Codex Committee on Pesticide Residues
ChE	cholinesterase
CNS	central nervous system
cv	coefficient of variation
CXL	Codex Maximum Residue Limit (Codex MRL). See MRL.
DFG	Deutsche Forschungsgemeinschaft
DL	racemic (optical configuration, a mixture of dextro- and laevo-)
DP	dustable powder
DS	powder for dry seed treatment
EBDC	ethylenebis(dithiocarbamate)
EC	(1) emulsifiable concentrate (2) electron-capture [chromatographic detector]
ECD	electron-capture detector
EMDI	estimated maximum daily intake
EPA	Environmental Protection Agency
ERL	extraneous residue limit
ETU	ethylenethiourea
F_1	filial generation, first
F_2	filial generation, second
f.p.	freezing point
FAO	Food and Agriculture Organization of the United Nations
FDA	Food and Drug Administration
FID	flame-ionization detector
FPD	flame-photometric detector
g (not gm)	gram
ìg	microgram
GAP	good agricultural practice(s)
GC-MS	gas chromatography - mass spectrometry

G.I.	gastrointestinal
GL	guideline level
GLC	gas-liquid chromatography
GLP	Good Laboratory Practice
GPC	gel-permeation chromatography
GSH	glutathione
h (not hr)	hour(s)
ha	hectare
Hb	haemoglobin
hl	hectolitre
HPLC	high-performance liquid chromatography
HPLC-MS	high-performance liquid chromatography - mass spectrometry
IBT	Industrial Bio-Test Laboratories
i.d.	internal diameter
i.m.	intramuscular
i.p.	intraperitoneal
IPCS	International Programme on Chemical Safety
IR	infrared
IRDC	International Research and Development Corporation (Mattawan, Michigan, USA)
i.v.	intravenous
JMPR	Joint FAO/WHO Meeting on Pesticide Residues (Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and a WHO Expert Group on Pesticide Residues)
LC	liquid chromatography
LC_{50}	lethal concentration, 50%
LC-MS	liquid chromatography - mass spectrometry
LD_{50}	lethal dose, median
LOAEL	lowest observed adverse effect level
LOD	limit of determination (see also "*" at the end of the Table)
LSC	liquid scintillation counting or counter
MFO	mixed function oxidase
µm	micrometre (micron)
min (not min.)	minute(s)
MLD	minimum lethal dose
M	molar
mo	month(s)

(not mth.)	
MRL	Maximum Residue Limit. MRLs include draft MRLs and Codex MRLs (CXLs). The MRLs recommended by the JMPR on the basis of its estimates of maximum residue levels enter the Codex procedure as draft MRLs. They become Codex MRLs when they have passed through the procedure and have been adopted by the Codex Alimentarius Commission.
MS	mass spectrometry
MTD	maximum tolerated dose
n	normal (defining isomeric configuration)
NCI	National Cancer Institute (United States)
NMR	nuclear magnetic resonance
NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect level
NP(D)	nitrogen-phosphorus (detector)
NTE	neuropathy target esterase
o	*ortho* (indicating position in a chemical name)
OP	organophosphorus pesticide
p	*para* (indicating position in a chemical name)
PHI	pre-harvest interval
ppm	parts per million. (Used only with reference to the concentration of a pesticide in an experimental diet. In all other contexts the terms mg/kg or mg/l are used).
PT	prothrombin time
PTT	partial thromboplastin time
PTU	propylenethiourea
RBC	red blood cell
s.c.	subcutaneous
SC	suspension concentrate (= flowable concentrate)
SD	standard deviation
SE	standard error
SG	water-soluble granule
SL	soluble concentrate
SP	water-soluble powder
sp./spp.	species (only after a generic name)
sp gr (not sp. gr.)	specific gravity
t	tonne (metric ton)
T_3	tri-iodothyronine
T_4	thyroxine
TADI	Temporary Acceptable Daily Intake
tert	tertiary (in a chemical name)
TLC	thin-layer chromatography
TMDI	theoretical maximum daily intake
TMRL	Temporary Maximum Residue Limit

TPTA	triphenyltin acetate
TPTH	triphenyltin hydroxide
TSH	thyroid-stimulating hormone (thyrotropin)
UDMH	1,1-dimethylhydrazine (unsymmetrical dimethylhydrazine)
USEPA	United States Environmental Protection Agency
USFDA	United States Food and Drug Administration
UV	ultraviolet
v/v	volume ratio (volume per volume)
WG	water-dispersible granule
WHO	World Health Organization
WP	wettable powder
wt/vol	weight per volume
w/w	weight ratio (weight per weight)
<	less than
≤	less than or equal to
>	greater than
≥	greater than or equal to
*	(following residue levels, e.g. 0.01* mg/kg): level at or about the limit of determination

PESTICIDE RESIDUES IN FOOD

REPORT OF THE 1994 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 a WHO Expert Group on Pesticide Residues (JMPR) was held in Rome, Italy, from 19 to 28 September 1994. The FAO Panel of Experts had met in preparatory sessions on 14-17 September.

The Meeting was opened by Dr. F. Riveros, Officer in Charge of the Plant Production and Protection Division, FAO, on behalf of the Directors-General of FAO and WHO. In his opening remarks, Dr. Riveros noted the increased work-load of the Joint Meeting and the need for clear and comprehensive explanations of the evaluations. He emphasized the value of the work of the JMPR for governments and international organizations, and its increased importance in view of its relevance to the GATT agreement. He reminded the participants that their participation was in the capacity of independent experts in their repective fields, not as representatives of their governments.

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 man arising from the occurrence of residues of pesticides in foods. The reports of previous Joint Meetings (see References, Section 7) contain information on acceptable daily intakes (ADIs), maximum residue limits (MRLs) and general principles for the evaluation of the various pesticides. The supporting documents (Residue and Toxicological Evaluations) contain detailed monographs on these pesticides and include comments on analytical methods. The present Meeting was convened to consider a further number of pesticides together with items of a general or a specific nature. These include items for clarification of recommendations made at previous Meetings or for reconsideration of previous evaluations in the light of findings of subsequent research or other developments.

During the Meeting the FAO Panel of Experts was responsible for reviewing pesticide use patterns (good agricultural practices), data on the chemistry and composition of pesticides and methods of analysis for pesticide residues, and for estimating the maximum residue levels that might occur as a result of the use of the pesticides according to good agricultural practices. The WHO Expert Group was responsible for reviewing toxicological and related data and for estimating, where possible, ADIs for humans of the pesticides. The recommendations of the Joint Meeting, including further research and information, are proposed for use by national governments, international organizations and other interested parties.

2. GENERAL CONSIDERATIONS

2.1 AMENDMENTS TO THE AGENDA

Benomyl (069), carbendazim (072), dimethoate (027), diquat (031)*, ethephon (106)*, ethion (034)*, iprodione (111)*, profenofos (171), propiconazole (160) and thiophanate-methyl (077) were originally scheduled for review by the FAO Panel of the 1993 JMPR, but these reviews could not be completed in the time available to the Meeting. A special session of the FAO Panel was convened in Rijswijk, The Netherlands, immediately before the 1994 Session of the Codex Committee on Pesticide Residues (CCPR, April 1994) to complete the review of these compounds. The completed evaluations were presented at the present Meeting for the consideration of the WHO Group of Experts.

Fenpropimorph was removed from the schedule of the FAO Panel as the data were submitted too late for review. Metiram was removed as the review could not be completed in time for the Meeting.

The toxicological reviews of carbofuran (096), parathion (058) and parathion-methyl (059) were deferred owing to the late submission of data.

* Periodic review compounds

2.2 ASSESSMENT OF ACUTE DIETARY RISK

Over the years, the CCPR has frequently expressed reservations with regard to establishing MRLs for acutely toxic pesticides. The CCPR considered that for these pesticides the traditional ADI was probably not an appropriate toxicological benchmark to be used in assessing risks reflecting short-term exposure to residues.

The 1993 Joint Meeting (section 2.4) considered this issue briefly, recommending that the CCPR should request advice from the Joint Meeting in specific cases, explaining more clearly the nature of their concern. It was also suggested that the International Programme on Chemical Safety (IPCS) should consider these questions when revising the *Guidelines for Predicting Dietary Intake of Pesticide Residues*.

Pending further requests from the CCPR, the Meeting gave preliminary consideration to the implications of short-term dietary exposure to acutely toxic pesticides, such as aldicarb and monocrotophos. As a result of these considerations, the Meeting recognized that a new approach should be developed.

In principle, the acceptability of human exposure to a pesticide residue in food is most appropriately determined in animal studies that exactly mimic the human exposure pattern of concern. Current pesticide databases, however, rarely contain information that would allow the identification of acceptable levels of human exposure in all situations. While general concepts may be applied, each case must be considered individually. For example, it is generally accepted

that for certain effects, such as liver and kidney toxicity, carcinogenicity and reproductive toxicity, an acceptable level of exposure can be derived using the traditional ADI method, which assumes daily exposure throughout life. Occasional exposure on individual days to levels in excess of the ADI are not a cause for concern. For other toxic effects, such as developmental effects and biochemical and clinical manifestations of cholinesterase inhibition, the traditional ADI method may not be appropriate, as these effects may be manifested after only one or very few exposures.

It is plausible to expect that a single exposure at a particular dose level would be tolerated better than repeated doses at the same level. An appropriate toxicological benchmark in addition to or instead of the traditional ADI may be necessary in these cases. Toxicological databases, however, rarely contain the information necessary to derive an "ADI" for single exposures. For the purposes of this discussion, such short-term "ADIs" will be called acute reference doses (acute RFD). The acute RFD would be derived using the same basic principles and method as are used to derive the traditional ADI. That is, a NOAEL would be identified and safety factors selected by applying the same scientific criteria as are employed in deriving the ADI.

In the case of developmental toxicants, timing of exposure is the critical factor. In the case of cholinesterase inhibitors, rate of reversibility of inhibition is the critical factor. For carbamates, which cause rapidly reversible inhibition of cholinesterase, an acute RFD based on a single (bolus)-dose NOAEL would be the appropriate benchmark for comparison in assessing "single serving" dietary exposure and risk. In addition, for the carbamates, the NOAELs and ADI/acute RFD for both acute and chronic dietary exposure and risk assessment can be the same.

For organophosphorus pesticides, which cause less rapidly reversible or irreversible cholinesterase inhibition, an acute RFD based on NOAELs in studies of two or three up to seven days' duration would be a more appropriate benchmark for comparison. In the case of the OPs, it could be argued that different NOAELs and ADIs or acute RFDs could or should be used for acute and chronic assessment.

In order to ensure follow-up of these considerations, the Meeting reiterated the recommendations of the 1993 Meeting that the CCPR should seek advice from the Joint Meeting in specific cases, explaining accurately and in detail the nature of the concern. Suggestions of pesticide-commodity combinations for which concern about the theoretical dietary intake had been expressed would be particularly useful, as would national calculations of dietary intake. The Meeting further recommended that methods for the assessment of acute dietary risk should be included in the revision of the *Guidelines for Predicting Dietary Intake of Pesticide Residues*, to be undertaken by WHO/IPCS in 1995.

Further consideration will be given to aldicarb and monocrotophos at a future Meeting. The Meeting recommended that the CCPR should propose other acutely toxic pesticides of concern (e.g. organophosphorus and carbamate pesticides) in order that a future Joint Meeting can further develop these general concepts by means of specific examples.

2.3 TOXICOLOGICAL END-POINTS FOR PESTICIDES PRESENT IN THE ENVIRONMENT AS UNAVOIDABLE CONTAMINANTS

Several pesticides that have been allocated ADIs by the JMPR are no longer used in agricultural practice but may be present in food commodities as contaminants because of their persistence in the environment. *Extraneous Residue Limits* (ERLs) have been assigned to commodities containing these pesticides by the Codex Committee on Pesticide Residues on the basis of food monitoring data, **not** Good Agricultural Practice.

ADIs were established in the past for these pesticides, most of which bioaccumulate in human tissues, on the basis of toxicological data, but studies with adequate power to detect toxic effects have not been performed on most of them. It is unlikely that further studies will be carried out, because these pesticides are no longer used in agricultural practice and do not have industrial sponsors. For these reasons, the Joint Meeting did not consider it appropriate to maintain traditional ADIs for them. At the same time, it is useful to maintain a numerical toxicological end-point to serve as a guideline with which potential dietary intakes can be compared.

For these reasons and to parallel the action that has been taken on residues, the Meeting converted the ADI for each of these pesticides to a provisional tolerable daily intake (PTDI)[i]. The term "tolerable" rather than "acceptable" was used to signify permissibility rather than acceptability of the intake of environmental contaminants unavoidably associated with the consumption of otherwise wholesome food. Use of the term "provisional" expresses the fact that reliable data on the consequences of human exposure to these pesticides are lacking and that the submission from any source of relevant safety data is encouraged.

In line with the foregoing, PTDIs were established as follows:

Pesticide	PTDI (mg/kg bw)
aldrin/dieldrin	0.0001
chlordane	0.0005
DDT	0.02
endrin	0.0002
heptachlor	0.0001

The Meeting recommended that these PTDIs be reviewed whenever possible modifications of ERLs are considered.

2.4 DATA REQUIRED FOR ESTIMATING MAXIMUM RESIDUE LEVELS

At the 26th (1994) Session of the CCPR, a question was raised on the need to develop (minimum) database requirements as a guidance to the JMPR in recommending MRLs (ALINORM 95/24, paragraph 60).

The question is a simple one but different situations require different approaches. While no minimum database requirements (core database) have yet been developed for use by the JMPR, the Meeting decided it would be worth while to describe typical issues and considerations that the JMPR currently takes into account in judging the adequacy of available information.

In the first case the question is asked of a national regulatory agency by a pesticide registrant. A specific answer is required because the registrant needs to plan and conduct the required residue trials. This is a correct position for a national regulatory agency.

When the question is asked at the international level, at the CCPR, the perspective is different. The JMPR is not a regulatory body. Recommendations for MRLs are based on uses which already exist. The Joint Meeting carries out a scientific evaluation and takes into account all available information. Residue data from supervised trials are very important, but other information must not be ignored. Better evaluations result from an understanding of the processes of residue behaviour rather than from only an empirical treatment of data.

Metabolism studies provide fundamental information on the fate of the compound and its metabolites and suggest likely residue behaviour. The results of metabolism studies suggest target tissues in animals; other important guides to the site and level of residues are whether the compound is absorbed by the leaves or roots of crops, whether it is mobile in the plant, and its persistence and mobility in soil.

The adequacy of the database for each case is discussed by the JMPR; in some cases evaluation cannot proceed because the number of trials or other supporting information is too limited. Decisions are made case by case and take into account the nature of the pesticide, the crop (or animal) and its importance, the formulation, application method and use pattern, residue level, residue behaviour on related crops (or animals), and previous experience. When residue behaviour in trials appears to be at variance with expected behaviour further explanations and information are sought.

Data on comparable crops are often used in mutual support to increase the size of the database.

The JMPR summarizes information on GAP and data on supervised residue trials in reasonable detail in the monograph and explains the reasoning behind the evaluation.

An awareness of the expected variability of residues is necessary. If the data truly reflect the range of conditions, application methods, seasons and cultural practices likely to be encountered commercially, then considerable variation in the resulting residue levels is expected. Where copious data are available, the spread and variability of the residues are a caution against misleading interpretations of small differences in estimates of the maximum level. Where only limited data are available, the interpretation of fine differences is not valid. It is not a criticism to

say that the data are widely spread and variable. If results have been obtained at a number of places over some years they are likely to be a better approximation to commercial practice and will be widely spread.

Frequently the situation is complex, even when copious data and information are available. There are alternative interpretations, and judgement is required to arrive at an estimate which is realistic, practical and consistent.

Although supervised residue trials are conducted according to GAP prevailing at the time, GAP is often subsequently modified. Judgement is then required: are the trial conditions still close enough to GAP to be relevant? GAP is frequently modified by changing the rate of application, type of formulation, method of application, number of applications, and PHI. The nominal rate of application in a trial would normally be considered still consistent with GAP when it exceeds the GAP rate by up to 20-30%, which includes the likely variation in commercial practice. When little or no residue is present, data from higher application rates would be included.

In many situations different formulations would cause no more variation than other factors, and data derived with different formulations would be considered comparable. Controlled-release formulations would be expected to lead to more persistent residues and would not be comparable to others.

The method of application can be quite influential on residue levels. For example, directed application is not comparable to cover spray; aerial application is not normally comparable to ground application. For a non-persistent pesticide the number of applications is unlikely to influence residue levels: three, four or five applications could be considered equivalent from a residue point of view. For a persistent pesticide the number of applications would be expected to influence residue levels. The nature of the crop should also be considered. For example, summer squash may be harvested only a few days after flowering; residues of a non-systemic pesticide applied before flowering would be expected to be low, and the number of applications should have little influence on the residue level.

The PHI usually, but not always, influences residue levels. In most cases the PHI in supervised trials should agree with that specified by GAP. When residue levels are changing rapidly it is not possible to extrapolate from one PHI to another; when they are changing slowly extrapolation is possible. For a typical horticultural or agricultural crop, for example, data from a PHI range of 12-15 days could be considered equivalent. Trials that do not conform to GAP can be used to provide information on persistence. For example, there are cases where residues are not significantly influenced by the pre-harvest interval, so that results obtained at intervals other than the specified PHI can be used.

Some pesticide uses, such as seed treatments and pre-emergence herbicide treatments, usually lead to detectable residues in the final harvested crop; but when many results are provided residues may be detected in occasional samples. While residues resulting from use according to GAP are most likely to be undetectable, the occasional detectable residues should not be ignored when a maximum residue level is estimated. Phorate on potatoes and residues arising from the pre-planting application of glyphosate are two examples.

The JMPR has recognized the need to explain more fully the basis for its

recommendations. The increased volume of the evaluations is largely due to more detailed explanations.

The Meeting noted that governments and industry had been requested at the 1994 Session of the CCPR to supply information on their minimum data requirements (ALINORM 95/24, para 66). The Meeting welcomed this development; in future it should help to determine the quantity of data available for evaluation. Where available, an explanation of the scientific basis for minimum data requirements would also be of value.

The Meeting noted that international organizations are co-operating with governments and industry to develop internationally agreed registration requirements. The Meeting recommended that the attention of these organizations should be drawn to the need for internationally recognized minimum data requirements for establishing maximum residue limits (minimum data requirements for supervised residue trials). It further recommended that any such minimal requirements that might be developed be brought to the attention of a future JMPR.

2.5 THE SUBMISSION OF DATA ON METABOLISM

Data on metabolism are used in evaluating both the toxicological and residue profiles of pesticides. Such data can be used to compare metabolism in experimental animals with that in food-producing animals, to compare biotransformation pathways in the animal species used for toxicity testing and the plant species on which the pesticide is used, for the extrapolation of results in animals to humans, for defining residues, and in animal transfer studies. With these points in mind, the Joint Meeting stressed the need to provide all data on animal metabolism to both the WHO Expert Group and the FAO Panel of Experts. The required data on plant metabolism should be submitted to the FAO Panel, while the WHO Group wishes to receive only schemes of plant metabolism.

2.6 EXPERIENCE IN THE IMPLEMENTATION OF THE CCPR PERIODIC REVIEW PROGRAMME: COMMENTS AND RECOMMENDATIONS

(a) FAO

The programme of periodic review proposed by the Ad hoc Working Group on Priorities of the Codex Committee on Pesticide Residues (CCPR) was first implemented at the 1992 Joint Meeting on Pesticide Residues (JMPR). The report of the 1992 Joint Meeting provided general guidance on the data requirements for compounds in the periodic review programme and identified a list of critical supporting studies needed by the FAO Panel. Experience in preparing the FAO Panel papers for the 1993 and 1994 Joint Meetings has emphasized the importance of having product monographs prepared by the data submitter, with a detailed overview of the submitted data. A draft outline of the format for data submission and product monographs for the FAO Panel was prepared in advance of the 1993 Joint Meeting and circulated for comment.

One objective of the periodic review is to make the best use of the existing database, regardless of the age of the studies. As a result, countries and industry are requested to provide all relevant information, irrespective of whether it has been previously supplied. It has come to light, however, that some periodic review submissions contain data that are of limited use for estimating maximum residue levels. For example:

- Residue data are frequently provided that do not relate to current good agricultural practice (GAP) and are not accompanied by adequate details of the conduct of the field trial or the handling of the samples before analysis.

- Residue data have been developed with non-selective analytical methods (e.g. colorimetric analysis or bioassay).

- Critical supporting studies are frequently not included in the package provided.

In reviewing the submissions provided for periodic review over the last two years, such residue data have been found to be submitted routinely. The usefulness of such information, even as supplementary data, can be judged only on a case-by-case basis when considered in the context of the available database.

It was intended that in preparing product monographs the data submitters would consider the relevance of residue data in the light of current use practices, residue definitions, analytical methods etc., and that **only data pertinent to commodities with current or proposed maximum residue limit(s)** would be provided for the consideration of the Panel. The purpose of the monograph is to facilitate access to the data, not to replace the review of the detailed study reports by the Panel member. The monograph should include an explanation of why specific critical supporting studies (e.g. processing information) were not provided.

The requested index or directory provides an opportunity to conduct a cursory overview of the data package and identify any outstanding gaps. It is not possible to determine the acceptability of residue data vis-à-vis the use pattern, the availability of the critical supporting studies, the monograph etc.; that remains the responsibility of the data submitter.

It was recommended by the FAO Panel that:

- **compounds be scheduled for evaluation under the periodic review programme only if accompanied by a product monograph.**

- a complete set of critical supporting studies be provided. In the absence of this information a detailed scientific explanation of why certain studies were not considered necessary should be included in the monograph. When studies are lacking or no adequate rationale is provided, maximum residue levels will not be estimated by the FAO Panel.

(b) WHO

The Joint Meeting on Pesticide Residues (JMPR) has been considering compounds identified for periodic review by the Codex Committee on Pesticide Residues (CCPR) for three years. The 1994 Meeting discussed the purpose of the CCPR periodic review programme in the context of toxicological data requirements. It recognized that one objective of the programme is to ensure that the databases supporting the chemicals are being maintained and, as necessary, updated. While it is recognized that toxicological data should be generated in studies conducted in accordance with testing guidelines contemporary with the time of review, older data must also be considered on their scientific merits. Thus, it can be ensured that experiments have adequate power to detect toxic effects of the chemicals.

Studies relevant to the toxicological evaluation of many of the pesticides that are reviewed by the Joint Meeting are published in the open literature. Scientists who review the data and prepare working papers for WHO perform literature searches; however, this does not provide a guarantee that all of the relevant studies have been located. Companies that produce pesticides monitor the open literature for studies relevant to the safety assessment of their products as a component of their product stewardship programmes. This places them in a good position to provide copies of relevant published studies to the Joint Meeting at the time that data are provided for review. The Joint Meeting requests that reprints of studies considered to be relevant by the manufacturer be included with data submissions. All relevant information, both published and unpublished, positive and negative, should be submitted to the Joint Meeting for consideration. When there is doubt about the relevance of studies, they should be submitted. All reports should be sufficiently detailed to allow a complete evaluation of the experimental results.

Chemicals undergoing periodic review are considered on exactly the same basis as chemicals new to the Joint Meeting process. In either case, an ADI will be allocated only when the Meeting concludes that it is fully supported by a sufficiently complete database of acceptable scientific quality.

2.7 REVISED ORDER OF TOPICS IN RESIDUE EVALUATION MONOGRAPHS - THE FAO PANEL MANUAL

The format and language of JMPR evaluations and reports have evolved over the lifetime of the CCPR-JMPR system. One aim of this evolution has been to make it easier for readers to find the information they are seeking expressed in a clear and consistent way.

Beginning in 1994 the order of the subjects in residue evaluations has been rearranged so that the logical flow is improved[ii]. For example, metabolism is reported before methods of analysis, because the nature and abundance of metabolites will influence the requirements for residue analysis. Analytical methods, frozen storage stability of analytical samples and use pattern should be reviewed before supervised residue trials.

Most of the main headings have been retained, but the section *FATE OF RESIDUES* has been divided into two sections, *METABOLISM AND ENVIRONMENTAL FATE* and *FATE OF RESIDUES IN STORAGE AND PROCESSING*. The section on fate of residues in storage and processing follows that on supervised trials.

Stability of pesticides in stored analytical samples is now a subheading of *METHODS OF RESIDUE ANALYSIS*. The stability of frozen laboratory samples is more closely related to the validity of analytical data than to the fate of residues in storage and processing.

Animal transfer studies are included in the supervised trials section, not in the animal metabolism section.

Figure 1 shows the headings and subheadings in a residue evaluation.

Since 1991, a JMPR Manual for FAO Panel Members (JMPR Report 1992, section 2.9) has been developed and repeatedly revised in the light of experience. The manual provides guidance for reviewers assembling information so that they can present it in a consistent format.

It describes the word processor settings to use and gives examples of table formats so that draft documents can be prepared with presentable tables and text, assisting assembly into the final publication. The manual will also be of interest to national governments and industry preparing data submissions to the JMPR.

A copy of the manual is included as Annex IV to the report.

Restructuring of the residue monographs has arisen during the development of the manual and the guidelines on the preparation of data submissions for the consideration of the FAO Panel of the JMPR. The latter guidelines, directed to data submitters including manufacturers and member governments, was first circulated in advance of the 1993 Joint Meeting with the objective of improving the quality and consistency of the data submissions.

The FAO Panel Manual has been particularly useful for new Panel members and facilitates the preparation of draft documents in the correct format.

2.8 DIETARY INTAKE OF PESTICIDE RESIDUES

Theoretical Maximum Daily Intakes (TMDIs) have been calculated for the Joint Meeting by WHO by the methods described in *Guidelines for Predicting Dietary Intake of Pesticide Residues*.

The Meeting noted that, in calculating TMDIs for the CCPR, MRLs and CXLs that have been proposed for revision or withdrawal are retained. The Meeting requested that all MRL proposals of the Meeting as well as those of previous JMPRs be included in calculating TMDIs for the JMPR. When two proposals have been made for a commodity, the most recent JMPR recommendation should be used.

The results are summarized in Annex III. Processing factors must be reviewed before Estimated Maximum Daily Intakes (EMDIs) can be calculated for a number of pesticides for which the TMDI exceeds the ADI.

COMPOUND (Codex number)

EXPLANATION
[The EXPLANATION section is not included for new compounds.]

IDENTITY
[The IDENTITY section is included only for new compounds and periodic review compounds.]

METABOLISM AND ENVIRONMENTAL FATE
Animal metabolism
Plant metabolism

Environmental fate in soil
Environmental fate in water/sediment systems

METHODS OF RESIDUE ANALYSIS
Analytical methods
Stability of pesticide residues in stored analytical samples
Residue definition

USE PATTERN

RESIDUES RESULTING FROM SUPERVISED TRIALS

FATE OF RESIDUES IN STORAGE AND PROCESSING
In storage
In processing
Residues in the edible portion of food commodities

RESIDUES IN FOOD IN COMMERCE OR AT CONSUMPTION

NATIONAL MAXIMUM RESIDUE LIMITS

APPRAISAL

RECOMMENDATIONS
Definition of the residue:

FURTHER WORK OR INFORMATION
Required (by [year])
Desirable

REFERENCES

Figure 1. Headings and subheadings in a residue evaluation monograph

3. SPECIFIC PROBLEMS

3.1 MRLs FOR FAT-SOLUBLE PESTICIDES IN ANIMAL PRODUCTS

In the limited time available for such a task, the Meeting considered a paper prepared for the 26th Session of the CCPR (ALINORM 95/24, Appendix II) entitled "Revised Proposed Codex Approach to the Expression and Application of MRLs for Fat-soluble Pesticides in Animal Products". This appeared to have been devised largely in order to be able to extend MRLs based on reviewed data to other animal species, especially low-fat ones, or tissue parts. The Meeting agreed that while the CCPR may seek to make such use as it wishes of the recommendations formulated by the JMPR such empirical calculation did not fall within the scientific ambit of the FAO Panel of the JMPR, whose recommendations are based on the actual evidence provided and dealt with on a case-by-case basis. The following points relate to MRLs on meat (fat); MRLs for milk are already adequately dealt with within the CCPR.

Items on this subject and associated matters have already been dealt with at several previous Meetings; details are included in the Reports of the JMPR for 1970, 1971, 1972 and 1981 in particular. The MRLs that have been set on meat (fat) are normally based on residue data obtained from the analysis of carcase fat as a whole commodity; they were not derived from extracted fats and therefore do not necessarily apply to interstitial fat in lean meats. Data on residues of fat-soluble pesticides in lean cuts of meat or in animals of low fat content (e.g. rabbits) are rarely available for review. Were such data to be presented, appropriate recommendations might be possible. Similarly, it is not reasonable to convert MRLs set for meat (fat) of certain animal species of recognized fatty composition to other, untested, animals of low fat content potential. Hence, the MRLs recommended apply only to the carcase fat of the animal concerned or those of comparable fat content, not to meat cuts or meat products with lower fat contents.

In order to elaborate on these matters, the Meeting referred to the items on the subject as discussed at the 23rd Session of the CCPR (ALINORM 91/24A, para 299-321 and Appendix IV, para 7). At that time, of the 171 pesticides that had been considered by the CCPR, fewer than one-half (83) had had MRLs recommended for animal products. Of these 83, over one-half (45) referred to individual animal species (cattle, goats, sheep, etc.) and any amendment of these, or extension to other species, whether for fat, muscle tissue or offal, would require the provision of appropriate data from feeding studies or residue trials before any recommendation could be made; new MRLs could not be derived merely by calculations based on irrelevant data.

Of the remaining 38 compounds, 22 had MRLs on animal products set "at or about the limit of determination" (LOD) and thus must be excluded from such arithmetical MRL assessment. Six of the remaining compounds were organochlorine pesticides with ERLs based on old or monitoring data. Revision of these limits will be required from time to time and full data from monitoring studies on all types of relevant animal products would be required to suggest new limits; calculations for low-fat tissues would not be acceptable. For another six of these pesticides, the MRLs cover veterinary uses as well as possible agricultural inputs and these were specific to the animal species concerned. Any extension to other species would require the provision of the relevant data and extrapolation by calculation would be unacceptable.

For two compounds the MRLs refer to "meat" with no reference to fat or tissue, and

hence these can be taken to refer to any portion of meat from the respective animals; extension to other animals would require new data.

This leaves only two pesticides, propargite and fenvalerate, of which the former presents a different problem in that the distribution of the residue between fatty and non-fatty tissues is approximately equal. For both compounds, data on residues in the actual species and sample sites would be required in order that MRL proposals could be made or extended.

To refine the problem, of the 27 pesticides listed in the 2nd edition of Volume 2 of the Codex Alimentarius as being fat-soluble and also having CXLs for various meats, six have only ERLs (aldrin/dieldrin, chlordane, DDT, endrin, fenitrothion (LOD) and heptachlor). A further 13 have CXLs that cover veterinary uses on specified animals (carbophenothion, chlorfenvinphos, chlorpyrifos, diazinon, ethion (LOD), fenthion, lindane, phosmet, cypermethrin (LOD), permethrin, deltamethrin (LOD), phoxim and methoprene). Five others, fensulfothion, methidathion, pirimiphos-methyl, etrimfos and isofenphos, have CXLs at the LOD. Thus, only two such compounds, fenvalerate (1 mg/kg) and propargite (0.1 mg/kg) are feasible candidates for the proposed treatment; as shown above, the distribution pattern of propargite does not fit the requirements.

Aside from the above technical considerations, but from a regulatory enforcement perspective, the Meeting was not aware of substantial problems that could not be handled by the current MRL procedures employed by the JMPR. Also, current CCPR procedures allow the establishment of MRLs in animal tissues on a whole-product basis for fat-soluble pesticides in animals of low intrinsic fat content if the data are available. Without such data, of course, the JMPR cannot make suitable recommendations. It thus appears that the primary problem, if there is one, is not the lack of a procedure but the lack of adequate data.

When the JMPR estimates a maximum residue level on the basis of the fat of meat or on a whole-product basis (i.e. fat plus muscle), it is the prerogative of the CCPR to apply such factors as it chooses. However, the advantages to be achieved by the present proposals were not obvious to the Meeting.

In short, the Meeting was not able to conclude that any potential enforcement advantages to be gained from the proposal to change the current procedure would balance the increased complexity and potentially increased resources needed for its implementation and tracking within the CCPR. The Meeting, therefore, could not support the proposal.

4. EVALUATION OF DATA FOR ACCEPTABLE DAILY INTAKE FOR HUMANS AND MAXIMUM RESIDUE LIMITS

4.1 ABAMECTIN (177)

TOXICOLOGY

Abamectin comprises at least 80% avermectin B_{1a} and not more than 20% avermectin B_{1b}. It was first evaluated by the 1992 Joint Meeting, which allocated an ADI of 0-0.0001 mg/kg bw on the basis of the lowest NOAEL of 0.05 mg/kg bw per day for maternal toxicity observed in a teratogenicity study in mice and a two-generation reproductive toxicity study in rats. A safety factor of 500 was applied because of concern about the teratogenicity of the Ä-8,9 isomer in CF-1 mice. The isomer is a photolytic degradation product which forms a variable part of the residue on crops. Abamectin was re-evaluated by the 1994 Joint Meeting in order to consider new information.

In a study of photo-oxidative stability, the half-life of the Ä-8,9 isomer was 4.5 h and that of avermectin B_{1a} was 6.5 h.

Because of the close structural relationship between abamectin and ivermectin, a widely used human therapeutic agent against human onchocerciasis and other parasitic diseases, and the very similar toxic effects of the two compounds in various animal species, additional data on ivermectin were considered, comprising the results of two studies in primates and a published report of a study in humans. A study in which the presence of P-glycoprotein (a permeability protein associated with multiple drug resistance) as correlated with sensitivity to avermectins in different mouse strains was also considered.

A two-week oral toxicity study with ivermectin conducted in immature rhesus monkeys at doses of 0, 0.3, 0.6 or 1.2 mg/kg bw per day showed no adverse effects on body weight, clinical signs, ophthalmoscopic end-points, haematological or clinical chemical parameters, or gross or histopathology. Thus, the NOAEL in this study was 1.2 mg/kg bw per day. In a second two-week study with ivermectin in which neonatal rhesus monkeys were administered doses of 0, 0.04 or 0.1 mg/kg bw per day by nasogastric intubation,the NOAEL was 0.1 mg/kg bw per day. The doses administered were 10-30 times the dose that would be received by the nursing infant of a lactating mother who had been treated with ivermectin for onchocerciasis.

New data were submitted which showed that the high sensitivity of CF-1 mice to the nervous system toxicity of avermectins is associated with a deficiency of P-glycoprotein in both the epithelium of the small intestine and the capillary endothelial cells of the blood-brain barrier. The deficiency is associated with a marked increase in the concentration of ivermectin in brain and plasma after administration of the compound. CD-1 mice and those of the CF-1 strain that have higher levels of P-glycoprotein are less sensitive to the central nervous system toxicity of abamectin than the approximately 17% of CF-1 mice deficient in this protein. The oral LD_{50} for CF-1 P-glycoprotein-deficient mice was about one order of magnitude lower than that of CD-1 mice and of CF-1 mice with higher levels of P-glycoprotein. This heterogeneity in the CF-1 mouse strain may explain the apparent absence of a dose-response relationship with respect to

maternal toxicity in the teratogenicity studies. These data, however, cannot be used to demonstrate a correlation between P-glycoprotein deficiency and teratogenicity although, given the apparent absence of dose-response relationship, such a correlation might be inferred.

Extensive information available on the use of ivermectin in animal and human health was reviewed at the fortieth meeting of the Joint FAO/WHO Expert Committee on Food Additives in 1992. The Committee concluded that "despite the extremely wide use of ivermectin, there is no evidence of significant incidences of adverse effects on reproductive performance in treated animals and the very limited data on reproductive toxicity in humans indicate that ivermectin does not increase the incidence of birth defects."

The Meeting confirmed that the lowest NOAEL was 0.05 mg/kg bw per day for maternal toxicity in the teratogenicity studies in mice with abamectin and the Ä-8,9 isomer. The Joint Meeting in 1992 considered that slight decreases in body weight gain early in the lactation period in one generation of rats in a reproductive toxicity study provided supporting evidence. The present Meeting concluded that the NOAEL in the rat reproduction study was 0.12 mg/kg bw per day on the basis of pup toxicity at the higher dose level.

The Meeting concluded that the CF-1 mouse strain is heterogeneous with respect to sensitivity to abamectin and therefore may be an inappropriate model for studying the toxicity (including teratogenicity) of avermectins. An ADI was therefore established on the basis of the NOAEL of 0.12 mg/kg bw per day seen for pup toxicity in the reproductive toxicity study in rats. A safety factor of 500 was applied because the concern over the teratogenicity of the Ä-8,9 isomer could not be assuaged by the additional data.

An addendum to the toxicological monograph was prepared.

TOXICOLOGICAL EVALUATION

Level that causes no toxic effect

Rat: 0.12 mg/kg bw per day (two-generation reproductive toxicity study)

Estimate of acceptable daily intake for humans

0-0.0002 mg/kg bw

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

1. Data on P-glycoprotein in other species, including humans.

2. Establishment and validation of a more sensitive method to assess neurotoxic effects of avermectins in rodents.

3. Acute toxicity of the Ä-8,9 isomer in CF-1 and CD-1 mice with measurements of P-glycoprotein and blood and brain levels of the compound.

4. Teratogenicity study in CD-1 and CF-1 mice with abamectin and the Ä-8,9 isomer with concurrent measurements of P-glycoprotein, in order to correlate its presence or absence with maternal toxicity and teratogenicity.

RESIDUE AND ANALYTICAL ASPECTS

Abamectin was first evaluated at the 1992 JMPR and MRLs were recommended for a number of crops and animal commodities. Residue data were available for strawberries, but at that time there was no official GAP, so no MRL could be recommended.

Abamectin as an 18 g ai/l EC formulation is approved for the control of mites on strawberries in the field in France, South Africa and Spain at 0.023 kg ai/ha, with 4 applications and a PHI of 3 days.

In the one trial from France according to GAP residues of avermectin B_{1a} were below the limit of determination (0.005 mg/kg). Avermectin B_{1b} was not detected (<0.002 mg/kg). In the trial according to GAP from Spain the highest residue of avermectin B_{1a} was 0.015 mg/kg, with avermectin B_{1b} below the limit of determination. In the two trials from Italy, which could be evaluated according to Spanish GAP, the highest residues of avermectin B_{1a} were 0.010 mg/kg and below the limit of determination. Avermectin B_{1b} was not detected.

Although not strictly comparable, the same use patterns in Brazil and the USA produced similar levels of residues.

The Meeting estimated a maximum residue level of 0.02 mg/kg for abamectin in strawberries.

4.2 ACEPHATE (095)

[see also METHAMIDOPHOS (100)]

RESIDUE AND ANALYTICAL ASPECTS

Acephate was first evaluated in 1976, with further reviews of residue aspects in 1979, 1981, 1984 and 1990. At the 21st (1989) Session of the CCPR (ALINORM 89/24A) several delegations expressed the opinion that the proposed MRLs for broccoli, Brussels sprouts, head cabbages, cauliflower, citrus fruits and tomatoes, all at 5 mg/kg, were too high; these proposals were therefore left at Step 7B. In 1990, the JMPR proposed Temporary MRLs for cauliflower, citrus fruits and tomatoes, also at 5 mg/kg, pending the receipt of additional information on current GAP from countries other than the USA. The 23rd (1991) and 24th (1992) Sessions of the CCPR (ALINORM 91/24A; 93/24) retained the MRLs for broccoli, Brussels sprouts and head cabbages at Step 7B. Current GAP and residue information on all of these "Step 7B" crops has been provided for this Meeting and evaluated. The relevant data on these crops as published in the earlier monographs were also reassessed. In addition, some information on the fate of residues, methods of residue analysis and residues in food in commerce or at consumption was supplied

and this has been evaluated.

Information on minor modifications that had been made to the method of residue analysis was made available. These were aimed at consolidating the extraction procedures and improving recovery efficiency and measurement reproducibility.

Current information on GAP was available on citrus fruits (7 countries), broccoli (5), Brussels sprouts (6), cabbages (10), cauliflower (13) and tomatoes (21), showing the widespread registration of acephate on these crops. Unfortunately, very little of the residue data presented came from any of these countries.

A review of the data on brassica crops that had been published in the evaluations of earlier JMPRs showed that very few results had been obtained under current GAP conditions and most of the data were therefore invalid. Fortunately, some had been resubmitted this year and these could be evaluated. Data on residues in cabbage and tomato from New Zealand, reviewed at the 1984 JMPR, were within GAP and could also be evaluated, as could the data on mandarin oranges from Japan, reviewed in 1990, which were within GAP. However, it was clear that there were insufficient valid data either to support the existing Step 7B proposals or to serve as a basis for alternative recommendations.

Citrus fruits. Data from trials on citrus fruits that were within GAP were available only from Japan. From the eight trials on mandarin and summer oranges, residues in the whole fruit ranged from 0.13 to 3.0 mg/kg at 30 days PHI, most being below 1 mg/kg; residues in the pulp ranged from 0.12 to 1.2 mg/kg at 30 days. The Meeting agreed to withdraw the recommendation for citrus fruits (5 mg/kg T).

Broccoli. None of the residue data on broccoli had been obtained under GAP conditions and so no valid data were available. The Meeting agreed to withdraw the recommendation for broccoli (5 mg/kg).

Brussels sprouts. Residue data from trials in South Africa on Brussels sprouts were within their GAP but only summary data were provided in a form that was not very clear. The Meeting agreed to withdraw the recommendation for Brussels sprouts (5 mg/kg).

Cabbages. Residue data on cabbages from New Zealand that were reviewed by the 1984 JMPR were from two trials that were within GAP and gave maximum figures of 0.8 and 1.1 mg/kg at 7 and 10 days PHI, respectively. No other valid data were available. The Meeting agreed to withdraw the recommendation for head cabbages (5 mg/kg).

Cauliflower. As no valid data were presented on residues in cauliflower, the Meeting agreed to withdraw the recommendation for cauliflower (5 mg/kg T).

Tomato. At the 1984 JMPR, data from one trial of acephate on tomatoes in New Zealand showed a residue of 0.19 mg/kg at a PHI of 3 days under GAP application conditions. Data from trials of acephate on tomatoes which were carried out according to relevant GAP in Japan in 1984 and 1985 and in South Africa in 1973 were provided to the Meeting. In the Japanese trials, at the recommended PHI of 7 days, residues were between 0.38 and 0.74 mg/kg. Residues in the South African trials were 0.12 and 0.23 mg/kg at 3 days PHI. The Meeting agreed to withdraw the recommendation for tomato (5 mg/kg T).

Studies on the processing of some commodities were made available to the Meeting. Little or no reduction in acephate residue levels was observed from "home" water washing of green beans or from boiling them in water for over 20 minutes, although the cooking water was found to contain about one-half of the original residue. In canning, the total acephate in the canned beans was between 50 and 87% of the original acephate residue on the beans; again the canning water contained 40 to 50% of the residue.

Pinto beans were treated six times at 1.1 kg ai/ha, allowed to dry naturally and separately boiled and canned. When the cooking fluid and beans were analysed, both before and after processing, no residues of acephate were detectable in the dried beans nor in any of the processed parts.

When soya beans were treated at twice the normal rate, maximum residues of 0.19 mg/kg were found in the shelled beans. Processing studies showed that acephate residues were concentrated in the hulls but were reduced by at least 70% in the meal and by 100% in the oil. No residues were detected in the crude oil and none would be expected in refined oil.

Four trials of acephate on mint in 1987 gave maximum residues of 26 mg/kg on the fresh mint hay, after treatment at the maximum label rate, at 14 days PHI. In the spent mint hay, residues were down to 4 mg/kg but no residues could be detected in the oil produced therefrom.

After ten applications of acephate to corn at 2.2 kg ai/ha (twice the maximum label rate) residues at 21 days PHI were: grain, 0.1 mg/kg; forage, 4.6 mg/kg; silage, 6 mg/kg; and fodder, 3.2 mg/kg. Processing this corn led to no residues being found in the crude oil, refined oil, soapstock, reclaimed solvent, starch, gluten, bleached oil, deodorized oil, steepwater distillate or processed water. No residue change was observed in the kernels or grits. Residues were, however, slightly higher (10 to 50%) in screenings, meal, flour, and steepwater concentrate. Grain, silage, meal, flour, press cake and germ were reanalysed after a storage interval approximating to, or longer than, the interval between collection and initial analysis. Only in the germ was any loss of residues observed but the residue level was too low (0.07 mg/kg) for a meaningful conclusion to be drawn.

Acephate residues in crops treated at the maximum label rates were monitored from harvest through typical commercial processes to the consumer. Bell peppers showed the least loss, 17 to 29%, from the farm gate to the consumer. In Brussels sprouts, residues decreased by about 60% after sorting, while blanching plus freezing lost 35% more. Cauliflower residues were reduced by about 60% after trimming and 10% more after processing. In lettuce, levels were decreased by about 80% by removing wrapper and outer leaves. Snap bean levels decreased by about 64% during handling from the field to the market shelf and by an additional 18% during canning or freezing.

Eight market basket surveys were carried out quarterly in 1984 and 1985, each survey consisting of the collection of samples from three different geographical locations within the USA. From 26 to 62 commodities were collected in each of the surveys, the edible portions of each commodity from each location being combined and stored frozen until analysed. Residues of acephate were found in only 6 of the 62 commodities sampled: cantaloupe, celery (fresh), lettuce (crisphead), sweet peppers (green), tomatoes, and canned snap beans. Except for one sample of green sweet peppers, in which 0.72 mg/kg was found, all residues were less than 0.1 mg/kg. Acephate was not consistently found in any commodity in the surveys.

The withdrawals shown in Annex I are recommended.

4.3 ALDICARB (117)

RESIDUE AND ANALYTICAL ASPECTS

Aldicarb was first evaluated in 1979, and last reviewed in 1993. It is included in the CCPR periodic review programme.

Aldicarb is a systemic insecticide, nematicide and miticide, available commercially only as low-assay (50, 100 or 150 g/kg) granular formulations. To protect field crops the granules are applied in seed furrow, band or overall treatments (either pre-plant or at planting), as well as in post-emergence side-dress treatments. In orchards and vineyards the pesticide is applied at the intensively developing stage of the trees or vines (e.g. at the spring flush of foliage, before bud swell or around bud break) in bands along the row of vines, and along the dripline on both side of or around the trees, or uniformly around the trees. The application rate ranges from 0.34 to 11.25 kg ai/ha, depending on the crop and pests to be controlled. The granules must be incorporated into the soil immediately after application. Soil moisture is required to release the active ingredient from the granules, so irrigation or rainfall should follow application. The number of applications is usually restricted to one per year in food- and feed-producing plants except bananas, coffee, cotton, macadamia nuts and potatoes.

Aldicarb is rapidly absorbed by the plant's root system and moves throughout the plant, mainly in the xylem. The plants are protected for several weeks.

The fate of residues was studied in rats, dogs, cows, goats, hens, various plants and soil.

The basic metabolic pathway appears to be the same in all species studied. Aldicarb is rapidly oxidized to the relatively stable sulphoxide; then, more slowly, a small proportion of the sulphoxide is oxidized to aldicarb sulphone. Aldicarb, aldicarb sulphoxide and aldicarb sulphone are also readily converted to the corresponding oximes and nitriles, which are in turn slowly degraded to the corresponding aldehydes, acids, and alcohols, none of which are toxicologically significant.

Aldicarb sulphoxide and aldicarb sulphone fed separately to rats or in a mixture to dairy cows were eliminated similarly to the parent aldicarb. The metabolites present were the same.

A lactating cow fed [^{35}S]aldicarb as a single dose of 0.1 mg/kg bw eliminated over 96% of the administered radioactivity within 540 hours after treatment. The percentages of the total dose detected in the urine, milk, and faeces were 90.2, 3.0 and 2.9 respectively.

Lactating cows were administered aldicarb and aldicarb sulphone (1:1 molar ratio) labelled with ^{14}C in the methylthio group at levels of 0.12, 0.6 or 1.2 ppm in the diet for 14 days. The dose level did not alter the magnitude or nature of the residues eliminated daily in the urine, milk and faeces. The percentages of the dose excreted by these routes were 92, 1, and 3

respectively.

Residues in the milk expressed as aldicarb were between about 0.1 and 0.2% of the levels in the feed. About 15% of the radioactive residue in the milk was aldicarb sulphone and about 4% was the sulphoxide. The total aldicarb equivalents in the liver were 0.029, 0.12 and 0.16 mg/kg from the three treatments, respectively, when the animals were slaughtered 18 hours after the last treatment. Twenty-six other tissue samples contained either much lower or undetectable residues.

Two lactating goats were administered [*S*-methyl-^{14}C]aldicarb in gelatin capsules at a level equivalent to 2.5 ppm in the feed (or 0.165 mg/kg bw) for ten days and a third served as a control. The goats were slaughtered within 6-8 hours after the last dose was given. Of the applied dose, 61.2% was eliminated in the urine, 11.3% in the faeces, and 1.1% in the milk. Only 0.2% of the applied dose was found in the respiratory gases and 0.10% in the tissues at the end of the 10-day dosing period. The overall recovery of the applied dose was 74%.

The total ^{14}C residues in the milk reached a plateau within 7 days and a maximum concentration of 0.1 mg/kg by the end of the treatment period. Tissues contained low concentrations of total ^{14}C residues with a maximum of 0.52 mg/kg in the liver. No aldicarb, *per se*, was found in the urine, milk or tissues. Only traces of the sulphoxide and sulphone were detected in the milk and some tissues. A maximum of 0.26 ìg/kg and 1.5 ìg/kg of the total carbamate residues were found in the milk and liver, respectively. No carbamates were detected in the brain, mammary glands or omental fat, and only 0.1 mg/kg of the sulphoxide in the peripheral fat. The largest single component of the ^{14}C residues in the milk and all the tissues was identified as aldicarb sulphone nitrile, which represented 54% to 68% in the milk and varied in the tissues from 7.7% in the liver to 79% in the peripheral fat. Other metabolites identified in the milk and tissues were non-carbamate products similar to those in the urine. With the exception of aldicarb sulphoxide nitrile, all the non-carbamate metabolites in the milk and tissues were less than 1% of the total ^{14}C. Aldicarb sulphoxide nitrile appeared to be significant only in the kidney (4.9%), liver (2.5%) and peripheral fat (1.2%). Insignificant amounts (<1.0%) of aldicarb sulphoxide nitrile were detected in all the other tissue and milk samples analyzed.

The results of these studies indicate that the rapid excretion of aldicarb and its biotransformation products by dairy animals would prevent the accumulation of residues in milk or tissues.

In a feeding study mature, laying white leghorn hens were given daily doses of a 1:1 molar mixture of aldicarb and aldicarb sulphone, each labelled with ^{14}C in the *S*-methyl group. Three groups of six birds each were treated with 0.005, 0.05 or 1.0 mg/kg/day corresponding to levels of 0.1, 1.0 or 20.0 ppm aldicarb equivalents in the feed. In each of the three treated groups, three of the birds were killed 12 hours after the cessation of feeding and the other three seven days after the last treatment. At the highest level fed, 85% of the total administered radioactivity appeared in the droppings and 5% was found in the eggs. The total radioactive residues 12 hours after the last treatment amounted to 0.07 and 0.79 mg/kg in eggs, and 0.06 and 0.69 mg/kg in breast meat at the 1 ppm and 20 ppm feeding levels, respectively. The levels of radioactivity in muscle, fat, and skin with fat were comparable to that in breast muscle, but those in liver (0.14 mg/kg and 1.4 mg/kg) and kidney (0.12 mg/kg and 1.4 mg/kg) were higher. The total radioactivity in these organs declined significantly during the seven days after withdrawal of the pesticide. Characterization of the radioactive material in the eggs and tissues showed that the

total toxicologically significant residues (containing the carbamate moiety) were present at 0.003 mg/kg after 28 days of continuously feeding 1:1 mixtures of aldicarb plus aldicarb sulphone at the level of 20 ppm in the diet.

In another study ten laying hens were dosed twice daily with [*S*-methyl-^{14}C]aldicarb for seven consecutive days at a rate equivalent to 3.54 ppm in the diet. At the end of the dosing period, animals were slaughtered and tissues collected for analysis. The highest concentration of [^{14}C]aldicarb in tissues was observed in the liver with an average concentration of 0.42 mg/kg. The kidney contained the next highest concentration with an average of 0.31 mg/kg. Plasma contained an average of 0.15 mg/kg and red blood cells an average of 0.12 mg/kg. Muscle, fat and skin with adhering fat contained less than 0.1 mg/kg. The average concentrations of total aldicarb equivalents in egg yolks and whites over the seven-day dosing period were 0.09 mg/kg and 0.11 mg/kg respectively, giving a calculated average concentration in whole egg of 0.1 mg/kg. Aldicarb sulphone nitrile was the most common free metabolite isolated from liver, muscle, egg yolk and egg white. In liver, it was present at a level of 0.028 mg/kg aldicarb equivalents (6.7% of the total radioactive residue, TRR). However, the major free metabolite in liver was aldicarb sulphone acid which was present at a level of 0.105 mg/kg aldicarb equivalents (25.4% TRR). Two additional minor free metabolites were isolated from the liver: methanesulphonic acid, 0.029 mg/kg aldicarb equivalents (7.0% TRR), and aldicarb sulphoxide nitrile, 0.003 mg/kg aldicarb equivalents (0.8% TRR). No intact carbamates (aldicarb, aldicarb sulphoxide or aldicarb sulphone) were detected in the tissues or eggs.

The metabolic pathways of aldicarb have been studied in potatoes, sugar beet, cotton, peanuts, tobacco, spearmint and lettuce.

The initial step in the metabolism of aldicarb in plants is thio-oxidation by plant enzymes to aldicarb sulphoxide. This conversion occurs rapidly since no parent aldicarb is found in the plant after a few weeks. Aldicarb sulphoxide is subsequently metabolized, mainly by hydrolysis to the sulphoxide oxime. It is also converted to aldicarb sulphone by slow thio-oxidation. Both of these metabolites suffer extensive degradation through hydrolysis, elimination, oxidation, reduction and conjugation reactions to yield the corresponding oximes and the resulting alcohols and their glycoside conjugates, amides, nitriles and carbonic acids. Possible intermediate metabolites are the aldehydes of the sulphoxide and sulphone. The major plant metabolite at harvest in the plants studied, in terms of percentage of the applied dose of aldicarb, was aldicarb sulphoxide alcohol (2-methyl-2-(methylsulphinyl)propanol), which may be conjugated with plant sugars in the form of water-soluble glycosides. No evidence of demethylation or reduction of aldicarb sulphone to aldicarb sulphoxide or aldicarb has been found in any of the plant studies.

There has been no evidence of conjugated carbamate metabolites in plants resulting from aldicarb treatment. Consequently, the only significant terminal carbamate-containing residues in plants following aldicarb treatment are aldicarb sulphoxide and aldicarb sulphone, both of which are toxicologically significant. In foliage, the ratio of aldicarb sulphoxide to aldicarb sulphone changes in favour of the latter with time.

Since the amount of each residue component represents the final yield of continuous uptake and biotransformation processes the half-life of the individual metabolites cannot easily be calculated.

The metabolic pathway for aldicarb is qualitatively similar in all the plant species studied

(potato, sugar beet, cotton, peanut and tobacco). An identical pattern of degradation products has been described whether the chemical was introduced by injection, leaf uptake, topical stem application, or soil treatment. The last is the only method of application commercially recommended.

Over the 90-day growing season there was an effective systemic uptake of aldicarb by potato plants from soil which resulted in the accumulation of the residues in the foliage for at least 60 days. Thereafter, the residues declined as a result of the loss of the older leaves and dilution of the residues by plant growth. Aldicarb sulphoxide and sulphone in the tubers amounted to 63% and 14.7% of the total radioactive residue at 60 and 90 days after planting respectively.

In sugar beet roots aldicarb sulphoxide and sulphone amounted to about 21% and 24% of the total radioactive residue at 90 and 140 days after planting and in sugar beet forage the corresponding proportions were 25.6% and 40.6%.

The concentration of total radioactive residues in cotton foliage declined rapidly. The following residues were measured at various intervals after application: 242 mg/kg (14 days); 53.5 (37 days); 9.2 (72 days) and 8.9 mg/kg (146 days).

The uptake by peanut plants from soil was slow. Only 1.4% and 2.8% of the applied radioactivity was detected in the plants at 21 and 35 days respectively. The maximum uptake (7.5%) was reached at 56 days. It should be noted that while the percentage of the applied radioactivity found in the plants continued to increase until 56 days, the concentration of ^{14}C residues declined after the 21-day sampling because the rate of dilution by plant growth was greater than the rate of uptake from the soil.

The absorbed radioactivity accumulated preferentially in the foliage and at 126 days only 0.25% of the applied material was translocated to the nuts (shells plus kernels). The proportion of unextracted ^{14}C was higher in the roots, pegs, shells and kernels than in the foliage.

Two studies have been conducted to measure the uptake of residues of aldicarb by rotational crops. The first consisted in treating a Norfolk sandy loam soil with 5.6 kg ai/ha of [*S*-methyl-^{14}C]aldicarb and ageing under field conditions for four- and twelve-month periods. Of the applied [^{14}C]aldicarb, approximately 60% was lost by degradation (as CO_2) and 20% by leaching during the four month ageing period. At the end of the period lettuce, turnip and barley were planted separately in the treated soil and grown to maturity. Only traces of carbamate residues were detected in the four-month plantings. These ranged from 0.02 to 0.05 mg/kg in all the plant parts except barley straw which contained 0.72 mg/kg.

In the second study covering seven test sites in six States of the USA, aldicarb was applied to three primary crops, cotton, potatoes and sugar beet, according to registered uses and generally at the maximum use rate. Residues were found in most rotational crops especially at the early plant-back intervals ranging from five to twelve months, but the residues were generally below the limit of determination (LOD). The maximum residues (mg/kg aldicarb sulphone) measured in rotational crops were: alfalfa (0.07), barley forage (0.15), carrot (0.04), and wheat forage (0.7). Residues in the other crops (onion, lettuce, broccoli, cucumber, cantaloupe, tomato, maize and oats) were below the LOD.

The fate of aldicarb in soil has been extensively investigated under both laboratory and field conditions. The main transformation pathway involves oxidation to aldicarb sulphoxide as a major product and to a lesser extent to aldicarb sulphone. These products are degraded to the corresponding oximes and nitriles. Extensive decomposition of the transformation products leads to the formation of carbon dioxide as the major end product.

The experiments showed that soil micro-organisms were active in the degradation of the pesticide and contributed significantly to its short persistence in soil. Aldicarb sulphoxide and water-soluble metabolites were the major products of metabolism by various fungi. Traces of aldicarb sulphone, aldicarb sulphoxide oxime, aldicarb sulphoxide nitrile, aldicarb sulphone oxime and aldicarb sulphone nitrile were also detected in the organosoluble fraction. Water-soluble metabolites consisted of aldicarb sulphone alcohol and amide as major products, moderate amounts of aldicarb sulphoxide alcohol and amide, and small amounts of acids, presumably derived from aldicarb sulphoxide and aldicarb sulphone. The metabolic pattern of aldicarb sulphoxide was similar to that of aldicarb.

The rate of dissipation of aldicarb and its carbamate metabolites in the soil varies, and depends on several factors such as mineral and organic matter contents, nature of the micro-organisms present, temperature and moisture.

No important differences could be attributed to pH within the range 6 to 8. There was however variation among the soil types in their capacity to degrade aldicarb at different moisture levels. It is apparent that the moisture level is a critical factor in the fate of aldicarb in soils. In general, degradation was slower in the deeper layers than in the top layers of the soil. Transformation of aldicarb to its sulphoxide and sulphone decreased markedly at lower temperature and moisture content.

Co-distillation from the moist soil resulted in essentially insignificant losses, which ranged from 0.01% to 0.08% of the applied dose. No carbamates were detected in the volatilized radioactivity.

Under the regular farming and environmental conditions of six States of the USA, the aldicarb sulphoxide and sulphone residues in soil ranged from undetected to 0.27 mg/kg five to ten months after the last application at maximum recommended rates.

In aqueous solution aldicarb was more susceptible than aldicarb sulphoxide and aldicarb sulphone to UV (290 nm) irradiation. The half-life of aldicarb was 8 to 12 days and aldicarb sulphone 36 to 38 days, while aldicarb sulphoxide was stable to UV irradiation with only 2% degradation in 14 days. This photostability was attributed to the lack of light absorption above the 290 nm region by aldicarb sulphoxide. Under field conditions therefore, other environmental agents such as microbes and plant absorption and metabolism are responsible for its ultimate dissipation.

In another study sterile water buffered at pH 5 containing [*S*-methyl-^{14}C]aldicarb at 10.6 mg/kg was exposed to artificial sunlight comparable to natural sunlight for a total period of 360 hours of continuous irradiation at 25°C. The parent concentrations in non-irradiated samples changed insignificantly, remaining within the range 95.0 to 98.4% of the initial level. The concentrations of aldicarb in irradiated samples decreased from 98.4% to 0.4% of the total radioactivity in 168 hours of exposure. There were two major products: aldicarb oxime, which

reached a maximum of 64.6% of the total activity by 168 hours, and aldicarb nitrile which reached a maximum of 48.2% by 360 hours.

The movement of aldicarb in soils has been extensively studied under both laboratory and field conditions, but only summary information was provided on leaching and the fate of residues in ground water. Laboratory studies show that aldicarb residues do not bind significantly to inorganic soil particles, but can be retained to some extent by soil organic matter, so that the rate of movement may be equal to or as little as one-tenth that of the movement of water. The movement of water in the soil under normal agricultural conditions is determined by the rainfall, irrigation, evaporation/transpiration, and the water-holding capacity of the soil. The movement of residues into deeper soil layers or ground water is influenced by the rate of degradation of the compound in the soil, which is a function of the pH, moisture, temperature, texture and microbial activity in or of the soil.

Field studies indicated that the half-life of aldicarb residues in shallow and medium-deep ground water (down to 10 m) ranges from about one month to three years. The residues in ground water moved laterally as well as vertically. A worst-case calculation indicated that under unfavourable conditions the degradation or effective dilution of residues in ground water may take up to 100 years. Because of the persistence of the residues in ground water, appropriate management practices are to be introduced and followed in order to protect ground water from contamination.

For residue analysis, the toxicologically significant carbamate residues (aldicarb, aldicarb sulphoxide and aldicarb sulphone) are usually extracted from plant foliage, fruits and vegetables with mixed solvents, from oils with hexane followed by partition into acetonitrile, and from soil with water. After clean-up the residues may either be oxidized to aldicarb sulphone and determined by GLC, or separated by HPLC. In the latter case the individual compounds can be detected by a fluorescence detector after post-column derivatization.

The limit of determination by GLC is usually 0.02 mg/kg but lower levels down to 0.001 mg/kg could be achieved in peanut oil.

The HPLC separation and detection provide the advantage of determining the individual toxicologically significant residues with limits of determination of 0.01 mg/kg in plant materials, 0.001 mg/kg in soil and 0.1 ìg/kg in ground water for each residue component.

Since the sum of the toxicologically significant residues has to be calculated the limits of determination are about the same with both methods, which are suitable for regulatory purposes.

Attention has to be paid to the expression of the residue. Since aldicarb sulphone is determined by GLC, the residues found by oxidation and GLC are most frequently expressed as aldicarb sulphone. In HPLC procedures the expression of the total residue should take into account the differences in the molecular masses of the components (aldicarb sulphone/aldicarb = 1.168; aldicarb sulphoxide/aldicarb = 1.084; aldicarb sulphone/aldicarb sulphoxide = 1.077).

In the supervised trials evaluated by the Meeting the residues were generally determined by GLC and the results, with few exceptions, were expressed as aldicarb sulphone.

The typical recommended application is by soil treatment in band or furrow, drilling 5-7.5 cm below the seed line at planting or sowing. Application must be followed by immediate

and complete incorporation into soil to a depth of about 30-80 mm.

The Meeting evaluated supervised field trials on citrus fruits, grapes, onions, garlic, cauliflower, cabbage, dry peas, soya beans, carrots, swedes, sweet potatoes, sugar beet, wheat, barley, sorghum, maize, sugar cane, pecans, cotton, peanuts and coffee beans.

Since the residue information for potatoes (1990 JMPR) and Brussels sprouts (1993 JMPR) has been recently reviewed, the residues in these commodities have not been evaluated by the Meeting.

The manufacturer informed the Meeting that owing to changes in the use pattern for bananas, the available residue data for aldicarb do not reflect the currently recommended GAP. A programme of residue trials in accordance with the new use pattern is in progress, and will be made available to the JMPR when it has been completed.

The Meeting therefore withdrew the previous estimate of 0.5 mg/kg.

Citrus fruits. Supervised field trials and specific studies on several varieties of orange, mandarin, grapefruit, lemon and lime were reported from 13 countries.

The results indicated that the pesticide incorporated into the soil was translocated from the tree roots to the developing fruit and the initial residue was then reduced by growth dilution as the fruit matured. Also, the essentially mature fruit on the tree at the time of treatment did not accumulate the translocating pesticide to the same extent as the smaller more actively growing fruit. Consequently the residues are higher in immature green fruit than in mature fruit on the tree at the same time.

The analysis of orange peel and pulp showed that the parent aldicarb was practically absent, and the toxic residue was composed of aldicarb sulphoxide and aldicarb sulphone in the ratio of about 5:1.

Field trials on oranges in 6 countries were considered. Following application at recommended rates, the residues were generally at or below 0.1 mg/kg 100 days after treatment. However, higher residues up to 0.2 mg/kg were also detected during the period of 31-250 days following the last application. No substantial differences in residue patterns at various time intervals after application were observed.

Residues in lemons, limes and grapefruit were similar, both in magnitude and in the variation of residue levels in the maturing fruit with time after treatment. Since their culture is essentially similar, the residue data from all three crops were considered together for estimating maximum residue levels. The residues in various fruits resulting from recommended application rates up tok 56 kg ai/ha showed similar patterns and were at or below 0.1 mg/kg in most of the samples. Two samples contained residues in the range >0.1 to <0.2 mg/kg and two from ≥ 0.2 to <0.3 mg/kg. In trials in the USA with 11.2 kg ai/ha the residues did not exceed 0.3 mg/kg in the mature fruits.

The Meeting took into account the similar growing conditions, use patterns and residue distributions in the different fruits, and the reduction of approximately 20% of the measured residue levels when they are expressed as aldicarb, and agreed to maintain the current

recommendation of 0.2 mg/kg for citrus fruits.

Trials in grapes were evaluated from eight countries, four of which have registered uses. The maximum residue in grapes is likely to occur at about 60 days after treatment and then decline slowly. There was no significant difference in the residue levels occurring in various grape varieties from 100 to 130 days.

The residues in both fresh juice and wine made from Cabernet Sauvignon grapes consisted of a 1:1 ratio of aldicarb sulphoxide to sulphone with no parent aldicarb.

The highest residues were observed in trials in the USA and South Africa. The use recommendation has been withdrawn in the USA, so the evaluation was based on South African GAP, where the granules are applied in a band between the rows and the maximum rate of 0.75 g ai/m^2 is equivalent to 3.75 kg ai/ha taking into account the band and row widths. Although a PHI of 120 days is registered in South Africa, the pesticide is to be applied at the time of bud swelling. The residues measured in harvested grapes (<0.03-0.16 mg/kg) were therefore considered for estimating the maximum residue level. The registered uses in Australia, Egypt and Peru (used as a reference for trials in Chile) lead to lower residues.

The Meeting estimated a maximum residue level of 0.2 mg/kg for grapes.

Several trials on onions were reported from Israel, the UK and The Netherlands, which were in accordance with registered uses. Residues in mature onions ranged from undetected (<0.01-0.04 mg/kg) to 0.08 mg/kg. Two trials on garlic resulted in similar residues.

The Meeting estimated a maximum residue level of 0.1 mg/kg for onions. The data for garlic were not sufficient to estimate a maximum residue level.

The 1990 JMPR confirmed the Codex MRL of 0.5 mg/kg on potato on the basis of available data. In view of the acute toxicity of aldicarb, its inclusion in the periodic review, and the understanding that new data were available the Meeting decided to make the current recommendation temporary pending the reconsideration of all available data reflecting current use patterns. Consequently, the supervised trials reported from The Netherlands will also be evaluated at a future Meeting.

The Meeting noted the residue data on Brussels Sprouts evaluated in 1993, and reaffirmed the previous recommendation of 0.1 mg/kg.

Residues were between <0.02 and 0.11 mg/kg in cauliflowers 56-90 days after soil treatments with recommended and 1.5-fold rates. In cabbages the residues ranged from <0.01 to 2.7 mg/kg within 67-81 days following applications with recommended and 1.5-fold rates. The trials were in the UK in 1977 and 1978.

The Meeting considered the limited data insufficient to estimate a maximum residue level for cabbage or cauliflower.

Trials on dry beans from 4 countries were considered. In Brazilian trials the part of the plant which was analyzed was not clearly indicated and the analytical method used had a LOD of

0.2 mg/kg, so the results were not taken into account. Aldicarb residues in the beans declined rapidly during the last few weeks of the season while the beans were developing and drying. In US trials the maximum residue found in dry beans at harvest following recommended application was 0.02 mg/kg. After applications at a 1.5-fold rate the residues at harvest were mostly below the limit of determination (<0.02 mg/kg). Quantifiable residues (3 x 0.03, 0.07 mg/kg) were found in four of 22 samples. The residues in samples from trials in other countries were also generally below the limit of determination.

Residues in dry bean forage at harvest were below 0.5 mg/kg in 21 of 26 samples. The remaining five contained residues of 0.8 mg/kg from the recommended rate and 0.6, 0.88, 1.2 and 2.8 mg/kg from 1.5 times that rate. The green forage 40 days before harvest contained residues in the range 0.03-35 mg/kg. However green and dry forages are restricted for use as animal feed.

The Meeting agreed to maintain the current recommendation of 0.1 mg/kg for beans (dry).

Residues in dry peas were determined in 8 trials in the UK. They were in the same range as in beans (<0.01 - 0.03 mg/kg). Since no information on GAP for peas was available, the Meeting could not estimate a maximum residue level.

In soya beans in US trials the residues in the immature succulent seeds were low and decreased quickly as the seed matured. In all samples taken at harvest residues were below the limit of determination (0.02 mg/kg) regardless of the method of treatment and including treatments at 2 and 2.3 times the recommended maximum rate.

Residues in the forage at harvest were below 0.1 mg/kg except in one sample which contained 0.56 mg/kg. The residues in green forage may exceed 5 mg/kg, but quickly decline below 0.1 mg/kg. Owing to their value as oil seed, no significant quantities of soya beans are likely to be used as green forage or cut for hay. In addition, the US label states that treated plants must not be used as animal feed.

The Meeting agreed to maintain the current recommendation of 0.02* mg/kg for soya beans (dry).

Carrots were grown in three plots in the UK following soil treatments with 2.6-5.1 g ai/100 m. Residues declined rapidly in the root and were in the range 0.17-0.29 mg/kg at 84 days after planting.

The Meeting considered the limited data insufficient to estimate a maximum residue level for carrots.

Swedes were grown in soils treated with aldicarb at 1.3-2 times the recommended rate. In one trial the residue was 0.04 mg/kg in the whole plant and 0.01 mg/kg in the root at 129 days, and in four other trials below the limit of determination in all root samples 191-222 days after treatment. Since the samples were taken at much longer intervals than the current 70 day PHI, the residue data could not be used for estimating a maximum residue level.

Supervised trials were carried out on sweet potato in 5 States of the USA between 1968 and 1975. Application rates included the recommended US rates (1.7-3.36 kg ai/ha) and ranged

up to 6.72 kg ai/ha. At the registered PHI and dosage the roots contained residues from <0.01 to 0.05 mg/kg. Residues of 0.09 and 0.16 mg/kg were detected after applications with 1.5- and twofold rates. The distribution of the results indicated that residues higher than 0.05 mg/kg residues might also occur when the compound used according to GAP.

The vines of sweet potato following treatment with the maximum recommended rate contained residues in the range 0.21-0.89 mg/kg after 90-105 days, and 0.34 mg/kg after 119 days. When a double rate was applied the residues ranged from 1.6 to 5.1 mg/kg after 90-105 days and 0.74 mg/kg was measured after 119 days.

The Meeting agreed to maintain the current recommendation of 0.1 mg/kg for sweet potato.

Results were considered from field trials on sugar beet in seven European countries and in eight States of the USA. Following application at sowing (GAP) in European trials, the residues in the roots were at or below 0.04 mg/kg in samples from 76 trials. Broadcast applications over the plants (up to five leaves) did not result in higher residues. In four trials in the UK in 1967-68 higher residues were detected in two samples: 0.05 mg/kg (4.5 kg ai/ha, top dressing application, 182 days PHI) and 0.06 mg/kg (1.12 kg ai/ha in furrow, 159 days). Single applications up to 4.5 kg ai/ha and with a 90-day or longer PHI, corresponding to the current recommended uses in the USA, resulted in residues in the roots of ≤0.02 mg/kg in 23 trials. Application at a double rate (9 kg ai/ha) gave residues of ≤ 0.03 mg/kg at harvest (≥140 days after application).

The residues in leaves from treatments corresponding to US GAP ranged from <0.1 to 0.93 mg/kg at 120 days after application or later. After treatments at a double rate the residues in the leaves amounted to 0.98 mg/kg at 160 days. The residues in tops and leaves ranged from 0.03 to 0.65 mg/kg in all of the 79 samples from European trials. The residues in the leaves consisted of about 78% aldicarb sulphone and 22% aldicarb sulphoxide. The parent aldicarb could not be detected.

The Meeting agreed to maintain the current recommendations of 0.05* mg/kg for sugar beet root and 1 mg/kg for sugar beet leaves or tops.

In 12 trials in Australia and 2 in Israel on wheat, after application at planting with rates up to 3 kg ai/ha, residues were not present at detectable levels (<0.01 or <0.02 mg/kg) in the mature grain.

In grain from barley grown in soil treated with 1 kg ai/ha, the residues were <0.02 mg/kg in 1 Australian and 5 French trials.

Wheat straw from the Australian trials contained residues of <0.02-0.03 mg/kg. Barley straw samples were also analyzed but no residue was detected (<0.04 mg/kg). Rotational crop studies conducted in the USA indicated, however, that wheat and barley planted in soils containing 0.17-0.24 mg/kg aldicarb residues may take up higher residues from the soil, resulting in 0.11-0.88 mg/kg residue levels in green forage.

The Meeting took into consideration the similar residue pattern in wheat and barley and estimated maximum residue levels of 0.02 mg/kg for wheat and barley grain, and 0.05 mg/kg for

the straws.

After applications at rates ranging from 0.56 to 3.36 kg ai/ha at or shortly before planting sorghum, residues were undetectable (<0.01 mg/kg) in mature grain in 55 of 60 trials. Following applications with 1.12 and 2.24 kg ai/ha the residues were 0.03, 0.04 and 0.13 mg/kg and 0.04 and 0.1 mg/kg, respectively. Residues were undetectable (<0.02 mg/kg) in sorghum straw in 16 cases. Detectable residues were present in 5 samples at the following concentrations from the application rates (kg ai/ha) and PHIs shown in parentheses: 0.03 mg/kg (1.34, 124 days), 0.03 mg/kg (1.12, 158), 0.09 mg/kg (0.56, 132), 0.11 mg/kg (1.68, 158) 0.4 mg/kg (1.12, 132). The residues in straw and dry fodder would be unlikely to exceed 0.5 mg/kg when the compound is used according to GAP.

The Meeting concluded that about 98% of the residues deriving from approved uses would be below 0.1 mg/kg, and recommended lowering the present MRL of 0.2 mg/kg MRL for sorghum grain to 0.1 mg/kg. The previous recommendation of 0.5 mg/kg for sorghum straw and fodder is maintained.

Supervised field trials on maize were reported from France, Germany, Israel, the UK and the USA. Treatments up to 1 kg ai/ha did not give rise to detectable residues in the grain. Applications with 1.7 kg ai/ha resulted in detectable (≥0.03 mg/kg) residues in three of 25 trials. The residues in the other samples were below the limit of determination.

The residues in green forage harvested from 60 to 116 days after treatment ranged from <0.02 to 0.34 mg/kg. The dry fodder (stover) contained residues in the range <0.02-0.54 mg/kg.

The Meeting agreed to maintain the current recommendation of 0.05 mg/kg for maize, and recommended new limits of 0.5 mg/kg for maize fodder and maize forage, the latter to replace the previous recommendation of 5 mg/kg.

Supervised field trials on sugar cane were submitted from Australia, India, Indonesia and South Africa. The compound may be used either at or shortly after planting, or after the first harvest. Consequently the minimum time which would elapse between application and harvest is 8 months, but usually over a year. The residues in the leaves and stalks of sugar cane from 14 trials at rates of 0.75-7.75 kg ai/ha were below the limit of determination (<0.001-0.003 mg/kg) 315-362 days after application. In South Africa eleven trials with rates from 2.24 to 3.36 kg ai/ha resulted in residues from <0.02 to 0.33 mg/kg at 170-192 days after application and <0.02 to 0.11 mg/kg after about a year. In these last trials the blank values were up to 0.06 mg/kg.

The Meeting estimated a maximum residue level of 0.1 mg/kg for sugar cane, based on a PHI of about a year.

68 trials on pecans have been carried out in Israel, South Africa and the USA with recommended rates. Samples taken at intervals of 48 to 268 days after application generally contained residues below 0.2 mg/kg, with a mean of 0.11 mg/kg. The residues were between 0.2 and 0.3 mg/kg in three samples, and between 0.3 and 0.4 mg/kg in two others. Two samples contained residues of 0.77 and 0.75 mg/kg 59 and 96-98 days after treatment.

Residues in pecan shells ranged from 0.02 mg/kg to 0.61 mg/kg.

The Meeting recommended an increase in the current limit for pecan from 0.5 mg/kg to 1 mg/kg.

Numerous field trials on cotton were reported from Australia, Israel and the USA. Applications made in accordance with recommended uses gave no detectable residues in about 75% of the samples. Over 90% of the samples contained <0.07 mg/kg, and a few 0.08 mg/kg. Even when more than one side-dressing application was made with higher rates the residues did not exceed 0.08 mg/kg.

The Meeting agreed to maintain the current recommendation of 0.1 mg/kg for cotton seed.

A large number of trials on peanuts in the USA resulted in residues at or below 0.08 mg/kg in whole peanuts treated according to GAP (the LOD was 0.01 mg/kg). Processing studies in the USA and trials from Senegal showed that the residues in peanut kernels were 5 to 10 times lower than in the whole nuts, so residues may occur up to 0.02 mg/kg in peanut kernels when GAP is followed.

The residues in green peanut vines were 0.65-21.5, 0.48-21.8, 0.15-3.0 and <0.02-2.7 mg/kg about 55, 75, 95 and 120 days after application. The hay contained residues in the range <0.05-2.6 mg/kg at harvest following applications at about the recommended rates.

The Meeting agreed to replace the previous recommendation for peanut kernel (0.05* mg/kg) by 0.02 mg/kg.

Seven trials on sunflower were reported from France. Aldicarb was applied at the maximum recommended rate of 0.5 kg ai/ha at planting. The seeds did not contain detectable residues (aldicarb sulphone <0.05 mg/kg).

The Meeting estimated a maximum residue level of 0.05* mg/kg for sunflower seed.

The residues in dried and hulled green coffee beans from supervised trials in accordance with use patterns in South America were low. Four of 47 samples contained residues above the LOD (0.02 mg/kg) 15 to 274 days after the last application: three were 0.03 mg/kg 118 to 143 days after the last application and the fourth was 0.05 mg/kg at day 186. Application of about double the recommended rate resulted in <0.02 (3), 0.04 (2) and 0.08 mg/kg.

The Meeting agreed to maintain the current recommendation of 0.1 mg/kg for coffee beans.

A feeding study was conducted to determine the residue levels in milk and liver after feeding a 1:1 mixture of unlabelled aldicarb sulphoxide and aldicarb sulphone at 1.0, 3.0 or 5.0 ppm in the diet to lactating cows.

The total toxic aldicarb residues in the milk were about 0.1% of the level of the metabolites in the feed, which is in agreement with the value of about 0.1-0.2% obtained for the total radioactive metabolites in milk from feeding radiolabelled aldicarb and its sulphone. No build-up of toxic aldicarb residues was found during the 46 days of the continuous feeding study.

Aldicarb residues were not detected in liver (<0.01 mg/kg) at any of the dose levels tested. Since the samples were stored frozen for an unreported period, this may have been caused by the decomposition of residues during storage.

In view of the very low concentration or absence of the carbamate metabolites in the meat of cattle and goats (<0.1% of the feeding level) and eggs (<0.05%), and the maximum estimated residues in potential animal feeds, it is unlikely that detectable residues would ever occur in meat, milk or eggs if the current use patterns are followed, even if some treated plant forages were used as animal feed.

Aldicarb sulphoxide and aldicarb sulphone were shown to be stable under deep-frozen storage for at least nine months in oranges, six months in milk, six weeks in potato processing products (chips, flakes, granules, wet and dry peel) and in soya bean processing products except soapstock. However, in frozen beef liver 85% of the aldicarb sulphoxide and >99% of the aldicarb sulphone were lost within one day.

The effect of processing on residue levels in processed products was studied in citrus fruit, grapes, dry beans and peas, soya beans, sugar beet, sorghum, maize and peanuts.

The commercial washing of citrus fruit did not remove aldicarb residues. The peel generally contained about 3 to 5 times the residue in the pulp, with extremes of 2-9 times. The peel/pulp ratio ranged from 31/69 to 49/51.

The juice contained lower residues than the fresh fruit. The residue levels in juice as a percentage of those in the whole fruit were 34-89% for oranges, <10-18% for grapefruit and 27-57% for limes.

Residues were concentrated when fresh fruit was processed to dried citrus pulp (dried peel) by a factor of about 1.8. Residues in the molasses were at about the same level as in the dried pulp.

Eight grape varieties, containing residues in the range 0.1-2.5 mg/kg, were processed to fresh juice, pomace and wine. The concentration factors (residue in processed product/residue in fresh fruit) ranged between 0.53 and 0.87 for fresh juice, 0.73 and 1.4 for pomace, and 0.19 and 0.63 for wine.

Raisins were prepared from Thompson seedless grapes grown in California in 1981. Concentration factors ranged from 0.6 to 2.4.

Studies to determine the effects of preparative procedures and cooking as usually done in the home showed a significant reduction of the residues in dry beans and peas. About 85% and over 90% of the residues in the seeds were lost after one hour and three hours cooking respectively. Fully cooked blackeye peas, red kidney beans and field peas contained less than 10% of the original residue in the dry seeds.

There was no concentration of residues on processing soya beans (after treatment at 4 times the recommended rate) to oil. Residues were undetectable in the refined oil (<0.005-0.01 mg/kg). The residues in the hulls and meal were about the same as, or somewhat higher than, in

the seed.

Diffusion juice obtained from sugar beet in a pilot unit simulating commercial processing contained residues which were about the same as or somewhat lower than in the corresponding root samples. Other processed fractions (thin juice, dry pulp, wet pulp) contained no detectable residue (<0.005 mg/kg).

When sorghum grain was milled, residues in the flour were about 1/2-1/3, in the shorts about 1/2, and in the bran up to 4 times those in the grain.

Processing field-treated maize to meal and oil caused no concentration of residues. The hulls contained about 2.5 times the residue in the grain. Since the hulls are generally fed to animals only in a mixture with other grain products, their feeding would be unlikely to result in a higher residue intake than feeding grain.

Crude oil processed from field-treated cotton seed contained about 1/10 to 1/15 of the residue in the seed. No residues containing the carbamate moiety were present in refined oil. The residues in the meal were about 1/2-1/3, and those in the hulls up to about 3 times, those in the seed.

Four lots of field-treated peanuts were processed to oil and meal. The residues in the kernels were about 1/5 to 1/10 of those in the whole nuts. The meal contained residues at about the same level as the kernels. Residues were not detectable in pressed or extracted oil (<0.003 mg/kg). The residues in the hulls were about 1 to 3 times those in the whole nuts. Since the average kernel/hull ratio is about 70/30 it may be concluded that most of the residue is generally in the hull.

Green coffee containing aldicarb residues of 0.11 mg/kg was processed to yield roasted coffee, spent grounds, and instant coffee. No aldicarb residues (<0.02 mg/kg) were found in any of these products.

The residues in commodities moving in commerce were studied in two extensive food survey programmes in the USA in order to assess more accurately the dietary exposure to aldicarb at the point of purchase. Seventy-five locations were selected nation-wide. Samples of bananas, oranges, potatoes, sweet potatoes and grapefruit and their processed products were taken in February, May and September during 1987 to cover seasonal variations. At each sampling 69-75 samples of each commodity were analyzed. Detectable residues, including those below the limit of determination (LOD), were found in about 15% of the samples of bananas (0.019, 0.175 mg/mg), bananas processed for infant food (0.012, 0.01 mg/kg), orange juice for infants (0.01 mg/kg), and fresh grapefruit. The numbers in parentheses are the mean residue calculated with 0.01 mg/kg assigned to all samples containing <0.01 mg/kg.

The second monitoring programme was conducted in Florida in 1993 to determine the residues in oranges. The design of the survey involved collection of samples of oranges from groves that (1) had been treated with aldicarb, (2) had mature fruit on the tree at harvest, and (3) were intended for the fresh market. Altogether 869 individual oranges were analyzed, of which 711 had either less than the LOD (467 oranges) or no detectable residues (244). The remaining 158 samples had quantifiable residues with a mean of 0.025 mg/kg and a standard deviation of 0.020 mg/kg.

From the results of these surveys it is apparent that the potential dietary exposure to aldicarb is significantly overestimated by using either tolerance-based or 95th percentile residue calculations.

On the basis of the data on residues resulting from supervised trials the Meeting concluded that the residue levels listed in Annex I are suitable for use as MRLs.

4.4 AZOCYCLOTIN (129)

TOXICOLOGY

Azocyclotin was evaluated by the Joint Meeting in 1979, 1981, 1989 and 1991. An ADI of 0-0.003 mg/kg bw was established in 1981 and was confirmed in 1989 after consideration of several teratogenicity studies in rabbits. Since azocyclotin residues are degraded to cyhexatin, the 1991 Joint Meeting concluded that the ADI for azocyclotin should be the same as that for cyhexatin, 0-0.001 mg/kg bw.

After reviewing additional data on cyhexatin for the assessment of that compound and after reviewing data on azocyclotin from previous reports, the present Meeting concluded that the toxicological profiles of the two compounds were of sufficient similarity as not to require separate ADIs. The Meeting therefore included azocyclotin in the ADI of 0-0.007 mg/kg bw for cyhexatin.

A separate toxicological monograph on azocyclotin was not prepared.

4.5 BENOMYL (069)

[See also CARBENDAZIM (072) and THIOPHANATE-METHYL (077)]

RESIDUE AND ANALYTICAL ASPECTS

Benomyl was first evaluated in 1973 and has been reviewed on five other occasions. The 1988 JMPR initiated a re-evaluation of residues arising from the use of the three related fungicides benomyl, carbendazim and thiophanate-methyl, all to be calculated as carbendazim, in response to concerns expressed at the 1988 CCPR (ALINORM 89/24, paras. 82-84). The 1989 CCPR requested that the recommendations for a group MRL for carbendazim in cereals should be replaced by separate recommendations for MRLs for individual crops, while at the 1992 CCPR (ALINORM 93/24, para. 105) several other MRLs were held at step 7B pending further review by the JMPR. Although some information was provided for the 1990 JMPR, that Meeting concluded that it would be premature to review the compounds until all of the required data became available and consideration was deferred to the 1992 JMPR. However, because of the work-load at that Meeting, the re-evaluation was again postponed until 1993. The data submitted for the 1990 and 1992 Meetings, together with additional data provided in 1993, have now been reviewed with particular attention to the information on GAP and some new residue data.

The information on GAP illustrated the extensive applications of this fungicide world-wide. Although post-harvest uses have been withdrawn in several countries, they are still registered for fruits in others. However, apart from two trials on apples in France in 1988, no data on residues arising from such treatments were made available.

Data were available from field trials on pome and stone fruits, and limited data on residues in grapes, strawberries, wheat, and a range of vegetables. Of the commodities with MRLs currently held at Step 7B, residue data from the use of benomyl were available only for apricot, grapes, strawberry, mushrooms, nectarine, peach, pome fruits, sugar beet leaves, and wheat.

Some data were presented on residues occurring in commercially treated apples and also on the effects of processing on treated prune plums, grapes, pineapples and tomatoes. Results of monitoring studies carried out in Hungary and the USA were also provided.

Any assessment of the residues from the use of benomyl must take into account those arising from uses of carbendazim and/or thiophanate-methyl, since all three pesticides yield carbendazim as the residue of prime importance. Recommendations are therefore dealt with under "carbendazim".

FURTHER WORK OR INFORMATION

Desirable

1. Residue data from supervised trials of benomyl using currently registered post-harvest treatments of fruits and vegetables.

2. Residue data from supervised trials of benomyl on rice to enable a recommendation for an MRL to be made.

3. Residue data from supervised trials of benomyl at the currently registered rates of use on lettuce, peppers, tomatoes and sugar beet.

4. Supporting residue data from supervised trials of benomyl at the currently registered rates of use on all other crops for which CXLs are listed.

4.6 BENTAZONE (172)

RESIDUE AND ANALYTICAL ASPECTS

Bentazone was first reviewed by the 1991 JMPR. At the 25th (1993) Session of the CCPR (ALINORM 93/24A para 193) it was agreed that there was a need to review the information on GAP as it was inadequately reported in the 1992 Residue Evaluations.

The following additional concerns were expressed.

(a) France and The Netherlands preferred an MRL of 1 mg/kg for alfalfa forage (green), and suggested that the proposed MRL of 3 mg/kg on maize fodder was not supported by the data in the 1991 residue evaluations.

(b) Germany indicated that German GAP required a higher MRL for beans (dry), common bean (pods and/or immature seeds), field pea (dry) and garden pea (young pods). Germany was requested to provide written comments.

The USA requested that the proposed MRL on dry peas be increased from 0.05 to 1.0 mg/kg.

(c) The Netherlands preferred an MRL of 0.05(*) mg/kg for potato and, supported by the USA, an MRL of 0.05* mg/kg for rice.

(d) Germany queried the fact that the reported limit of determination is lower than the sum of the limits of determination of the three components of the residue.

In order to respond to the questions raised by member countries the Meeting considered the information provided in the 1991 Evaluation as far as the condensed and summarized presentation made it possible.

The residue values reported for dry beans indicate that parent bentazone and its hydroxy metabolites were below the limit of determination in all dry bean samples. In all samples of pods and seeds or succulent seeds, deriving from 74 trials covering the registered application rates, residues were undetectable except in one sample taken 46 days after treatment with bentazone at 1.4 kg ai/ha which contained 0.14 mg/kg bentazone while the 6- and 8-hydroxy metabolites were

below the LOD (<0.02 mg/kg).

The Meeting noted the comments of Germany indicating that field beans in trials reported in the 1991 Evaluations were varieties of *Vicia faba* and should be classified as Broad bean (dry) instead of Common bean (Codex Classification of Foods and Animal Feeds).

Since in both dry broad beans and dry common beans the residues were below the limit of determination, the correction of the commodity description does not affect the recommended limits.

The Meeting concluded that the available data do not support an increase of the current recommended limit of 0.2 mg/kg for common bean (pods and/or immature seeds).

New supervised field trials on peas were reported from the USA reflecting the current use pattern. Bentazone was applied twice at a rate of 1.1 kg ai/ha. Samples were taken at intervals of 30 to 40 days after the second treatment. All three of the residue components in three dry pea samples were below the limit of determination (0.05 mg/kg). The fourth sample contained 0.06 mg/kg of 6-hydroxy-bentazone. The remaining two samples had a total residue of 0.28 and 0.79 mg/kg bentazone equivalents allowing 0.05 mg/kg (the LOD) for the undetected parent bentazone. Residues in pea hay ranged from 0.95 mg/kg to 5.4 mg/kg.

The Meeting estimated a maximum residue level of 1 mg/kg for dry peas to replace the previous recommendation (0.05* mg/kg).

The Meeting concluded that the 0.2 mg/kg limit for immature peas might not reflect uses according to GAP, but there was no information on residues in immature peas resulting from applications according to current US GAP.

Residues in potatoes were below the limit of determination in the majority of samples. However, detectable residues were measured in some samples at 52 and 84 days following treatments with 1.4 kg ai/ha and 1.9 kg ai/ha. (The recommended maximum rate is 1.44 kg ai/ha, and the PHI ranges from 30 to 42 days in several countries.) The results indicate that detectable residues may occur following the use of bentazone according to GAP.

The meeting reaffirmed the previous recommendation of 0.1 mg/kg for bentazone in potatoes.

Residues in barley, oats, rye, sorghum and wheat were below the limit of determination in all samples except one summer wheat sample in which 0.06 mg/kg 6-hydroxy-bentazone was measured. In this sample bentazone and 8-hydroxy-bentazone were <0.02 mg/kg. The 0.13 mg/kg parent bentazone residue in one rye sample was not considered in estimating the maximum residue level because the sample was taken after a double rate application with a very short (11 days) PHI.

In maize the residues were generally undetectable. In two trials bentazone and 6-hydroxy-bentazone were detected in the ranges of <0.02 to 0.04 mg/kg and 0.02 to 0.11 mg/kg respectively. The higher residues were observed in trials corresponding to GAP.

In rice the residues were below the limit of determination except in one sample in which

0.07 mg/kg parent bentazone was measured. Hydroxy metabolites were undetectable.

The results of trials in cereals indicate that detectable residues in grains may occur when the pesticide is used according to GAP.

The Meeting took into account the likely presence of detectable residues at similar levels in various cereal grains and estimated a new maximum residue level of 0.1 mg/kg for barley, oats, rye, sorghum and wheat and 0.2 mg/kg for maize to replace 0.05* mg/kg. The Meeting reaffirmed the previous recommendation of 0.1 mg/kg for rice.

In maize fodder residues of bentazone ranged from <0.02 to 0.03 mg/kg, 6-hydroxy-bentazone from <0.02 to 0.08 mg/kg, and 8-hydroxy-bentazone from <0.02 to 0.05 mg/kg. The sum of the three residue components never exceeded 0.15 mg/kg.

The Meeting estimated a maximum residue level of 0.2 mg/kg for maize fodder to replace the previous estimate of 3 mg/kg.

The recommendation for alfalfa was based on three sets of results from 4 trials. The total residues ranged from 0.07 to 1.14 mg/kg with some residues below the LOD.

The Meeting reaffirmed the previous recommendation of 2 mg/kg for green alfalfa forage.

The Meeting considered the expression of residues at or about the limit of determination and in the case of cereals recommended replacement of the limits of 0.05* by 0.1 mg/kg to reflect the fact that detectable residues may occasionally occur in samples following recommended use patterns. In the case of dry beans, however, none of the components of the residue was detectable in any of the samples. Consequently, the 0.05* mg/kg limit, allowing some latitude for regulatory laboratories, indicates that none of the components of the residues should be present in detectable amounts.

After reconsideration of the data on residues resulting from supervised trials, the Meeting concluded that the residue levels listed in Annex I are suitable for establishing MRLs.

FURTHER WORK OR INFORMATION

Desirable

Data on residues in immature peas resulting from current recommended uses.

4.7 CAPTAN (007)

RESIDUE AND ANALYTICAL ASPECTS

The 1987 JMPR had recommended that a detailed review of all aspects of the use of captan be carried out and the 1990 JMPR reviewed the information currently available and recommended withdrawal of a number of MRLs and the establishment of TMRLs for those commodities for which residue data were being generated.

Extensive supporting information, as well as residue trials data, was supplied to the Meeting. The available studies included fate in animals, plants, soils and sediments, analytical methods and frozen storage stability, animal transfer and fate of residues in processing. Residue trials data were available for citrus, apples, pears, cherries, peaches, nectarines, plums, grapes, blueberries, strawberries and tomatoes. The information was supplied by Canada, Spain and two manufacturers.

Metabolism studies with [^{14}C]captan on rats (cyclohexene-1,2 label), lactating goats (trichloromethyl label) and laying hens (cyclohexene-1,2 and trichloromethyl labels) were made available to the Meeting. An additional metabolism study on rats and goats (carbonyl label) was received at a late stage of the Meeting, and was not reviewed.

The following abbreviations are used for some of the captan metabolites.

THPI:	1,2,3,6-tetrahydrophthalimide
3-OH-THPI:	3-hydroxy-1,2,3,6-tetrahydrophthalimide
5-OH-THPI:	5-hydroxy-1,2,3,6-tetrahydrophthalimide
THPAM:	3-hydroxy-1,2,3,6-tetrahydrophthalamic acid

The major urinary and faecal metabolites identified in rats were THPI, 5-OH-THPI, 3-OH-THPI and THPAM.

When trichloromethyl[^{14}C]captan was administered to goats and hens, CO_2 was the major metabolite.

Total ^{14}C residues in eggs rapidly reached a plateau (within 2-4 days) when cyclohexene[1,2-^{14}C]captan was administered daily to laying hens. Most of the dose was excreted, but small amounts were distributed through the tissues. THPI was the predominant metabolite and accounted for 52-77% of the ^{14}C in the tissues, egg yolk and egg white. Minor metabolites identified in each of the tissues and eggs were 3-OH-THPI and 5-OH-THPI. Residue levels of metabolites in tissues and eggs were in good agreement when determined by chemical analysis and by measurement of ^{14}C.

Metabolism studies on tomatoes and lettuce were made available to the Meeting. Both cyclohexene[1,2-^{14}C]captan and trichloromethyl[^{14}C]captan were used (foliar application), so that the fate of both parts of the captan molecule could be studied.

In tomatoes, most of the ^{14}C was removed by an acetone wash, suggesting that residues

were largely on the surface. The residues were not translocated to the roots of lettuce or tomatoes, indicating an immobile residue.

Metabolites in lettuce and tomatoes arose from N-S cleavage and epoxidation of the cyclohexene bond. Captan was the major component (70-82%) of the residue, with THPI and captan epoxide identified as minor parts of the total residue (<10%) in tomatoes, tomato leaves and stems, and lettuce leaves. Captan levels determined in lettuce leaves by an enforcement method and by ^{14}C measurement were in good agreement. THPI levels measured by the enforcement method were somewhat lower than by ^{14}C.

The major products identified in the degradation of carbonyl[^{14}C]captan in soil were CO_2, THPI and tetrahydrophthalamic acid. Captan degraded was very rapidly with 99% of the initial 5 mg/kg in a sandy loam soil disappearing in 7 days.

Trichloromethyl[^{14}C]captan was degraded rapidly with a half-life of about 1 day when incubated under aerobic conditions in a sandy loam soil (pH 7.2, 1.2% organic matter) at 25°C at an initial concentration of 5 to 6 mg/kg. Carbon dioxide was rapidly eliminated, and was the only significant ^{14}C product. In another similar study the half-life of captan was less than 4 hours.

At 25°C the half-lives of captan in sterile buffer solutions were 11.7 hours, 4.7 hours and 8.1 minutes at pH 5, 7 and 9 respectively. THPI was the major hydrolysis product identified at each pH. Captan was not photodegraded in sterile aqueous solution at pH 5; the rates of loss were the same in irradiated and non-irradiated samples.

The fate of cyclohexene[1,2-^{14}C]captan was studied in sterile and non-sterile sediment-water systems under controlled laboratory conditions at 20°C in the dark. In the sterile systems CO_2 was not produced, but in the microbial systems after 90 days approximately 50% of the applied ^{14}C had been mineralised to CO_2. Captan disappeared very quickly in both sterile and non-sterile systems and was not detected by day 1. THPI was the initial product of hydrolysis.

Methods have been developed for the residue analysis of captan and THPI in crops, and for THPI and hydroxylated metabolites in animal commodities. The methods rely on gas chromatography for the final determination. Limits of determination are usually in the range 0.01 to 0.05 mg/kg. The methods employed to generate the residue data in the supervised trials were validated in terms of recoveries and interferences.

Captan is easily degraded by high pH or when exposed to some enzymes. Crops should be analysed without delay after maceration. Phosphoric acid is added at the extraction step to maintain acid conditions and enhance captan stability. Captan and THPI require different clean-up steps and different GLC conditions; the analyses in effect require parallel procedures after the extraction step.

The hydroxylated metabolites, 3-OH-THPI and 5-OH-THPI, must be silylated for determination by GLC. Limits of determination of 0.01 mg/kg and 0.05 mg/kg were achieved for milk and animal tissues respectively.

Extensive information on the stability of captan and THPI residues in frozen storage was provided for a range of commodities: almonds, almond nuts coarsely ground, almond nuts whole, apples, apple juice, apple sauce, beet tops, cherries, cucumbers, dry grape pomace, lettuce, maize

grain, maize grain coarsely ground, maize grain whole, melons, potato tubers, raisins, soya bean forage, soya beans, spinach, spinach coarsely chopped, spinach finely chopped, strawberries, sugar beet tops, tomatoes, dry tomato pomace, tomato sauce, tomato whole fruit and wheat forage.

Captan residues remained at 70% or more of the initial concentration after storage at -20°C for the specified interval for the following commodities involved in the residue or processing trials: apples (14 months), cherries (12 months), strawberries (14 months), tomato whole fruit (9 months), apple juice (6 months), apple sauce (9 months), grape pomace (9 months), raisins (10 months), tomato dry pomace (9 months) and tomato sauce (9 months). Less than 20% of the initial captan residues remained in tomato matrix held at -20°C for 12 months. In those cases where captan was degraded, THPI was formed.

THPI itself was shown to be stable in frozen storage. The absence of THPI residues in a sample containing captan is good evidence that captan was stable during storage.

Captan was rapidly converted to THPI in eggs and chicken tissues; the THPI was shown to be stable. The other metabolites, 3-OH-THPI and 5-OH-THPI were also stable under the tested storage conditions (-20°C for 6 to 10 months). Captan was also unstable in milk, with about 50% disappearing in 1 month at -20°C. THPI, 3-OH-THPI and 5-OH-THPI were stable in bovine tissues and milk stored at -20°C for 1 year.

Captan is a broad-spectrum fungicide, widely used on food crops, seed crops and ornamentals. It is registered for use in many countries. Application rates are often in the 1-3 kg ai/ha range and high-volume spray concentrations are often 0.1-0.2 kg ai/hl.

Residue data from supervised trials were made available to the Meeting on citrus, apples, pears, cherries, peaches, nectarines, plums, grapes, blueberries, strawberries and tomatoes.

The Meeting considered a number of points which influence a decision on the definition of the residue.

In crops, captan is the major component of the residue at short intervals between application and harvest; THPI is usually a minor constituent. However, when the residue is older and lower THPI levels may be of the same order as those of the captan. The level of captan itself on a raw agricultural commodity is a good indicator of compliance with GAP, provided the sample is analysed without delay or stored correctly.

The main component of the residue in animal commodities is THPI, where it is the indicator compound.

When commodities are processed, particularly in cooking and heating operations, captan is converted to THPI.

Captan is converted to THPI during frozen storage of some types of sample. Satisfactory sample storage must be questioned when THPI levels in raw agricultural commodities, particularly in samples harvested at short intervals after captan application, constitute a considerable part of the total residue.

After considering these points the Meeting decided that, for enforcement purposes, the residue should be defined as captan alone. The residue definition will need reconsideration if MRLs are recommended for animal commodities or processed commodities.

Residue data recorded in the tables of supervised trials show the captan and THPI residues separately. In the following discussion of residue trials, the residue levels quoted are for captan.

Residue trial data on oranges and mandarins in Spain were made available to the Meeting. The use pattern was the same and the resulting residues were similar. No information was available on the storage conditions of the samples between harvest and analysis, or on the storage stability of captan residues in citrus. Also, in the absence of data on THPI residues it was not possible to decide whether captan residues had been stable during storage. The Meeting was unable to estimate a maximum residue level for captan in oranges or mandarins.

Residue trials on apples (according to GAP) were available from Argentina, Brazil, Canada, Chile, France, Japan, The Netherlands and the UK. The French and Netherlands data were evaluated against UK GAP. Residues in many trials were in the 0.5 to 5 mg/kg range, and two trials from Japan produced residues above this, at 7.2 and 13 mg/kg. Residues of 4.3, 4.4 and 4.8 mg/kg were produced in 3 UK trials. THPI was generally a minor part of the residue in the upper levels.

On the basis of the preponderance of the data the Meeting estimated a maximum residue level of 10 mg/kg for captan in apples to replace the previous recommendation (25 mg/kg T).

Residue trials on pears according to GAP for foliar applications were available from Chile and the UK. In three trials from the UK where captan was used at 2.7 kg ai/ha and the fruit were harvested at the official PHI, 7 days, residues in the 7 to 10 mg/kg range were recorded. THPI residues were low compared with those of captan. Two US post-harvest trials according to GAP (0.15 kg ai/hl) produced captan residues of 4.7 and 11 mg/kg.

The Meeting estimated a maximum residue level of 10 mg/kg for captan in pears to replace the previous recommendation (25 mg/kg T).

Supervised trials on cherries were provided from Japan and the USA. When captan was used according to GAP in Japan (14 days PHI), residues up to 1.3 mg/kg were reported. Foliar application according to US GAP (2.2 kg ai/ha and PHI of 0 days) produced residues in the 10 to 20 mg/kg range. Post-harvest dipping according to US GAP (0.15 kg ai/hl) gave captan residues of 3.8 to 15 mg/kg.

The Meeting estimated a maximum residue level of 20 mg/kg for captan in cherries.

Data on Peaches were made available from trials in Australia, Chile, Spain and the USA. The highest residues in peaches from Chile and Spain were 2.0 mg/kg and 3.5 mg/kg respectively when captan was used according to the GAP of those countries. The majority of the captan residues from the US trials according to GAP (4.5 kg ai/ha and PHI of 0 days) were in the 2 to 10 mg/kg range, but in three of the 11 trials, residues were 10, 12 and 14 mg/kg. THPI was a minor part of the residue.

The Meeting estimated a maximum residue level of 15 mg/kg for captan in peaches to replace the previous recommendation (15 mg/kg T).

Trials on nectarines were available from Chile, Spain and the USA. The intervals between application and harvest in the Chile trials were much longer than the intervals permitted by the label. The spray concentrations in the Spanish trials were much lower than Spanish GAP. Captan residues up to 0.30 mg/kg and 0.77 mg/kg were reported in the trials from Chile and Spain respectively. Captan residues in the US trials were in the range 1.3 to 3.9 mg/kg.

The Meeting estimated a maximum residue level of 5 mg/kg for captan in nectarines.

Residues in plums in Chile were similar to those in nectarines for similar conditions of use. In the US trials, application rates on plums were about 20% higher than on nectarines. The highest captan residues in each of three US trials were 0.45, 0.60 and 5.6 mg/kg. Captan is essentially a surface residue, and the Meeting decided that the nectarine data could be used to supplement the plum data in estimating a maximum residue level.

The Meeting estimated a maximum residue level of 5 mg/kg for captan in plums.

Extensive data on residues in grapes were provided from trials in Argentina, Chile, France, Germany, Japan and the USA. Residues in grapes from the Argentine trials were in the range 0.5 to 0.8 mg/kg. Three trials from Chile produced captan residues in the 5 to 10 mg/kg range. The fourth trial produced much higher residues, 12 to 25 mg/kg. In France the PHI is 33-45 days; the highest residue according to GAP was 4.4 mg/kg. THPI was the major part of the residue in some of these grape samples. If the THPI was formed during sample storage the original captan residues in these samples would have been somewhat higher.

There are no registered uses of captan on grapes in Germany, so the German trials were evaluated in terms of French GAP. A PHI of 30 days after a final application of 3.6 kg ai/ha was considered to be according to GAP. The majority of trials according to these conditions produced residues in the 1 to 5 mg/kg range, with three trials producing residues of 9.8, 7.4 and 7.0 mg/kg. In two trials where a PHI of 28 days was observed residues of 8.3 and 15 mg/kg were recorded.

Residues in four of the eight grape trials in Japan were in the 5 to 10 mg/kg range and in two exceeded 10 mg/kg (12 and 14 mg/kg). PHIs were very long in the US trials on grapes, so residues were low and did not influence the estimation of a maximum residue level.

The Meeting estimated a maximum residue level of 20 mg/kg for captan in grapes.

In nine blueberry trials in the USA according to GAP (1.1-2.8 kg ai/ha, PHI 0 days), residues in four were in the 5 to 10 mg/kg range and in two exceeded 10 mg/kg at 15 and 18 mg/kg.

The Meeting estimated a maximum residue level of 20 mg/kg for captan in blueberries to replace the previous recommendation (20 mg/kg T).

Data on trials according to GAP on strawberries were provided from Canada, Chile, Hungary and the USA. The highest residue from treatments according to GAP in the Canadian trials was 3.0 mg/kg. The highest residues in the three trials from Chile were 3.8, 4.2 and 4.8

mg/kg; THPI residues in these trials ranged up to 0.73 mg/kg (equivalent to 1.5 mg/kg captan). In Hungary the highest residue was 0.93 mg/kg. In the six US trials according to GAP (1.7-3.4 kg ai/ha and 0 days PHI) residues of captan in three were in the 2 to 5 mg/kg range, in two in the 5 to 10 mg/kg range, and residues in one exceeded 10 mg/kg. The highest captan residues in three separate US trials were 5.2, 7.7 and 12 mg/kg. If some of the THPI detected in the samples was formed during sample storage, the original captan levels would have been slightly higher.

The Meeting estimated a maximum residue level of 15 mg/kg for captan in strawberries to replace the previous recommendation (20 mg/kg T).

Supervised trials according to GAP on tomatoes were reported from Brazil, Canada, Greece, Israel and Mexico. Data were reasonably consistent from the different countries, with the majority of trials producing highest residues in the 0.2 to 1 mg/kg range. The highest residues in three trials were 1.7 and 1.3 mg/kg in Canada and 0.46 mg/kg in Brazil. Data from one trial in Greece were considered invalid because of excessive residues in control samples. If the THPI residues in samples from trials in Israel and Brazil were formed during sample storage the original captan levels would have been considerably higher.

The Meeting estimated a maximum residue level of 2 mg/kg for captan in tomatoes to replace the previous recommendation (15 mg/kg T).

Animal transfer studies with laying hens and dairy cattle were made available to the Meeting. Captan itself disappears quickly from animal commodities; THPI is the residue of interest.

In the study on laying hens THPI residues in eggs reached a plateau after about 7 to 10 days of daily captan administration. The ratio of captan feeding level to THPI levels in the eggs was about 40-50 at the plateau. THPI residues were evenly distributed in the tissues and levels were 120 to 150 times less than the captan feeding levels. THPI residues decreased rapidly in tissues and eggs when the hens received a residue-free diet.

When dairy cattle were dosed with captan, THPI residues in milk reached a plateau rapidly, within 1 to 4 days, at levels 500 to 1000 times lower than captan levels in the diet. Residue levels of the metabolite *trans*-3-OH-THPI in milk and tissues were similar to those of THPI. Residue levels of THPI in muscle, liver and kidney were generally 300 to 500 times lower than captan levels in the diet, and were even lower in fat. Residues disappeared quickly when dosing was withdrawn.

There are currently no recommendations for MRLs in animal feeds. If additional uses of captan lead to residues in feeds, the maximum residue levels in animal commodities should be estimated. The current animal transfer studies should provide the basis for an estimate. The Meeting also noted that the residue in animal commodities is not captan but THPI. Residues of THPI in animal commodities will generally not exceed 0.05 mg/kg when captan in the diet is in the parts per million range.

Processing studies on apples, grapes, prunes and tomatoes were made available to the Meeting.

Captan residues are on the surface, and washing the raw agricultural commodity as the

initial step in processing removes some of the residue. Peeling apples removes most of the residue. Captan is converted to THPI in cooking or heating. The net result is that captan itself is not present in processed commodities such as apple sauce, canned apple slices, apple jelly, canned juice, tomato puree and tomato ketchup. The level of THPI residues depends on the captan levels present at the boiling or cooking step.

In the drying of prunes, where the process included a water wash and oven drying for 16 hours at 74°C, most of the captan was converted to THPI, and because of the removal of moisture the level of the total residue increased. The data suggest that the total residue (as captan) in dried prunes is approximately 3 times the level in the raw commodity.

Captan residue levels in raisins, where the process involved sun-drying of the grapes and subsequent removal of raisin waste, were on average 1½ times those in the grapes. Captan was not converted to THPI in the drying process. The Meeting noted that the captan levels in grapes (less than 1 mg/kg) used for the US processing trials were appropriate for the use pattern in the USA where raisins are produced. The estimated MRL for grapes was based on captan uses on grapes which were not used for raisin production.

Whole milk in the USA (224 samples) was surveyed in 1991 for captan, THPI, 3-OH-THPI and 5-OH-THPI residues to validated LODs of 0.005 mg/kg. In all 224 samples, captan and the three metabolites were below the limits of determination.

Information on national MRLs for captan was provided to the Meeting.

The residue levels shown in Annex I are recommended for use as MRLs.

FURTHER WORK OR INFORMATION

Desirable

1. Current information on registered uses of captan on citrus in Spain (the available information was dated May 1991).

2. Details of Spanish trials on citrus (sample storage conditions, storage interval before analysis, storage stability data for captan residues in citrus). Reports should include author or study director, date and report numbers. Without trial identification numbers and document identification numbers it is sometimes difficult to know if reports are for different trials, or are progress reports for the same trial, or have been reviewed on previous occasions.

4.8 CARBENDAZIM (072)

[See also BENOMYL (069) and THIOPHANATE-METHYL (077)]

RESIDUE AND ANALYTICAL ASPECTS

Carbendazim was first evaluated in 1973 and has been reviewed on seven other occasions. The

1988 JMPR initiated a re-evaluation of residues arising from the use of benomyl, carbendazim and thiophanate-methyl, all to be expressed as carbendazim, in response to concerns expressed at the 1988 CCPR (ALINORM 89/24, paras. 82-84). The 1989 CCPR requested that the recommendations for a group MRL for carbendazim in cereals should be replaced by separate recommendations for MRLs for individual crops, while at the 1992 CCPR (ALINORM 93/24, para. 105) several other MRLs were held at step 7B pending further review by the JMPR. Although some information was provided for the 1990 JMPR, it was concluded that it would be premature to review the compounds until all of the required data became available and consideration was deferred to the 1992 JMPR. However, because of the work-load at that Meeting, the re-evaluation was again postponed until 1993. The data submitted for the 1990 and 1992 Meetings, together with additional data provided in 1993, have now been reviewed with particular attention to the information on GAP and some new residue data.

Information on the uses of carbendazim that was available from several sources clearly showed the extensive applications of this fungicide. Although it is known that post-harvest uses have been withdrawn in several countries, there are still registered post-harvest uses on fruits in others. The treated commodities include apricots, cherries, citrus fruits, nectarines, peaches, pineapples, plums, and pome fruits, all of which were held at step 7B by the 1988 CCPR. The other 7B commodities, bean fodder, berries and other small fruits, carrots, cereal grains, head lettuce, mushrooms, peppers, sugar beet leaves or tops, and tomatoes, are not subject to post-harvest treatments with carbendazim, according to the available information on GAP.

Very few results from residue trials on fruit and vegetables were provided. Some new data covered treated apples and peas. There were also data from the post-harvest dipping of carrots in The Netherlands, but these were from 1983 and earlier and had already been reviewed by the 1988 JMPR. More extensive data were supplied on residues in barley, oats, rye and wheat, although again the bulk of the information was obtained before 1984.

Some information regarding the residues of carbendazim found during monitoring studies in Hungary and The Netherlands was also provided. This showed that occurrences were generally rare, only mushrooms in The Netherlands showing some occasions on which the national MRL of 0.5 mg/kg was exceeded.

Any assessment of the residues arising from the use of carbendazim must also take into account those arising from benomyl and/or thiophanate-methyl treatments, since all three pesticides yield carbendazim as the residue of prime importance. Recommendations concerning all three compounds are therefore dealt with together, and are shown in Annex I.

All of the MRLs for which recommendations have been made are at CCPR Step 7B at present. There was insufficient information on which to base any recommendations relating to the existing CXLs. However, there were indications that more recent data from supervised trials were needed in order to be able to assess the continued suitability of the present recommendations for lettuce, peppers, tomato and sugar beet, in particular.

FURTHER WORK OR INFORMATION

Desirable

1. Residue data from supervised trials of carbendazim using currently registered post-harvest treatments of citrus, pome and stone fruits, potatoes, carrots and any other fruits or vegetables for which post-harvest treatment is registered.

2. Residue data from supervised trials of carbendazim on rice to enable a recommendation for an MRL to be made.

3. Residue data from supervised trials of carbendazim at the currently registered rates of use on lettuce, peppers, tomatoes and sugar beet.

4. Supporting residue data from supervised trials of carbendazim at the currently registered rates of use on all other crops for which CXLs are currently listed.

4.9 CHLORFENVINPHOS (014)

TOXICOLOGY

Chlorfenvinphos, an inhibitor of cholinesterase, was previously evaluated by the Joint Meeting in 1971 when an ADI of 0-0.002 mg/kg bw was established. The compound was re-evaluated by the present Meeting as a result of the CCPR periodic review programme.

The main step in the biotransformation of chlorfenvinphos is detoxification by desethylation into the corresponding diester, microsomal enzymes playing an important role. Interspecies differences in the rate of metabolism of chlorfenvinphos were found *in vitro*. Oxidative metabolism by human liver enzymes was comparable to that by rabbit liver enzymes.

In studies with single oral doses, chlorfenvinphos was very toxic to rats, toxic to mice and guinea pigs and moderately to slightly toxic to rabbits and dogs. The clinical signs observed were consistent with cholinesterase inhibition and included tremors, fasciculation and salivation. Pre-treatment with enzyme inducers can increase the acute oral LD_{50}. Interspecies differences in the acute oral LD_{50} reflect the activity of the hepatic enzymes involved in the detoxification of chlorfenvinphos. WHO has classified chlorfenvinphos as extremely hazardous.

A four-week study in which mice were fed 0, 1, 10, 100 or 1000 ppm chlorfenvinphos in the diet showed inhibition of plasma and erythrocyte cholinesterase at 100 and 1000 ppm. Brain cholinesterase activity was inhibited at 10 and 1000 ppm in males and at all dose levels in females; hence no NOAEL could be established for female mice (NOAEL <0.18 mg/kg bw per day) and the NOAEL in males was 1 ppm, equal to 0.18 mg/kg bw per day.

In a one-year study in which dogs were fed 0, 3, 100 or 3000 ppm in the diet, inhibition of erythrocyte cholinesterase activity and increased relative adrenal weight were seen in males and increased relative thyroid weight in females at the highest dose. The NOAEL was 100 ppm, equal to 2.8 mg/kg bw per day.

In a carcinogenicity study in which mice were fed 0, 1, 25 or 625 ppm in the diet, no increase in tumour incidence was observed. At the highest dose, erythrocyte and brain

cholinesterase activity was inhibited. The NOAEL was 25 ppm, equal to 3.7 mg/kg bw per day.

In a two-year toxicity/carcinogenicity study in rats fed diets containing 0, 0.3, 1, 3 or 30 ppm, erythrocyte and brain cholinesterase activity was inhibited at 30 ppm. There was no evidence of carcinogenicity. The NOAEL was thus 3 ppm, equivalent to 0.15 mg/kg bw per day.

In a two-generation reproductive toxicity study in rats fed diets containing 0, 1, 10 or 100 ppm, reduced brain cholinesterase activity, post-implantation loss and breeding losses were observed at 10 and 100 ppm. The NOAEL was 1 ppm, equivalent to 0.05 mg/kg bw per day.

In two teratogenicity studies, one in rats and one in rabbits, dose levels that caused maternal toxicity were not embryotoxic and there was no indication of teratogenicity. The NOAEL for maternal toxicity in rats was 1 mg/kg bw per day, and that for developmental toxicity at the highest dose tested, 3 mg/kg bw per day. For rabbits, no NOAEL could be established for maternal toxicity (<25 mg/kg bw per day); the NOAEL for developmental toxicity was 100 mg/kg bw per day.

Chlorfenvinphos was mutagenic in one study with *Salmonella typhymurium* TA100 in the presence of an exogenous metabolic system at doses of at least 1000 µg per plate. It was inactive in other bacterial tests and did not induce mitotic conversion in yeast or chromosomal aberrations in human lymphocytes *in vitro*. *In vivo*, chlorfenvinphos did not induce chromosomal aberrations in Chinese hamster bone- marrow cells or dominant lethal effects in male mice. The Meeting concluded that chlorfenvinphos was not genotoxic.

Delayed neurotoxicity in chickens has not been evaluated.

Observations in humans were not suitable for use in estimating an ADI.

An ADI of 0-0.0005 mg/kg bw was established on the basis of the NOAEL of 0.05 mg/kg bw per day in the two-generation reproductive toxicity study in rats and a 100-fold safety factor.

A toxicological monograph was prepared summarizing the data received since the previous evaluation and containing summaries from the previous monograph on chlorfenvinphos.

TOXICOLOGICAL EVALUATION

Levels that cause no toxic effect

Mouse: 25 ppm, equal to 3.7 mg/kg bw per day (two-year carcinogenicity study)

Rat: 3 ppm, equivalent to 0.15 mg/kg bw per day (two-year toxicity/ carcinogenicity study)

1 ppm, equivalent to 0.05 mg/kg bw per day (two-generation reproductive toxicity study)

1 mg/kg bw per day (maternal toxicity in teratogenicity study)

Dog: 100 ppm, equal to 2.8 mg/kg bw (one-year toxicity study)

Rabbit: <25 mg/kg bw per day (maternal toxicity in teratogenicity study)

Estimate of acceptable daily intake for humans

0 - 0.0005 mg/kg bw

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

1. Delayed neurotoxicity study in chickens, with estimation of neuropathy target esterase.

2. Further observations in humans.

3. *In vivo* pharmacokinetic studies in mammals.

4.10 CHLORMEQUAT (015)

TOXICOLOGY

Chlormequat (chlorocholine chloride) was previously evaluated by the Joint Meeting in 1970 and 1972. In 1972 an ADI of 0.05 mg/kg bw was established on the basis of the NOAEL in a reproductive toxicity study in rats. The compound was reviewed by the present Meeting as a result of the CCPR periodic review programme.

In experiments with ^{14}C-labelled chlormequat in rats, which were reported only in summary form, absorption was rapid and elimination was essentially complete within 48 h, almost entirely via the urine; less than 1% of the administered dose remained in the tissues. Accumulation of ^{15}N-labelled material in the kidneys was reported, but experimental details were incomplete and detailed evaluation was not possible. The biotransformation of chlormequat has been little studied; it was suggested that the only metabolites found in rat urine may have been other salts of chlorocholine.

Pharmacological tests in mice, rats, rabbits and cats administered chlormequat intravenously revealed a stimulatory effect on the parasympathetic nervous system and a myoneural blocking action. Further work showed that chlormequat is a partial agonist of the nicotinic acetylcholine receptor; the affinity for muscarinic receptors was low and rather unselective.

Chlormequat was of moderate acute oral toxicity in rats, mice, hamsters and guinea-pigs (LD_{50} 200-1000 mg/kg bw), but there was some indication that rabbits and dogs are more sensitive (LD_{50} 50-80 mg/kg bw). Signs of toxicity may have been associated with pharmacological action, and there were no consistent treatment-related findings at autopsy. WHO has classified chlormequat as slightly hazardous.

In a recently completed four-week dietary toxicity study in rats the NOAEL was 1500 ppm, equal to 137 mg/kg bw per day, on the basis of reduced body-weight gain and depression of serum creatinine concentrations. These results are largely in agreement with those of older studies in rats lasting up to 90 days. In dogs the NOAEL in an unsatisfactory two-year study was 300 ppm in the diet, equal to 7.5 mg/kg bw per day.

The potential carcinogenicity of chlormequat was investigated in dietary studies in rats and mice carried out in the early 1970s. Those experiments did not comply with contemporary standards. In carcinogenicity studies in rats and mice reported by the National Cancer Institute in the USA in 1979, rats were fed dietary levels of 0, 1500 or 3000 ppm for 108 weeks and mice were fed dietary levels of 0, 500 or 2000 ppm for 102 weeks. There were no signs of reaction to treatment in either species and chlormequat was not carcinogenic to rats or mice.

In a multigeneration study in rats, which was not conducted according to currently acceptable scientific standards, chlormequat had no effect on reproductive performance at dietary levels up to 900 ppm; however, histopathological examination revealed giant cells in the testicular tubules in four of ten F_3-generation rats treated with 900 ppm and two of ten F_3-generation rats treated with 300 ppm. The report suggested that this finding may be an expression of delayed maturation during spermatogenesis; the Meeting found the significance of the finding difficult to assess, but the NOAEL may thus be 100 ppm, equivalent to 5 mg/kg bw per day.

The teratogenic potential of chlormequat has been investigated in mice (following administration by intraperitoneal injection, gavage and via the diet), in rats by dietary administration and in hamsters and rabbits by gavage. Many of the study reports were available only in summary form, and detailed evaluation was not possible. In a dietary study in mice the number of malformations in animals fed 10,000 ppm from days 1 to 15 of gestation or 25,000 ppm from days 11 to 15 was reported to be slightly higher than that seen in controls, but the exact significance of this observation was difficult to assess. In hamsters, malformations and evidence of delayed development were seen following three doses of 100 mg/kg bw per day (on days 7-9 of gestation) or a single dose of 200, 300 or 400 mg/kg bw on day 8. Evidence of maternal and fetal toxicity was also obtained at these doses. Further evaluation of these data in hamsters was not possible, owing to lack of detail in the publication. A well-conducted study in which rabbits were dosed by gavage with up to 12 mg/kg bw per day was available for detailed review. Signs of maternal toxicity were seen at the highest dose level, but there was no evidence of teratogenicity or fetotoxicity.

Chlormequat has been adequately tested for genotoxicity in a range of *in-vitro* and *in-vivo* assays. The Meeting concluded that it was not genotoxic.

Although review of the available information raised no suspicion of significant toxicological concern, the Meeting concluded that in view of the inadequacy of the information available in comparison with acceptable contemporary standards, it was impossible to maintain the ADI for chlormequat.

A toxicological monograph was prepared summarizing the data received since the previous evaluation, as well as relevant data from the previous monograph and monograph addendum on this pesticide.

TOXICOLOGICAL EVALUATION

Levels that cause no toxic effect

Mouse: 2000 ppm, equivalent to 286 mg/kg bw per day (102-week carcinogenicity study)

Rat: 1500 ppm, equal to 137 mg/kg bw per day (four-week toxicity study)
3000 ppm, equivalent to 150 mg/kg bw per day (108-week carcinogenicity study)

Rabbit: 6 mg/kg bw per day (maternal toxicity in teratogenicity study)
12 mg/kg bw per day (fetotoxicity and teratogenicity in teratogenicity study)

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

Updating of studies to meet acceptable standards

RESIDUE AND ANALYTICAL ASPECTS

Chlormequat is a plant growth regulator used as a stalk stabilizer in cereals and for the inhibition of vegetative growth and promotion of flowering in fruits and vegetables. It was evaluated by the JMPR before 1976, re-evaluated for residues several times up to 1985 and proposed for re-evaluation under the periodic review programme at the 19th Session (1989) of the CCPR. The 1990 CCPR indicated that there appeared to be continued use, but there was no indication of the availability of data. Cancellation of the CXLs was proposed if no data were provided. The 1991 CCPR scheduled a review for the 1994 JMPR. The Meeting received information on GAP and data from supervised trials on pears, grapes, tomatoes, mushrooms, cereals, cotton and rape.

In metabolism studies on cows, goats and hens chlormequat was rapidly excreted unchanged, mainly in the urine (or excreta of the hens), and did not accumulate in milk, eggs or tissues.

The metabolism of chlormequat in barley and wheat differed according to the treatment (on roots or leaves) and the developmental stage of the plant. The literature reports that metabolic rates in cereals range from stable (only 2 to 10% metabolized) to 50% conversion into choline, betaine, glycine, serine and CO_2, and incorporation into proteins 7.5 days after application.

The degradation of chlormequat in soil by micro-organisms proceeds very rapidly: its half-life varies between <1 and 28 days. The compound is mineralised to CO_2; other degradation products could not be identified.

The analytical determination of chlormequat in plant material is difficult owing to the necessary separation of chlorocholine from native choline. If separation is not quantitative high blank values are found, which may lead to false positive results.

The extraction of chlormequat residues from plant or animal matrices is carried out with

methanol or ethanol. The active ingredient is separated from native choline and other plant constituents by cation exchange or column chromatography on aluminium oxide and dichloromethane/water partition.

Former publications described photometric (dipicrylamine complex) or TLC (Dragendorff reagent) determination. The limit of determination for the semi-quantitative TLC method was reported to range from 0.1 mg/kg (cereal grains, green plants) to 0.3 mg/kg (cereal straw) with recoveries between 70 and 80 %. In some cases these methods were not validated.

Gas-chromatographic determination is carried out after conversion to *N*,*N*-dimethyl-2-(phenylthio)ethylamine, with detection by a sulphur-specific flame-photometric detector. The limit of determination is 0.05 mg/kg for cereal green plants, grains and milk, and 0.2 mg/kg for straw.

HPLC determination has been carried out by ion-pair chromatography with conductivity detection. The limit of determination was 0.05 mg/kg for the green matter, grain and straw of wheat.

Chlormequat was stable in samples of wheat stored at -18°C for 32 weeks.

Processing studies on cereals and rape showed the same residue levels in unprocessed grain, wholemeal and wholemeal bread (winter rye, winter wheat), an accumulation in the cereal brans, and a reduction in winter wheat flour, oat flakes and rape seed oil.

Because the residues from supervised trials were calculated as chlormequat chloride in most cases the original values were expressed as chlormequat and evaluated as follows.

As the Meeting withdrew the ADI for chlormequat, all estimates of maximum residue levels are recorded as Guideline Levels, not recommended as MRLs.

Pears. Data from seven trials in Norway were made available to the Meeting, but the spray concentrations ranged from 0.44 to 0.5 kg ai/hl whereas GAP concentrations are 0.005-0.18 kg ai/hl. Of the ten Dutch supervised trials received, three trials (twelve values) were according to GAP (2 applications, 1.1-1.8 kg ai/ha) although the PHI, 101-124 days, was longer than the Dutch PHI of 90 days. The residues ranged from 3.5 to 8.1 mg/kg calculated as chlormequat cation. The Meeting estimated a maximum residue level of 10 mg/kg for pears to replace the previous estimate (3 mg/kg).

Grapes and dried grapes. The use of chlormequat on grapes and vines is registered in Australia, Italy, Peru and Spain. Only two German trials on grapes were available, and they were not according to GAP. The Meeting agreed to withdraw the previous estimates for grapes and dried grapes of 1 mg/kg.

Tomatoes. The use of chlormequat on tomatoes is registered in Argentina, Italy and Peru. The Meeting received data from six trials from the UK, but there is no GAP in the UK or a country with comparable conditions. A maximum residue level could not be estimated.

Mushrooms. Four supervised trials on oyster mushrooms cultivated on cereal straw were provided from Germany. In all cases the straw used came from commercial producers and

contained residues from 0.8 to 5.3 mg/kg (calculated as chlormequat chloride). Eleven residue values in mushrooms determined 26-160 days after inoculation of mushroom spores ranged from 0.6 to 5.5 mg/kg, calculated as chlormequat chloride, or from 0.47 to 4.3 mg/kg if calculated as chlormequat cation. The data suggest that residues in straw and mushrooms are about the same. It was recognized that residues will occur in mushrooms grown on treated straw. In the absence of data on mushrooms grown on straw containing residues close to the highest level expected to occur in practice (20 mg/kg) the Meeting did not estimate a maximum residue level for mushrooms.

Barley. In most cases the PHI is the time between treatment and harvest; a PHI is specified only in Germany, where it is 42 days.

Three trials on summer barley from Denmark (1 treatment, 0.46-0.61 kg ai/ha), two from Germany (1 treatment, 0.61 kg ai/ha) and seven from Sweden (1 treatment, 0.46 kg ai/ha) approximated GAP in The Netherlands, Belgium and Germany. After PHIs of 34-111 days the residues (15 values) in grain ranged from <0.05 to 0.62 mg/kg chlormequat chloride, which corresponds to <0.05-0.48 mg/kg chlormequat cation. From the UK, three residue values from trials according to GAP ranged from 0.18 to 0.37 mg/kg as chlormequat chloride, or 0.14 to 0.29 mg/kg as chlormequat cation. Canada provided six summer barley trials with 24 residue values (0.3-1.5 mg/kg calculated as chlormequat cation), but Canada has no GAP for chlormequat.

The Meeting evaluated eleven supervised trials on winter barley from France and seven from the UK. The residues in grain ranged from <0.05 to 0.58 mg/kg as chlormequat chloride or from <0.05 to 0.45 mg/kg calculated as chlormequat cation. Four residue values from Sweden, three from Germany, two from Switzerland and one from Denmark, evaluated according to the GAP of Belgium, The Netherlands, the UK or France, showed similar residues of 0.05 to 0.42 mg/kg as the chloride, or <0.05 to 0.33 mg/kg as the cation.

The Meeting estimated a maximum residue level of 0.5 mg/kg for barley.

Maize. Chlormequat is authorized only in Belgium. There were nine supervised trials from Germany which did not correspond to Belgium GAP. A maximum residue level could not be estimated.

Oats. The use of chlormequat on oats is registered in many countries, with one to two treatments and application rates from 1 to 1.8 kg ai/ha. In most cases the PHI is determined by approved use as the time between treatment and harvest, but in Germany (only) the PHI is 42 days. The Meeting evaluated three values from trials according to GAP in the UK and 18 German trials with 24 residue values (1 treatment, 1.2-1.4 kg ai/ha, PHI 42-91 days) on the basis of the GAP of Belgium, The Netherlands and Luxembourg. The residues ranged from <0.05 to 9.2 mg/kg as chlormequat chloride, or from <0.05 to 7.1 mg/kg if calculated as chlormequat cation. The Meeting agreed to maintain the current estimate of 10 mg/kg as a GL for oats.

Rye. The Meeting received data on 30 trials on winter rye from Denmark, Germany, Sweden and the UK, but only two from Germany, one from Sweden and two from the UK reflected approximately the national GAP. Two values from Denmark could be evaluated on the basis of Swedish, and five from Sweden on the basis of British GAP. Three German trials on summer rye could also be used. The residues were <0.05 to 2.6 mg/kg as chlormequat chloride, or <0.05 to 2 mg/kg as chlormequat cation. The Meeting estimated a maximum residue level of 3 mg/kg for

rye to replace the previous estimate (5 mg/kg).

Wheat. Numerous results were provided to the Meeting because the main use of chlormequat world-wide is for the stem stabilization of wheat. Of 38 German trials on summer wheat, two were in accordance with German GAP for summer wheat, but six reflected GAP for winter wheat and were evaluated. Although only two of the 17 residue trials from Germany on winter wheat were in accordance with German GAP, they could be evaluated on the basis of British GAP. Eleven residue values on winter wheat from trials according to GAP were available from the UK. The Meeting also evaluated three residue values from Denmark and three from France on the basis of Dutch GAP. The residues in grain ranged from <0.05 to 1.4 mg/kg calculated as chlormequat chloride, which corresponds to <0.05-1.1 mg/kg if calculated as chlormequat cation. The Meeting estimated a maximum residue level of 2 mg/kg for wheat to replace the previous estimate (5 mg/kg).

Cotton seed. Twelve residue values from four Indian trials were approximately in accordance with GAP (0.063-0.088 kg ai/ha) and ranged from 0.33 to 0.52 mg/kg as chlormequat chloride, or 0.26-0.4 mg/kg if calculated as chlormequat cation. The Meeting estimated a maximum residue level of 0.5 mg/kg for cotton seed.

Rape seed. The use of chlormequat on rape is registered in Belgium and the UK. The Meeting received residue data from Germany and the UK, but only two British trials reflected UK GAP. Nine German trials were approximately in line with Belgian GAP (0.69 kg ai/ha). In other German trials applications were 0.92 kg ai/ha, slightly higher than Belgium GAP but within the GAP of the UK (1.9 kg ai/ha). After evaluating the total of twelve values from 1.4 to 5.8 mg/kg as chlormequat chloride, or 1.1 to 4.5 mg/kg if calculated as chlormequat cation, the Meeting estimated a maximum residue level of 5 mg/kg for rape seed.

Rape seed oil, crude. Three processing studies carried out in Germany and the UK showed that, because chlormequat is ionic, the residues in the oil are below the limit of determination. The Meeting estimated a maximum residue level for rape seed oil, crude, of 0.1* mg/kg as being a practical limit of determination.

Food of animal origin

Milks and milk products. Twelve dairy cattle were divided into three groups and treated with 9, 30 or 50 mg ai/cow/day for 14 days (corresponding to 0.2 ppm, 0.6 ppm or 1 ppm in the daily feed that would be ingested by a cow consuming a total of 50 kg green feed per day). The maximum residue in the milk of the high dose group was 0.068 mg/kg on day 3. As the residues in green feed may be much higher (the MRL recommended for rye forage and oat forage (green) is 20 mg/kg) and there were inconsistencies in the reported analytical method an MRL for milks could not be recommended. The Meeting agreed to withdraw the previous estimates of 0.1* mg/kg for the milk of cattle, goats and sheep, and for milk products.

Poultry. Although feeding studies on hens with radiolabelled active ingredient for ten days at 0.3 mg ai/bird/day (corresponding to 3 ppm in the daily feed) showed that the total ^{14}C residues observed in eggs, poultry meat and edible offal of poultry were <0.1 mg/kg, the Meeting did not recommend an MRL because a residue analytical method for unlabelled chlormequat in these commodities was not provided.

Animal feeds

The Meeting considered all available residue data for barley, oat, rye and wheat straw and fodder, and estimated individual maximum residue levels of 20 mg/kg to replace the previous estimates of 50 mg/kg.

Barley straw and fodder, dry. Residues in supervised trials in Europe in the straw of summer and winter barley ranged from 0.36 to 16 mg/kg as chlormequat chloride or 0.28 to 12 mg/kg as chlormequat cation.

Oat straw and fodder, dry. Thirty residue values on straw were received from Germany and the UK, which ranged from <0.1 to 25 mg/kg as chlormequat chloride or <0.1 to 19 mg/kg as chlormequat cation.

Rye straw and fodder, dry. The Meeting evaluated residue data on straw from Denmark (3 values), Germany (3 values for winter rye, 4 for summer rye), Sweden (1 value) and the UK (2 values) in the light of British, German and Swedish GAP. The residues ranged from <0.1 to 18 mg/kg as chlormequat chloride or from <0.1 to 14 mg/kg as chlormequat cation.

Wheat straw and fodder, dry. An evaluation of 55 values from Denmark, France, Germany and the UK showed that after 42-131 days the residues in straw ranged from 0.29 to 29 mg/kg as chlormequat chloride, which corresponds to 0.22 to 22 mg/kg (only one value >20 mg/kg) as chlormequat cation.

Oat and rye forage (green). Residue data (15 values) on whole green oat plants from German trials with PHIs of 19-23 days were 0.69-17 mg/kg as chlormequat chloride, or 0.53-13 mg/kg as chlormequat cation. Residues (15 values) in whole green rye plants from German trials with PHIs of 17-22 days (summer rye) and 27-32 days (winter rye) ranged from 1.9 to 28 mg/kg as chlormequat chloride, or from 1.5 to 22 mg/kg as chlormequat cation (only one value >20 mg/kg).

The Meeting considered all the available residue data and estimated individual maximum residue levels of 20 mg/kg for oat forage (green) and rye forage (green).

Processed foods and feeds of plant origin

Unprocessed rye and wheat bran. Processing studies on wheat and rye showed that the residues in brans are twice in wheat and four times in rye those in the raw grain. In view of the estimates for rye (3 mg/kg) and wheat (2 mg/kg), the Meeting estimated maximum residue levels of 10 mg/kg and 5 mg/kg for unprocessed rye and wheat bran respectively.

Rye flour and wholemeal. A processing study on winter rye showed the same residue level in grain, wholemeal and flour. In view of the maximum residue level estinated for rye (3 mg/kg), the Meeting estimated a maximum residue level of 3 mg/kg for rye wholemeal. Because the high residue level in rye flour could not be explained, the Meeting could not estimate a maximum residue level for rye flour.

Wheat flour. A processing study on winter wheat showed a 78% reduction of the residues from 0.72 mg/kg in grain to 0.16 mg/kg in flour. On the basis of the maximum residue level estinated for wheat (2 mg/kg), the Meeting estimated a maximum residue level of 0.5 mg/kg for wheat flour.

Wheat wholemeal. A processing study on winter wheat showed only a minor reduction of the residues from 0.72 mg/kg in grain to 0.54 mg/kg in wholemeal. The Meeting therefore estimated a maximum residue level of 2 mg/kg for wheat wholemeal, the same as that for wheat.

Wholemeal bread. Processing studies on winter wheat and rye showed a reduction of the residues from 0.72 mg/kg in wheat grain to 0.31 mg/kg in wholemeal bread, but no reduction in the case of rye (0.73 mg/kg in the grain, 0.86 mg/kg in wholemeal bread).

The estimated maximum residue levels are recorded as GLs in Annex 1.

FURTHER WORK OR INFORMATION

Desirable

1. New feeding studies on cows with determination of residues in milk, meat and edible offal of cattle.

2. New feeding studies on poultry with determination of residues in eggs, meat and edible offal of poultry.

3. Residue analytical method for meat, eggs and edible offal of poultry and cattle.

4. Processing studies on cotton seed for residue determination in cotton seed oil.

5. Investigations on mushrooms grown on straw with a residue level of 15 to 20 mg/kg.

4.11 CHLORPYRIFOS-METHYL (090)

RESIDUE AND ANALYTICAL ASPECTS

The 1994 CCPR was informed that only one response had been obtained, from the USA, to a CCPR Circular Letter (CL 1993/11-PR) inviting governments to inform the JMPR of their current GAP for all cereals. Several delegations indicated that the MRLs for barley and oats were too high. The delegation of the USA stated that the post-harvest use on rice was not accommodated. The delegations were requested to send information on GAP for barley, oats and rice to the JMPR by the end of May, 1994, for evaluation.

The comments previously provided by the USA do not appear to have been considered by

the 1993 JMPR. The present MRL for rice does not include post-harvest applications. The proposed MRLs for barley, oats and rice were reassessed using data from the 1991 JMPR review and data provided by Australia and the USA.

The USA has reported that US residue data (obtained from samples treated according to GAP) for the post-harvest storage use of chlorpyrifos-methyl on rice showed residues of ≤6.3 mg/kg at ≥4 days after treatment at a rate of 6 g ai/tonne. This rate is also the US level recommended for the post-harvest treatment of cereals. A report from Australia indicated that lower rates of chlorpyrifos-methyl (e.g. 5 mg/kg) were not effective for long-term storage protection under Australian conditions. In addition it stated that sublethal doses promoted resistance, threatening efficacy.

In summary the Australian report concluded that, owing to difficulties in obtaining samples for analysis, any lowering of the MRL below 10 mg/kg would seriously jeopardize the effective use of this insecticide.

A review of all the residue data from the 1991 JMPR report indicates that residues of chlorpyrifos-methyl in stored barley, oats and rice do not exceed 7 mg/kg. The current MRL of 10 mg/kg for barley and oats is supported by the data provided, which also support an MRL of 10 mg/kg for the post-harvest use of chlorpyrifos-methyl on rice.

The Meeting recommended an MRL of 10 mg/kg for chlorpyrifos-methyl on rice to replace the CXL of 0.1 mg/kg.

4.12 CLETHODIM (187)

(±)-2-[(*E*)-1-[(*E*)-3-chloroallyloxyimino]propyl]-
5-[2-(ethylthio)propyl]-3-hydroxycyclohex-2-enone

The compound was considered for the first time by the present Meeting.

Clethodim is a selective post-emergence herbicide, active against annual and perennial grasses and similar narrow-leaved weeds, such as Bermuda grass (*Cynodon dactylon*), Quackgrass (*Agropyron repens*), Rhizome Johnson grass (*Sorghum halepense*) and "volunteer" cereals. It exerts its activity by inhibiting acetyl-coenzyme A carboxylase, an enzyme common to both fatty acid and flavonoid biosynthetic pathways. Interference occurs at the acetyl-CoA → malonyl CoA transferase site.

TOXICOLOGY

Clethodim was readily absorbed upon oral administration to rats. Excretion was rapid, predominantly in the urine, with lesser amounts eliminated in the faeces and as carbon dioxide. There were no significant dose-related or sex-specific differences in the elimination pattern or tissue distribution, and there was no evidence of bioaccumulation.

The dominant metabolic pathway proposed for clethodim in rats is oxidation to

clethodim sulphoxide. Other postulated pathways are cleavage of the N-O bond to form the imine, conversion of the *S*-ethyl group to *S*-methyl, formation of the oxazole, and hydroxylation at the 5- position. The urinary metabolites identified were the sulphoxides and sulphones of clethodim and 5-hydroxy-clethodim, the sulphoxides of the imine and *S*-methyl-clethodim, and the sulphone of the oxazole.

Clethodim demonstrated slight to moderate acute oral toxicity in rats and mice. WHO has not classified clethodim with regard to its toxic hazard.

The primary effect of treatment with clethodim after short- and long-term dietary exposure in mice, rats and dogs was on the liver. Hepatic effects were manifest as increased liver weights and centrilobular hypertrophy. A study in rats administered clethodim at 250 mg/kg bw per day did not provide evidence for liver cytochrome P450 induction.

In a four-week study in mice given dietary concentrations of 0, 100, 250, 625, 1500 or 4000 ppm the NOAEL was 250 ppm, equivalent to 38 mg/kg bw per day, on the basis of evidence of slight anaemia at 625 ppm and above. In a 78-week toxicity/carcinogenicity study in which mice received dietary levels of 0, 20, 200, 1000 or 2000/3000 ppm the NOAEL was 200 ppm, equivalent to 30 mg/kg bw per day, on the basis of hepatic effects and an increased incidence of alveolar lung macrophages at 1000 ppm and above.

In a five-week study in which rats received dietary levels of 0, 5, 200, 1000, 4000 or 8000 ppm the NOAEL was 200 ppm, equal to 13 mg/kg bw per day, on the basis of liver hypertrophy and evidence of slight anaemia at 1000 ppm and above. A 13-week study at dietary concentrations of 0, 50, 500, 2500 or 5000 ppm and a two-year feeding study at dietary levels of 0, 5, 20, 500 or 2500 ppm in rats revealed an NOAEL of 500 ppm, equal to 25 mg/kg bw per day in the first study and equal to 16 mg/kg bw per day in the second. The NOAEL was based on decreased body weights and liver hypertrophy at dietary levels of 2500 ppm and above.

In dogs, 13-week oral administration of capsules of clethodim at doses of 0, 1, 25, 75 or 125 mg/kg bw per day resulted in an NOAEL of 25 mg/kg bw per day, on the basis of increased liver weight and cholesterol levels at 75 mg/kg bw per day and above. In a one-year study at doses of 0, 1, 75 or 200/300 mg/kg bw per day, the NOAEL was 1 mg/kg bw per day on the basis of treatment-related effects on the liver at 75 mg/kg bw per day and above.

Clethodim was not carcinogenic when fed to mice or rats at dietary levels up to 2500 ppm.

A two-generation study in which rats were administered clethodim in the diet at 0, 5, 20, 500 or 2500 ppm did not reveal any adverse effect on reproduction. The NOAEL was 500 ppm, equal to 39 mg/kg bw per day, on the basis of decreased parental body weights and food consumption at 2500 ppm.

Teratogenicity studies were conducted with clethodim in rats at doses of 0, 10, 100, 350 or 700 mg/kg bw per day and in rabbits at 0, 25, 100 or 300 mg/kg bw per day. In rats, the NOAEL for maternal toxicity was 100 mg/kg bw per day. Fetal toxicity was observed at the maternally-toxic doses of 350 and 700 mg/kg bw per day. An increased incidence of malformations, specifically tail defects (short, filamentous or absent tails), was observed at

the maternally-toxic and lethal dose level of 700 mg/kg bw per day. In rabbits, maternal toxicity was observed at 100 and 300 mg/kg bw per day, resulting in an NOAEL of 25 mg/kg bw per day. There were no adverse effects on the rabbit fetus and no evidence of teratogenic potential at doses up to 300 mg/kg bw per day.

Clethodim was adequately tested for genotoxicity in a series of *in-vitro* and *in-vivo* assays. The Meeting concluded that clethodim was not genotoxic.

Although the imine sulphone and 5-hydroxy sulphone metabolites of clethodim have been reported to occur in higher amounts in plants than in animals, neither of the metabolites was more toxic than the parent clethodim in acute, short-term and teratogenicity studies. Similarly, these metabolites displayed no evidence of genotoxic potential.

An ADI was established on the basis of the NOAEL of 1 mg/kg bw per day in the one-year study in dogs and a safety factor of 100.

A toxicological monograph was prepared, summarizing the data that were reviewed at the present Meeting.

TOXICOLOGICAL EVALUATION

Levels that cause no toxic effect

Mouse: 200 ppm, equivalent to 30 mg/kg bw per day (78-week toxicity/carcinogenicity study)

Rat: 500 ppm, equivalent to 16 mg/kg bw per day (two-year toxicity/carcinogenicity study)

Rabbit: 25 mg/kg bw per day (teratogenicity study)

Dog: 1 mg/kg bw per day (one-year toxicity study)

Estimate of acceptable daily intake for humans

0 - 0.01 mg/kg bw

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

Observations in humans.

RESIDUE AND ANALYTICAL ASPECTS

Metabolic studies using radiolabelled clethodim were carried out on rats, a lactating goat and

chickens. In all cases, most (>90%) of the radioactivity was rapidly excreted in the urine and faeces.

The metabolic study in rats was undertaken with the objectives of determining the absorption, distribution, excretion and metabolic fate, including metabolic characterization, of propyl[1-^{14}C]clethodim administered orally to male and female rats at different dose rates, Low Dose (4.4 mg/kg bw), Repeated Dose (4.8 mg/kg bw) and High Dose (468 mg/kg bw) and treated with a single oral dose of propyl[1-^{14}C]clethodim. The autoradiogram TLC profiles of urinary metabolites were very similar for males and females within a dose group and also between dose groups. Clethodim, clethodim sulphoxide, clethodim sulphone, clethodim imine sulphoxide, *S*-methyl sulphoxide and 5-hydroxy sulphone were isolated from urine and positively identified by chemical ionization and electron-impact mass spectrometry, TLC co-chromatography and HPLC co-chromatography. Further evidence for the presence of these metabolites and of the 5-hydroxy sulphoxide was obtained by LC-MS, whereby the imine sulphoxide, oxazole sulphoxide, oxazole sulphone, *S*-methyl sulphoxide, trione sulphoxide, 5-hydroxy sulphoxide, and clethodim sulphoxide were detected in the 12-hour urine collection from the High Dose group males and females. Thus, it appears that clethodim is rapidly absorbed and then (a) oxidized to clethodim sulphoxide (dominant) and thence to clethodim sulphone; (b) converted to the *S*-methyl analogue via a sulphonium cation intermediate; (c) converted to imine, or (d) hydroxylated at the 5 position. The proposed *S*-methyl-clethodim would follow the dominant metabolic process and form the observed *S*-methyl sulphoxide and smaller amounts of *S*-methyl sulphone. Similarly, the imine would rapidly be oxidised to imine sulphoxide and imine sulphone. Any 5-hydroxy-clethodim formed (this was not detected) would be rapidly oxidized to the observed 5-hydroxy sulphoxide and sulphone.

In goats, 91% of the radioactive dose was excreted in the faeces and urine; the concentration in the milk reached a plateau of 0.035 mg/l by the second day. There was little evidence of accumulation in tissues, although some radiocarbon was observed in the liver (0.41 mg/kg) and kidney (0.38 mg/kg).

In the chicken study, identification of the metabolites was focused on the edible tissues and eggs, using TLC and HPLC. Three major compounds were identified: in order of increasing amounts clethodim, clethodim sulphone and clethodim sulphoxide. In the skin clethodim sulphoxide accounted for as much as 57% of the radioactivity, while the proportions of the sulphone in the tissues ranged from 10.2 to 31.2%. On average, the parent clethodim amounted to only a few per cent of the radioactivity, although a higher percentage was observed in the fat. The metabolic pathway was simpler than that observed in other animals. None of the imine analogues, 5-hydroxy analogues or *S*-methyl analogues that were found in the rat and goat were seen in the chicken.

Results from four studies on the fate of clethodim in soils showed that metabolism by micro-organisms dominated the degradation process, with no photoproducts being formed. The half-life of clethodim was 1 to 3 days under aerobic conditions, the major product being the sulphoxide and the only volatile product CO_2. Under anaerobic conditions the sulphoxide was again the major product.

Under anaerobic conditions the half-lives of clethodim were 177 days at 25°C and 559 days at 5°C, the degradation being primarily microbiological with the metabolites being degraded at the same rate as they were formed. Under aerobic conditions the degradation pattern was

similar but quicker, with half-lives of clethodim of 5 days at 25°C and 23 days at 5°C, the only volatile metabolite again being CO_2.

In the analytical methods used in the reported studies, all clethodim-related metabolites which retain the 2-cyclohexene-1-one structure are oxidized to one of two compounds, depending upon whether 5-hydroxylation has occurred. Clethodim and its metabolites are extracted from plant material with water and methanol and the extract is partitioned into dichloromethane. After clean-up by alkaline precipitation and acidic back-extraction, oxidation with hydrogen peroxide at Ph 9-10 yields dicarboxylic acids which are methylated with methanol to yield the two esters DME, dimethyl 3-[2-(ethylsuphonyl)propyl]pentanedioate, and DME-OH, dimethyl 3-[2-(ethylsulphonyl)propyl]-3-hydroxypentanedioate. After a silica gel or methylene chloride partition clean-up step, these are then determined by gas chromatography using a flame-photometric detector in the sulphur mode. The limit of determination is of the order of 0.05 mg/kg. The total residue of DME + DME-OH is then expressed as clethodim equivalents: mg/kg clethodim = (mg/kg DME x 1.22) + (mg/kg DME-OH x 1.16). The procedure has proved to be adaptable to the many food commodities so far examined and should be suitable for regulatory use. However, it is essential also to use the confirmatory HPLC procedure to show that the residues found are from clethodim and not some other similar herbicide such as sethoxydim.

Clethodim and related metabolic compounds show three types of isomerism, geometric, tautomeric and enantiomeric, and as a result some chromatograms can show multiple peaks or spots owing to the resolution of some of these isomers. Care in analytical interpretation is therefore necessary.

Residue levels (0.05 to 0.25 mg/kg) of clethodim, *S*-methyl-clethodim sulphoxide and 5-hydroxy-clethodim sulphone in bovine tissues (fat, kidney, liver and muscle) and milk showed no degradation when stored at -20°C up to 5 months. In similar studies on residues in chicken eggs and tissues (fat, gizzard, liver and muscle), all components were stable up to 8 weeks at -18 ± 3°C, although 5-hydroxy-clethodim sulphone appeared to be slightly less stable in the gizzard, liver and muscle samples for the 6-week period, when less than 90% of the added material was recovered; it was stable in the other matrices studied and over 3- to 4-week periods. When fuzzy cotton seed containing residues of clethodim ranging from 0.38 to 1.44 mg/kg was stored up to six months at -20°C, analysis showed 80 to 128% of the initial residues.

Clethodim is available as a 24% emulsifiable concentrate. Residue data obtained from trials on about 30 crops in several countries were provided, although there were only very limited or summary data in many cases. Of the crops on which its use is registered, it appears that the major uses of clethodim are on beans, field peas, soya beans, potatoes, cotton, rape seed, sugar beet and sunflower.

Insufficient or inadequate data were provided for recommendations to be made in respect of artichoke, beetroot, broad beans, carrot, cauliflower, clover, common bean, fodder beet, garden peas, garlic, leek, lentil, lettuce, linseed, lupin, onion, peach, peanut, peppers (sweet), spinach, summer squash or tomato.

Peach. In six trials in Spain no residues were above the limit of determination of 0.03 mg/kg.

Garlic. One trial in Spain showed no residue above 0.03 mg/kg, 21 days after treatment.

Leek. Treatment of leeks in France gave residues up to 0.34 mg/kg at a 28-day PHI and 0.17 mg/kg at 56 days.

Onion. Onions treated in New Zealand showed no residues above the limit of determination (0.03 mg/kg) 42 or 84 days later. Similarly, onions treated in Italy gave no residues at 20, 30 or 40 days PHI. In Moldavia, trace amounts of clethodim, <0.1 mg/kg, were reported, 55 days after application.

Cauliflower. One trial in New Zealand gave a residue of 0.28 mg/kg 42 days after treatment but <0.03 mg/kg after 84 days.

Squash, Summer. Treatment of zucchini in a trial in Italy gave residues below 0.03 mg/kg at 28, 33 and 42 days PHI.

Peppers, Sweet. Residues of 0.1, 0.05 and 0.05 mg/kg were found 18, 28 and 38 days (respectively) after treating sweet peppers in Italy.

Tomato. Treatment of tomatoes in Italy gave residues of 0.06 mg/kg at 30 days but <0.03 mg/kg after 51 days. In six trials in Spain from 1989 to 1992, a maximum residue of 0.05 mg/kg was found once at day 0 but all other results were at or below 0.03 mg/kg at 0, 21, 22 or 60 days after application.

Lettuce, Head. Lettuces were treated in France with clethodim at rates of 0.12, 0.18, 0.18 and 0.48 kg ai/ha; the corresponding residues were 0.19, 0.13, 0.27 and 0.34 mg/kg at 28 days PHI. Trials in Italy in 1990 at 0.24 kg ai/ha yielded residues of 0.31, 0.16, 0.05 and 0.07 mg/kg at 0, 10, 15 and 20 days after treatment.

Spinach. In France, spinach was treated with clethodim at 0.12, 0.18, 0.18 and 0.48 kg ai/ha; residues were respectively 0.14, 0.19, 0.10 and 0.15 mg/kg at 15 days and 0.04, 0.08, 0.03 and 0.08 mg/kg at 30 days.

Peas. Marrowfat peas treated in New Zealand showed residues in the podded peas of 0.29 mg/kg after 43 days. The pea silage contained 0.47 mg/kg at the same time.

Broad bean. One trial on broad beans in Spain gave residues below the limit of determination (0.03 mg/kg) in the bean and in the husk.

Common bean. Green beans treated in Belgium showed no residues in the pods above the limit of determination of 0.025 mg/kg. French beans treated in France also gave no residues in the beans above 0.03 mg/kg. Green beans treated in Italy with clethodim yielded residues of 0.11 and 0.09 mg/kg at 20 and 24 days PHI, respectively. However, none of these treatments were in accordance with the GAP of the countries concerned.

Beans (dry). In Brazil, beans were treated with clethodim at rates of 0.084, 0.108, 0.168 and 0.216 kg ai/ha. At PHIs of 65 and 85 days, the dry beans showed no residues above the limit of determination of 0.05 mg/kg, although at 25 and 45 days PHI residues in the beans ranged from 0.37 to 0.93 and 0.06 to 0.14 mg/kg, respectively. The Meeting estimated a maximum residue level of 0.1 mg/kg for beans,dry.

Field peas (dry). Field peas were treated in Australia with clethodim at rates up to 0.24 kg ai/ha. At harvest, 110 days after application, residues in the dry pea seeds and in the straw were all below the limit of determination of 0.03 mg/kg. Four trials were made on field peas in the UK at rates of 0.36 and 0.72 kg ai/ha. At the lower rate, residues in the pea seed and the husk were not above 0.03 mg/kg at PHIs of 53 and 85 days. At the higher application rate, residues of 0.04 and 0.05 mg/kg were found in the peas at 53 days, and <0.03 and 0.08 mg/kg at 85 days.

When protein peas were treated in Belgium the residues in the seeds 41 days later were below 0.025 mg/kg. Protein peas were treated at six sites in France with clethodim at rates of 0.18, 0.48 and 0.96 kg ai/ha; residues were below 0.06 mg/kg at the lowest rate, up to 0.28 mg/kg at the middle rate and up to 0.75 mg/kg at the top rate, all at 82 days PHI.

The Meeting estimated a maximum residue level of 0.1 mg/kg for field pea (dry).

Lentil (dry). Lentils were treated in Spain with clethodim at 0.18 kg ai/ha. On the day of treatment, residues in the husk were 2.2 mg/kg; 21 days later they were 1.1 and 1.4 mg/kg.

Lupin (dry). When clethodim was applied at rates up to 0.24 kg ai/ha to lupins in Australia no residues were above the limit of determination of 0.1 mg/kg in the dried seed or in the straw at 167 days PHI.

Soya bean (dry). In three trials in Australia, soya beans were treated with clethodim at rates up to 0.24 kg ai/ha. No residues above the limit of determination of 0.1 mg/kg were found in either the dried seed or the straw at 109 days PHI.

In Brazil, a soya bean plantation was treated with clethodim at 0.084, 0.108, 0.168 and 0.216 kg ai/ha. Both the plant and dry beans were sampled at 13, 27, 52 and 91 days after application. At 91 days PHI, residues in both plant and beans were below the limit of determination of 0.05 mg/kg at all treatment rates. However, residues were found in both sets of samples at the other PHIs, reaching maxima of 1.3 mg/kg at 13 days, 2.4 mg/kg at 27 days and 0.29 mg/kg at 52 days in the dry beans. From these results, it appears that clethodim can be absorbed and translocated in soya bean plants and that the amount of clethodim residue in the beans is dependant on the growth stage of the crop at the time of application.

Trials were carried out on soya beans at three sites in Ontario, Canada using the maximum proposed label rate of application of 0.09 kg ai/ha. No residues were above the limit of determination of 0.05 mg/kg, although one result from nine was at that level. When a second application was made at the same rate immediately after the first, residues of 0.05, 0.06, 0.11, 0.11, 0.13 and 0.18 mg/kg were observed.

Two trials in France showed residues of 0.07 mg/kg in the mature beans after 87 days but <0.03 mg/kg in the dry seeds after 105 days.

From a trial in Italy using one application at 0.24 kg ai/ha, residues of 0.58, 0.23 and 0.35 mg/kg were found after 30, 50 and 69 days PHI, respectively. Three similar trials were carried out using two applications at 0.18 kg ai/ha which gave residues in the seed of 0.38, 0.29 mg/kg at 30 days, 0.15, 0.15 mg/kg at 45 days and <0.03, 0.05 mg/kg at 60 days PHI.

Summary data from applications up to 0.29 kg ai/ha to soya beans in the Ukraine indicated that no residues were detected in the beans at harvest.

Supervised trials of clethodim on soya beans were carried out at 12 sites in 10 States in the USA, all treatments being at 0.28 kg ai/ha, with two applications 14 days apart. At PHIs from 40 to 80 days, residues ranged from <0.04 to 10 mg/kg, apart from one result of 16 mg/kg at 53 days PHI for which the corresponding duplicate determination was 10 mg/kg. In addition, in order to determine the effect of the application rate on residues, at one site two applications at 0.45 kg ai/ha were also used; residues from these treatments gave 8.0 and 10.1 mg/kg at 61 days. The ratio between the mean results of these two trials (5.85:9.05 mg/kg) was 1.55, very close to the ratio between the applied doses (0.4:0.25 = 1.6), indicating that the residue levels were proportional to the applied rate. Aerial and ground applications were compared in two States; the residues found in the dry shelled soya beans were not significantly different, aerial spraying showing 4.6 and 0.73 mg/kg as compared with the 5.8 and 0.96 mg/kg found from ground spraying.

The Meeting estimated a maximum residue level of 10 mg/kg for soya bean, dry, 1 mg/kg for soya bean oil, crude and 0.1 mg/kg for soya bean oil, edible.

Beetroot. Summary data from trials of clethodim on beetroot treated in the Ukraine gave residues up to 0.9 mg/kg at 44 days but below 0.04 mg/kg at harvest.

Carrot. Application at 0.07 to 0.28 kg ai/ha to carrots in Moldavia and Russia showed no residues above the limit of determination (0.1 mg/kg) at harvest.

Fodder beet. Three trials of clethodim on fodder beet were carried out in France at rates up to 0.96 kg ai/ha. Residues were always below the limit of determination (0.03 mg/kg) in both the roots and tops at PHIs of 102 to 129 days.

Potato. Summary data from a trial in Belgium in 1990 showed residues of clethodim to be below 0.025 mg/kg.

When potatoes were treated with clethodim at three sites in Ontario and one in Nova Scotia, using the maximum proposed label rate of application of 0.09 kg ai/ha, only one of the sites in Ontario yielded residues above 0.05 mg/kg, these being 0.11 and 0.14 mg/kg as clethodim at PHIs of 46 and 61 days. When another set of samples was collected following a second application of clethodim at the same rate immediately after the first, residues were found in five of the eight samples examined, ranging from 0.13 to 0.25 mg/kg at PHIs of 45 or 46 days.

Potatoes treated in France in two trials gave residues in the tubers of <0.03, 0.08 mg/kg at 47 days PHI and <0.03, <0.03 at 80 days.

From trials carried out at three sites in Italy, apart from one result at 0.07 mg/kg, all residues were at or below the limit of determination of 0.03 mg/kg at PHIs of from 30 to 80 days. One trial in Morocco showed no residue after 91 days.

Summary data from trials in the Ukraine using applications of clethodim up to 1.2 kg ai/ha showed no residues in the tubers above the somewhat high limit of determination of 0.2 mg/kg.

The Meeting estimated a maximum residue level of 0.2 mg/kg for potato.

Sugar beet. Eleven trials of clethodim on sugar beet were carried out in France, using application rates of 0.18, 0.36, 0.48 or 0.96 kg ai/ha. Residues in the roots at PHIs from 112 to 136 days were always below the limit of determination (0.03 mg/kg), while in the beet tops residues were found in only two samples treated at the highest rate at 0.03 and 0.04 mg/kg.

Sugar beet treated in Germany gave no residues above 0.05 mg/kg in either the roots or the tops at 92 or 132 days PHI.

In two trials carried out in Italy, residues in the roots were 0.08, 0.11; 0.04, 0.08; and 0.06, 0.17 mg/kg at PHIs of 30, 45 and 59/60 days, respectively. Corresponding residues in the tops were 0.06, 0.23; 0.07, 0.07; and <0.03, 0.07 mg/kg.

In one trial in Morocco residues were below 0.03 mg/kg in the root after 153 days.

The Meeting estimated a maximum residue level of 0.2 mg/kg for sugar beet.

Artichoke, Globe. Globe artichokes treated in Italy gave residues of 0.5, 0.29 and 0.21 mg/kg after 20, 25 and 30 days, respectively.

Cotton seed. Cotton was treated in seven States in the USA with clethodim, using two applications at 0.28 kg ai/ha from 13 to 83 days apart, fuzzy cotton seed samples being taken 60 days after the last application. Total clethodim residues ranged from <0.11 to 0.48 mg/kg at 40 to 74 days PHI.

A second trial was conducted in California to study the effect of timing of the application on residues in cotton seed. The data showed that the residue levels decreased as the interval from the last application increased from 40 to 74 days, dropping from a maximum of 0.4 mg/kg to a minimum of <0.16 mg/kg; however, this difference may not be significant at those residue levels. Similarly, differences between residues found after aerial and ground spraying were not significant (aerial, 0.14, 0.12 mg/kg; ground, 0.22, 0.14 mg/kg).

The Meeting estimated a maximum residue level of 0.5 mg/kg for cotton seed, 0.1 mg/kg for cotton seed oil, crude and 0.05 mg/kg for cotton seed oil, edible.

Linseed. Summary data were provided from trials on linseed in Canada. Residues in the seed after treatment with 0.105 kg ai/ha were 0.07, <0.05, 0.08 and <0.05 mg/kg, at 67, 84, 95 and 108 days PHI. Summary data also indicated that residues were not detected (<0.03 mg/kg) in linseed from flax treated in the Ukraine at rates up to 0.29 kg ai/ha.

Peanut. Trials in Argentina gave residues of <0.1 and 0.6 mg/kg 70 days after treatment with clethodim at 0.12 and 0.24 kg ai/ha respectively.

Rape seed. Oilseed rape (two varieties of canola) was treated at four sites in Canada in 1988 with clethodim, either once or twice at 0.105 kg ai/ha. Similar trials were performed in 1989, using rates of 0.06 and 0.105 kg ai/ha. Residues in the whole seed ranged from <0.05 to 0.54 mg/kg at PHIs from 58 to 103 days; there was little difference between the residues arising from single and

double applications at either rate, but there was more difference between results from Saskatchewan and those from Alberta in the 1989 trials.

Eleven trials of clethodim on oilseed rape were conducted in France using rates from 0.18 to 0.96 kg ai/ha either in the autumn on young plants or in the spring as vigorous growth began. The majority of the results were below the limit of determination of 0.03 mg/kg, the highest being 0.19 mg/kg from the highest treatment rate with several others around 0.1 mg/kg. In some trials rape seed oil was prepared from the treated seed, and in all cases the residues in the oil were below the limit of determination of 0.03 mg/kg. In similar trials in France, nearly all of the residues were below the limit of determination, the highest being 0.07 mg/kg.

From three trials of clethodim on oilseed rape in the UK, using either 0.36 or 0.72 kg ai/ha, residues at harvest after 258 to 294 days were below the limit of determination of 0.03 mg/kg.

The Meeting estimated a maximum residue level of 0.5 mg/kg for rape seed, and 0.05 mg/kg for rape seed oil, both crude and edible.

Sunflower seed. Trials of clethodim on sunflowers were carried out in Argentina using 0.12 or 0.24 kg ai/ha. Residues in the seeds did not exceed 0.14 mg/kg at 102 to 108 days PHI. Residues of clethodim in sunflower seeds treated in France at either 0.18 or 0.48 kg ai/ha were below the limit of determination, 0.03 mg/kg, at 108, 112 and 123 days later.

Two trials were conducted in Italy, using clethodim at a rate of 0.24 kg ai/ha. Residues in the seeds did not exceed the limit of determination (0.03 mg/kg) after 74, 92 or 110 days; residues were also not observed in the raw or refined oil prepared from the crop. From another trial in Italy the same treatment gave residues of 0.07, 0.06 and 0.06 mg/kg, at 60, 75 and 90 days PHI, respectively.

The Meeting estimated a maximum residue level of 0.2 mg/kg for sunflower seed and 0.05 mg/kg for sunflower seed oil, crude and edible.

Clover. In one trial in New Zealand, white clover was treated with clethodim at 0.24 kg ai/ha. After 62 days, the silage prepared from the clover showed residues of 0.26 mg/kg, while 71 days later the regrowth showed 0.07 mg/kg.

Chickens. Laying hens were fed doses of clethodim (5%) and clethodim sulphoxide (95%), at nominal doses of 0, 10, 30, and 100 ppm of total clethodim in the diet, for 28 days. Egg samples were taken on 10 test days from days -1 to 30. The levels of DME (as clethodim) found in eggs from hens treated at 10 ppm were all less than 0.05 mg/kg. The levels of DME found in eggs from the 30 ppm and 100 ppm treatments ranged from 0.05 to 0.09 mg/kg and from 0.14 to 0.24 mg/kg, respectively, during the feeding period; in both cases they declined to less than 0.05 mg/kg by day 29. Neither DME-OH nor S-MeDME were above the limit of determination (0.05 mg/kg) in any of the egg samples.

Ten chickens from each group were killed on day 29 and the rest on day 31; from each batch, samples of thigh and breast muscle, liver, gizzard, and subcutaneous and abdominal fat were taken for analysis. The only tissue fraction found to contain any clethodim-related residues was the liver from the 100 ppm dose level which showed 0.06 mg/kg of DME. All other results

were below the limit of determination of 0.05 mg/kg.

The Meeting estimated a maximum residue level of 0.05* mg/kg for chicken meat and chicken eggs.

Cows. Fourteen dairy cows were used in a study of the distribution of clethodim residues in bovine tissues. Two were used as controls and the others were split into three groups of four cows each for treatment daily for 28 days with capsules containing clethodim (5%) and clethodim sulphoxide (95%), the nominal doses being 0, 10, 30, and 100 ppm of total clethodim in the diet.

Duplicate samples of whole milk were collected from all cows on days -1, 1, 2, 4, 7, 12, 16, 20, and 28 of the treatment period and on test days 29, 30 and 31 from the available animals. Three cows from each treated group and one control cow were killed on test day 29, within 24 hours of the last dose; the remaining cow in each group was killed on the morning of test day 31.

Analysis of the milk samples from treated cows showed no residues corresponding to clethodim or its metabolites for the control or 10 mg/kg feeding levels. The 30 ppm feeding level showed only "clethodim-type" residues, with a maximum of 0.033 mg/kg clethodim equivalents and a plateau by test day 1. The 100 ppm feeding level showed a maximum of 0.081 mg/kg of "clethodim-type" residues with a plateau by day 1, and a maximum residue of 0.032 mg/kg clethodim equivalents for the *S*-methyl metabolite residues with a plateau by day 2. No 5-hydroxy metabolite residues were found at any feeding level. One cow at each feeding level was held for a two-day withdrawal period and in all cases any residue present during the treatment declined to below 0.0125 mg/kg by the end of the withdrawal period.

The Meeting estimated a maximum residue level of 0.05* mg/kg for cattle milk and cattle meat and 0.1 mg/kg for cattle kidney and cattle liver.

No information was available on the fate of residues of clethodim in stored produce.

Data were provided on the fate of residues of clethodim when soya beans, cotton seed, rape seed and sunflower seed were processed to yield the respective oils. Apart from soya bean soapstock and crude lecithin there was virtually no transfer of clethodim from the treated raw agricultural commodity to the processed fractions.

Soya bean. Soya beans were treated at eight times the normal rate, in order to ensure that residues were high enough for the study to be effective, and the samples were processed in the usual way, all processed fractions being sampled and analysed. When the soya beans were processed, clethodim residues were reduced in crude oil (by 90%), degummed oil (94%) and refined oil (>99%), while residue levels in the hulls and meal were unchanged from those in the unprocessed beans; residues were concentrated somewhat in soapstock (126%) and crude lecithin (156%).

Cotton seed. Cotton was similarly treated at eight times the normal rate and the samples were processed. All processed fractions except linter and linter motes were collected and analysed for clethodim residues. The processing reduced the combined clethodim residues in crude and refined oil to about 20% and 10%, respectively, of the amounts in the raw agricultural commodity. Residues remained essentially the same in soapstock, delinted cotton seed and hulls but were concentrated slightly (1.7 times) in the meal.

Rape seed. Rape seed was treated with clethodim at twice the normal rate at two sites in western Canada. The rape seed was then processed to oil and meal using standard commercial techniques, and specific fractions from the process were sampled and analysed for clethodim residues. From rape seed containing 0.2 and 0.3 mg/kg of clethodim, no residues could be detected in the crude oil fraction. Final analyses of the solvent-free meal fractions showed a total residue of 0.77 mg/kg as clethodim. A mass balance showed that virtually all of the initial residue was retained in the meal.

Sunflower seed. Sunflower seeds from clethodim-treated crops in Argentina were processed to the oil. While residues remained in the press cakes, those in the oils were below the limit of determination. From two trials in Italy, residues in the seeds, raw oil or refined oil did not exceed the limit of determination (0.03 mg/kg).

No data were provided on residues in the edible portions of food commodities other than those included with the supervised trials or processing data reported above.

No information was provided on residues of clethodim occurring in commerce or at consumption.

The residue levels shown in Annex I are recommended for use as MRLs.

FURTHER WORK OR INFORMATION

Desirable

Data on residues occurring in food in commerce and/or at consumption.

4.13 CYHEXATIN (067)

TOXICOLOGY

The toxicological data on cyhexatin (tricyclohexyltin hydroxide) were reviewed by the Joint Meeting in 1970, 1973, 1978, 1980, 1981, 1988, 1989 and 1991. The 1991 Meeting reviewed draft reports of several toxicokinetic studies with both technical and micronized cyhexatin and of a multigeneration study in rats; final reports of a teratogenicity study in rabbits and a multigeneration study in rats were also reviewed. An ADI of 0-0.001 mg/kg bw was established on the basis of the multigeneration study in rats. The 1991 Meeting recommended that cyhexatin be reviewed again in 1994 when the following additional information would become available: (i) observations in humans; (ii) clarification of the influence of particle size on the toxicokinetics and toxicity of cyhexatin; (iii) determination of the effect of restricted food intake on reproduction parameters, preferably by a limited paired feeding study on rats during gestation and lactation; and (iv) information on the particle size of cyhexatin residues in food.

Cyhexatin is poorly absorbed after either oral administration (rats and rabbits) or dermal

application (rabbits). In rabbits, bioavailability is similar after treatment by either route, although a higher peak concentration in the blood is reached after oral administration. Bioavailability after oral administration is much greater in rabbits (7-9%) than in rats (0.5-1.2%). Micronized cyhexatin has greater bioavailability than the technical formulation in female rats but not in female rabbits.

Elimination of cyhexatin is slow, 75-85% being eliminated in rats within four days after treatment, with complete recovery of the administered dose within about 10 days. After rats were fed diets containing 100 ppm of [^{119}Sn]cyhexatin for 90 days, the tissue content of ^{119}Sn reached a steady state within about two weeks. When cyhexatin was removed from the diet, the half-life of ^{119}Sn in most tissues was about 10 days, except in brain and muscle where it was about 40 days. ^{119}Sn was present in muscles mainly as cyhexatin and, later, as dicyclohexyltin.

In pregnant rabbits given ^{14}C-labelled cyhexatin either orally or dermally, peak blood concentrations were found to be higher than expected from results obtained in non-pregnant animals. Contrasting results were obtained in fetus, placenta and amniotic fluid in two studies.

Comparative studies in rats showed that micronized cyhexatin has greater acute oral toxicity (LD_{50} 265 mg/kg bw) than technical-grade cyhexatin (LD_{50} 654 mg/kg bw) in females but not in males (LD_{50} 501 and 599 mg/kg bw respectively). This finding is consistent with kinetic data from the same laboratory using the same source of cyhexatin, in which the bioavailability of micronized cyhexatin was greater than that of technical-grade cyhexatin in female rats. In studies of acute toxicity in female rats in another laboratory using cyhexatin from a different source, however, lower acute toxicity was seen with micronized (LD_{50} 411 mg/kg bw) than with technical-grade (LD_{50} 274 mg/kg bw) cyhexatin.

More information has been provided from the multigeneration study (reviewed by the 1991 Meeting) in rats fed diets containing 0, 10, 30 or 100 ppm of micronized cyhexatin. The NOAEL in this study was 10 ppm, equal to 0.7 mg/kg bw per day, on the basis of decreased body weight gain in pups during lactation and reduced pup survival in F_0 - F_1 offspring at 30 ppm.

A one-generation reproductive toxicity study was conducted in pair-fed rats. Rats were given control diet *ad libitum*, a diet containing 30 ppm of micronized cyhexatin, or the same amount of control diet as that consumed by the cyhexatin group. Pup growth was affected by both cyhexatin and control diet but to a greater extent by the former. Therefore, reduced food intake accounted only partially for the effects. In a study of reproductive toxicity reviewed by the 1991 Meeting, rats were administered diets containing cyhexatin at concentrations that yielded 0, 0.1, 0.5 or 6.0 mg/kg bw per day. A slight effect on body weight associated with reduced food intake was observed in F_0 females at 0.5 mg/kg bw per day and the NOAEL was set at 0.1 mg/kg bw per day. Taking into consideration the results of the pair-feeding study and the other multigeneration study in rats, the Meeting considered that the effect seen at 0.5 mg/kg bw per day might be due to diet unpalatability. The Meeting concluded that the NOAEL was 0.5 mg/kg bw per day.

In a teratogenicity study in rabbits given percutaneous doses of technical cyhexatin of 0, 0.5, 1 or 3 mg/kg bw per day, neither maternal toxicity nor teratogenic effects were observed. In another teratogenicity study, rabbits were given 0, 0.75, 1 or 3 mg/kg bw per day orally. An increased incidence of folded retinas was found in treated groups, but a dose-response relationship could not be demonstrated and fixation artefacts were considered likely. The

NOAEL for this study was 0.75 mg/kg bw per day on the basis of possible maternal toxicity at higher doses. After taking into consideration the results of all the studies on teratogenicity in rabbits, the Meeting concluded that cyhexatin is not teratogenic to this species.

Two studies have been carried out on human occupational exposure to cyhexatin during mixing and spraying. The average exposure by inhalation was very low; cutaneous exposure ranged from 0.7 to 19 mg/day. Cutaneous exposure during picking fruit in cyhexatin-treated orchards ranged from 21 to 0.8 mg at 0 and 14 days after application respectively. No reliable measurements were reported of tin or cyhexatin in blood or urine.

No information was submitted on the particle size of cyhexatin residues in food because it cannot be determined analytically; however, it is conceivable that residues are of the same sizes as the applied product.

The Meeting based the ADI on the NOAEL determined in the multigeneration study in rats (0.7 mg/kg bw per day), applying a 100-fold safety factor.

An addendum to the toxicological monograph was prepared.

TOXICOLOGICAL EVALUATION

Levels that cause no toxic effect

Mouse: 3 mg/kg bw per day (two-year study reviewed at the 1981 JMPR)

Rat: 0.7 mg/kg bw per day (multigeneration study)

Rabbit: 0.75 mg/kg bw per day (maternal toxicity in teratology study)

Estimate of acceptable daily intake for humans

0-0.007 mg/kg bw

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

Further observations in humans.

4.14 DDT (021)

RESIDUE AND ANALYTICAL ASPECTS

At the 22nd and 23rd Sessions of the CCPR (1991 and 1992) countries were requested to supply monitoring and other data on DDT, and at the 23rd Session the existing Extraneous Residue Limits for DDT were converted to temporary limits awaiting evaluation by the JMPR.

The 1993 Joint Meeting reviewed the residue data supplied, but no recommendation was

made for cereal grains.

Residue data from monitoring cereal grains were available only from the USA. In 579 samples of cereal grains DDT was present in 5 samples with the highest residue at 0.09 mg/kg.

The data were consistent with the current temporary ERL, 0.1 mg/kg. The Meeting estimated a maximum residue level of 0.1 mg/kg for DDT and recommended it for use as an ERL to replace the current temporary ERL (0.1 mg/kg).

4.15 DIAZINON (022)

RESIDUE AND ANALYTICAL ASPECTS

Diazinon was re-evaluated under the CCPR periodic review programme by the 1993 JMPR. The present Meeting received information on use patterns, residue data from supervised trials and analytical methods for hops.

Hops, dry. Residue data were available from five trials in the USA carried out according to GAP (1.1 kg ai/ha, 14-day PHI). Residues ranged from 0.11 to 0.43 mg/kg. The recovery and limit of determination of the analytical method used in the trials were 94% and 0.05 mg/kg.

The analytical methods for hops are suitable for regulatory purposes.

The meeting estimated a maximum residue level of 0.5 mg/kg for dry hops.

4.16 DICOFOL (026)

RESIDUE AND ANALYTICAL ASPECTS

Dicofol was originally evaluated by the JMPR in 1968 and was re-evaluated under the CCPR periodic review programme by the 1992 JMPR. At the 1994 CCPR several delegations expressed their reservations (ALINORM 95/24) with regard to the following points.

France stated that the proposed MRL for grapes should be reassessed as the French residue data provided to the 1992 JMPR were not considered valid and French GAP was reported incorrectly. France also expressed reservations on the proposals for pome fruit, peas, tea, milks and poultry meat (fat), and questioned the reported GAP for citrus fruits.

The delegations of France and the USA and the representative of the EU considered that the definition of the residue was unsatisfactory for the edible offal of cattle in view of the presence of a major metabolite, 2,2-dichloro-1,1-bis(4-chlorophenyl)ethanol (FW 152), in cattle liver. The JMPR was requested to re-evaluate the definition of the residue.

Germany expressed reservations regarding the adequacy of the available feeding study on poultry and doubted whether it could be extrapolated to the residues expected in feed items.

Delegations were requested to provide their written comments on the residue definition in animal tissues for consideration by the JMPR.

The Meeting received explanatory notes from France on French GAP for grapes, on the French residue trials on grapes reviewed in 1992, and the proposed MRLs for citrus fruits, apples, grapes, peas, tea and products of animal origin. Germany and the USA submitted comments on the residue definition and proposed MRLs for animal products.

The Meeting reviewed the new information in the context of that previously evaluated.

Grapes. Dicofol is registered for use on grapes in Australia, Canada, France, Japan, Spain and the USA with application rates from 0.4 to 1.9 kg ai/ha. The Meeting re-evaluated the residue data reviewed in 1992. It noted that France had considered the French trials to be invalid because of high control values, but the results associated with these control values had not been included in the evaluation, nor had the studies in which only the p,p'-isomer was determined.

The re-evaluation was based largely on six US trials according to GAP with applications at 1.3-1.5 kg ai/ha and a 7-day PHI which gave residues from 0.27 to 2.6 mg/kg.

Two Australian trials (0.03-0.035 kg ai/hl, 28-day PHI) with residues of 0.1 and 0.2 mg/kg, and two trials from Spain (0.72 and 0.9 kg ai/ha, 14-day PHI) with residues of 0.54 and 1.9 mg/kg were also in accordance with GAP, and one Italian trial was evaluated on the basis of Spanish GAP (0.72 kg ai/ha, 15-day PHI, residue 0.32 mg/kg). Of all the German trials received in 1992, both isomers (*p,p′*- and *o,p′*-dicofol) were determined in only three and these could be used for re-evaluation on the basis of French GAP. The residues ranged from 0.2 to 0.42 mg/kg 21 days after application. The Meeting confirmed the previous recommendation (5 mg/kg).

Garden pea (young pods). France, supported by Germany, expressed a firm reservation against the proposed MRL (ALINORM 95/24, para 91), because the recommendation was based on only two trials.

Dicofol is registered for use on garden peas in Australia, Canada, Japan and Spain, with application rates ranging from 0.3 to 0.96 kg ai/ha and PHIs from 3 to 14 days. In the two trials in Japan reviewed in 1992 the product was applied at 0.53 and 0.67 kg ai/ha and the residues after a 3-day PHI were 1.3 and 1.4 mg/kg respectively.

The Meeting concluded that the data were insufficient to recommend an MRL and agreed to withdraw the previous recommendation for garden pea (young pods) of 2 mg/kg.

Tea, Green, Black (black, fermented and dried). France and Germany expressed their reservations against the GAP on which the evaluation was based (ALINORM 95/24, para 99).

Information was available on GAP in Japan (0.4 to 1.1 kg ai/ha, 20-day PHI), India (0.19 kg ai/ha, 14-day PHI), Indonesia, Sri Lanka and Bangladesh (0.086 to 0.49 kg ai/ha).

The Meeting evaluated results from four trials in Japan (1.1 kg ai/ha, 21-day PHI) and six trials in India (0.19 kg ai/ha, 7-day PHI). The PHI is of little importance because of the sequential way in which tea is harvested. The residues in processed dried leaves from the Japanese trials

ranged from 3 to 10 mg/kg, and in the Indian trials from 5.2 to 41 mg/kg. These levels are consistent with the previously reviewed results and the Meeting agreed that they supported the current MRL for 50 mg/kg for tea, green, black (black, fermented and dried).

Animal transfer studies and definition of the residue for animal products. Re-evaluation of the metabolism and feeding studies on hens and goats with [^{14}C]dicofol showed that the residues include both dicofol and FW 152. The metabolism studies showed that residues of FW 152 may constitute a significant proportion of the total radioactive residue in the milk and tissues of ruminants and eggs and tissues of hens.

The Meeting concluded that FW 152 should be included in the definition of the residue for animal commodities and changed the definition for animal products as shown in Annex I. The residue definition for plant commodities (sum of *p,p′*-dicofol and *o,p′*-dicofol) is unchanged.

Cattle meat, fat, kidney, and liver. Feeding studies on dairy cows for 35 days (10, 30 and 100 ppm in the feed) with analysis of muscle, heart, kidney, liver, fat and milk showed that in the 10 ppm group on day 29 after treatment the only detectable residue in the tissues except fat was FW 152 (muscle 0.14 mg/kg, fat 2.1 mg/kg, kidney 0.19 mg/kg, liver 0.65 mg/kg). In fat *p,p′*-dicofol (0.5 mg/kg) and *o,p′*-FW 152 (0.06 mg/kg) were also found. If it is assumed that fruit pomace accounts for a maximum of 30% and 10% of the daily feed of beef and dairy cattle respectively, and that residues can reach 30 mg/kg in apple pomace (see 1992 evaluation, US data) the residues in the daily feed of beef and dairy cattle should not exceed 10 mg/kg and 3 mg/kg, respectively. The residue intake from other feedingstuffs would be considerably less, e.g. pulses at a maximum of 20% of the daily feed and with a residue level of 0.3 mg/kg would contribute 0.06 mg/kg in the daily feed of cattle. The results show that the data from the lowest-dose (10 ppm) feeding group can be used to estimate maximum residue levels.

The Meeting agreed to increase the recommendation for cattle meat (fat) from 0.5 to 3 mg/kg to accommodate residues of FW 152, and to replace the previous recommendation for the edible offal of cattle (0.05* mg/kg) by 1 mg/kg in order to accommodate possible residues of FW 152 in the liver and kidney.

Cattle milk. The recommended MRL for milk is based on a residue level of 3 mg/kg in feed according to the following data.

p,p′-dicofol found on day 21 after application:
in 10 ppm feeding group: 0.025 mg/kg, extrapolated to 0.0075 mg/kg;
in 30 ppm feeding group: 0.15 mg/kg, extrapolated to 0.015 mg/kg;
in 100 ppm feeding group: 0.33 mg/kg, extrapolated to 0.01 mg/kg.

p,p′-dicofol found on day 28 after application:
in 10 ppm feeding group: 0.034 mg/kg, extrapolated to 0.01 mg/kg;
in 30 ppm feeding group: 0.13 mg/kg, extrapolated to 0.013 mg/kg;
in 100 ppm feeding group: 0.61 mg/kg, extrapolated to 0.018 mg/kg.

p,p′-FW 152 found on day 21 after application:
in 10 ppm feeding group: 0.14 mg/kg, extrapolated to 0.042 mg/kg;
in 30 ppm feeding group: 0.68 mg/kg, extrapolated to 0.068 mg/kg;
in 100 ppm feeding group: 1.8 mg/kg, extrapolated to 0.054 mg/kg.

p,p′-FW 152 found on day 28 after application:
in 10 ppm feeding group: 0.1 mg/kg, extrapolated to 0.03 mg/kg;
in 30 ppm feeding group: 0.53 mg/kg, extrapolated to 0.053 mg/kg;
in 100 ppm feeding group: 3.3 mg/kg, extrapolated to 0.099 mg/kg.

The maximum combined residue level in milk based on a residue of 3 mg/kg dicofol in the feed is expected to be 0.1 mg/kg. The Meeting estimated a maximum residue level for milks of 0.1 mg/kg (F) for the sum of *o,p′*-dicofol, *p,p′*-dicofol and *p,p′*-FW 152, expressed as dicofol, to replace the previous recommendation (0.05 mg/kg (F) for the sum of *o,p′*-dicofol and *p,p′*-dicofol).

Poultry meat and edible offal, eggs. Feeding studies were carried out on laying hens for 42 days (0.5, 1.5 and 5 ppm in the feed) with analysis of muscle, gizzard, heart, kidney, liver, fat and eggs. In the 0.5 ppm group the only detectable residues were found on day 29 after treatment in heart, with 0.07 mg/kg *p,p′*-dicofol, and fat, with 0.4 mg/kg *p,p′*-dicofol. Assuming that poultry feed contains a maximum of 30% pulses with a residue level of 0.3 mg/kg (see 1992 evaluation), not more than 0.1 mg/kg is to be expected in the daily feed (1/5 of the lowest level in the feeding trial). The Meeting estimated a maximum residue level for poultry meat of 0.1 mg/kg (fat), to replace the previous recommendation of 0.5 mg/kg (fat). The Meeting agreed to maintain the current recommendations for eggs of 0.05 mg/kg and for the edible offal of poultry of 0.05* mg/kg, as being a practical limit of determination.

Recommended or revised MRLs are recorded in Annex 1.

FURTHER WORK OR INFORMATION

Desirable

The items listed in the evaluation of the 1992 JMPR:

1. Details of rate of application (kg ai/ha or kg ai/hl) for the trials in Thailand on grapes submitted to the JMPR together with information on GAP.

2. Additional data from supervised trials on fruits where limited information is available, namely figs, coffee beans, zucchini, watermelons, tea, strawberries and gherkins.

3. Information on GAP for application to coffee beans.

4. Residue trials on crops where GAP was reported but no residue data were supplied, namely almond, apricot, banana, crab-apple, egg plant, mushrooms, papaya, quince and raspberry.

4.17 DIMETHOATE (027)

RESIDUE AND ANALYTICAL ASPECTS

Dimethoate is an insecticide used on many crops world-wide. It has been evaluated many times for residues since 1967. It is a metabolite of formothion and a pesticide in its own right. Similarly, omethoate is a metabolite of dimethoate (and indirectly of formothion) and is also a pesticide in its own right. The Meeting was informed by the manufacturer that omethoate would no longer be supported in the CCPR or in the EU. It was therefore removed from the review schedule.

Until 1986 dimethoate limits were for the combined residues of dimethoate and omethoate, owing in part to the nature of the data base, the early non-specific analytical methods and the ways in which national regulations have been framed. After repeated requests from the CCPR, and earlier rejection of a change by the JMPR, the 1986 Meeting revised the definition of the residue to refer only to dimethoate. Separate limits were proposed for omethoate to accommodate its residues resulting from the use of dimethoate or omethoate. MRLs were not affected by the changed definition of the residue, but the 1986 Meeting recommended limits for a number of individual vegetables to replace the 2 mg/kg MRL for "vegetables (except as otherwise listed)".

Since 1986 many delegations to the CCPR have expressed either support for or objections to the proposed limits. Objections have mainly centred on the wisdom of adopting limits based on very old data, with specific concerns that in many of the older trials combined residues were reported instead of separate residues of dimethoate and omethoate, that the original uses might no longer be current, and that many of the results were based on analytical methods which would no longer be acceptable.

This situation has led to repeated requests by the CCPR for governments and other interested parties to provide more recent and reliable data, with the result that a number of proposals have been retained at Step 7B or 7C since 1986. The 1987, 1988 and 1990 JMPRs reviewed additional information on GAP and selected residue data, estimated new maximum residue levels for olives and wheat (1988), recommended that the 2 mg/kg limit for grapes should be lowered to 1 mg/kg and that the limit for apricots should be withdrawn (1990), but otherwise did not consider that the limited submissions, often from only one country, provided an adequate basis for lowering limits when it had been clear that uses were on a broad range of crops world-wide. The longer the subject has been debated, the more outdated the data bases have become.

The 1992 CCPR recommended that the limits at Step 7C for beans (except broad beans and soya beans), broccoli, cauliflower, cucumber and leaf lettuce should be withdrawn if information was not provided. The MRLs for Brussels sprouts, head cabbage, head lettuce, peaches, plums (including prunes) and wheat were held at Step 7B awaiting further consideration by the JMPR. The 1993 CCPR was informed by the manufacturer that no new data would be provided for commodities with limits at Step 7C, although data from trials in the 1960s could be supplied. Residue data and information on GAP were promised from Italy on wheat and rice and from the UK on lettuce. The Netherlands would make detailed comments on the limits for Brussels sprouts, head cabbages and plums. The 1993 CCPR retained the Step 7B and 7C

proposals pending the 1993 JMPR review.

The Meeting received rather comprehensive information on GAP, in the form both of labels (in the native languages) and summary lists, as well as data on residue trials from around the world. Many of the trials were very old however (some previously reported) and relied on outdated analytical procedures, some were reported in summary form only, and some reports were illegible. The Meeting was informed that the results of additional trials being conducted in the United States on peas, sorghum, oranges, maize, wheat, cotton seed and potatoes were expected to be available in 1995. The Meeting also received information on national MRLs as well as comments from countries on a few proposals.

The Meeting concentrated its review mainly on the more recent data and relevant GAP, and government comments on proposals at Steps 7C and 7B. National MRLs, other information on GAP, and data on crops for which MRLs are not at issue will be reserved for review at a future Meeting. The Meeting placed little emphasis on the summary data.

Step 7C proposals

The Meeting received no additional information on broccoli, cauliflower or cucumber and recommended that the proposed MRLs should be withdrawn. The only new residue data to support the current 2 mg/kg proposal for beans (except broad beans and soya beans) were summary reports of trials on green beans from Canada. The Meeting also recommended withdrawal of this proposal.

The 1992 CCPR recommended withdrawal of the 2 mg/kg proposal for leaf lettuce unless additional data were provided to the 1993 JMPR. A relatively detailed summary was provided of extensive trials in the UK in 1983-1984, some of which approximated maximum GAP conditions. Most of the data were from analyses of multiple single-head samples from individual plots, the mean values of which could be considered relevant to the estimation of maximum residue levels. Only the ranges of residues were provided for the few multiple-head samples. In three of the 5 trials, and part of the 4th, samples were taken at intervals of ≤18 days compared with the 28-day PHI which is GAP for protected leaf lettuce in the UK. After ≥28 days the maximum residues (mean of single-head sample analyses and high end of the range for 10-head samples) were 1, 1.1, 1.8, 2.4, 1.2, 0.9, 0.8 and 1.2 mg/kg of dimethoate and 0.2, 0.2, 0.2, 0.3, 0.2, 0.2, 0.1 and 0.1 mg/kg of omethoate. The submitted country evaluation emphasized the high residues found after 7 days as an indication that the currently proposed limit may be too low, since pre-harvest intervals are not always certain.

The Meeting did not consider PHIs shorter than 28 days to be in accordance with the reported UK GAP for protected leaf lettuce, nor did it consider that the results could be applied to field uses for which the GAP PHI is 7 days and for which there were no data. Although additional possibly valid results were provided the Meeting concluded, taking into account that the report was only a summary and that previously reviewed trials had been considered inadequate by current standards, that the data were insufficient to estimate a maximum residue level. They suggest that reported uses could result in dimethoate residues exceeding the current 2 mg/kg proposal and that the 0.2 mg/kg CXL for omethoate might also be exceeded, but in the

absence of adequate data to replace those previously available the Meeting recommended that the proposal should be withdrawn.

Step 7B proposals

The Meeting received comments from one country questioning the current proposals of 2 mg/kg for Brussels sprouts and head cabbages, which were recommended by the 1986 JMPR. The linking of the recommendation to a PHI of 7 instead of 14 days was also questioned. The additional data from one country on Brussels sprouts and Savoy cabbage reviewed by the 1988 JMPR, which indicated maximum residues reflecting GAP of 0.05 mg/kg dimethoate and 0.3 mg/kg omethoate in Brussels sprouts and of 0.5 mg/kg dimethoate and 0.7 mg/kg omethoate in head cabbage, were cited as evidence that the current limit is too high. A general reservation was also expressed on the 1986 Meeting's use of old data which may be unreliable by current standards.

While the Meeting agreed with the comment on the PHI, especially since the PHI of the country where the trials reviewed in 1988 were conducted is 14 days, information provided to the Meeting reported GAP PHIs as short as 7 days in the USA and UK with application rates the same as or higher than those in the cited trials. The Meeting concurred with the 1988 JMPR in concluding that adequate data had not been provided to support revision of the current proposals, and agreed to maintain the current recommendations of 2 mg/kg for Brussels sprouts and head cabbage.

In recent years several delegations to the CCPR have expressed the view that the current 2 mg/kg limit for head lettuce is too high. Data reviewed by the 1988 JMPR (maximum residue from treatments according to GAP 0.34 mg/kg) and summary Canadian data submitted to the present Meeting (maximum residue from GAP treatments 1 mg/kg dimethoate and 0.3 mg/kg omethoate) suggest that this may be the case. However the Meeting concluded that the more recently submitted data, alone, are too limited to support the recommendation of a limit and therefore inadequate as a basis for lowering the current proposal. The Meeting agreed to maintain the current recommendation of 2 mg/kg for head lettuce.

The current limit of 2 mg/kg for peaches has been retained for several years pending the submission of additional data from trials according to current GAP. Some delegations to the CCPR have suggested that available data support a lower limit, although after evaluating additional data and re-examining previous JMPR reviews the 1990 Meeting did not recommend a revision. The Meeting did not receive a response to the urgent request of the 1992 CCPR to governments for detailed comments, although one general comment was received. Additional data were received from Hungary (residues up to 1.6 mg/kg after 7 days from applications apparently according to GAP). Although most of the limited data suggest that a case might be made for a 1 mg/kg limit, residues up to 1.5 mg/kg from GAP treatments in the older trials, up to 1.2 mg/kg in more recent trials from a GAP rate and PHI (albeit after 3 applications instead of the 2 allowed by GAP), and up to 1.6 mg/kg in the new Hungarian trials suggest that 1 mg/kg could be exceeded. The Meeting concluded that insufficient data reflecting current GAP were available to support a revision of the current proposal and agreed to maintain the current recommendation of 2 mg/kg.

The current 2 mg/kg proposal for plums (including prunes) has also been held at Step 7B for several years pending the submission of data reflecting current GAP and reporting standards.

It was again retained at this step by the 1991 CCPR to wait a review by the JMPR of detailed comments to be submitted by The Netherlands. The Meeting reviewed comments from The Netherlands supporting a 1 mg/kg limit and new Hungarian data based on use patterns consistent with the GAP of EU countries.

The Netherlands generally questioned the retention of MRLs based on old data and did not agree with the 1988 JMPR conclusion that data from one country were not sufficient to lower the proposed limit. Maximum residues in the new Hungarian trials were ≤0.1 mg/kg at the PHIs (≥7 days) of other European countries. In 6 German trials reviewed by the 1988 JMPR residues were <0.2 mg/kg after 14 to 21 days from applications according to GAP. Although the 1988 JMPR considered a PHI of 21 days to be GAP, information provided to the present Meeting indicates that 14 days is also GAP for the control of some pests. While the summary of GAP in EU countries received by the Meeting indicated that 1 application is GAP in Germany, other information provided indicates that 3 or 4 applications may be made (as in the trials reviewed by the 1988 JMPR).

When the new data are taken into account, residues in trials in three countries over several years have been well below 0.5 mg/kg even at very short PHIs. While only marginally sufficient data are available from trials according to GAP, the Meeting concluded that a limit of 0.5 mg/kg could be supported.

The 0.2 mg/kg limit for wheat recommended by the 1988 JMPR has been retained at Step 7B for several years as a result of varying opinions at the CCPR, and to await the submission of current information. The Meeting reviewed some additional information on GAP and additional residue data from Hungary, but the Hungarian trials were not reported in sufficient detail for the estimation of a maximum residue level. The Meeting agreed that data from the 3 supervised trials in Germany reviewed by the 1988 JMPR, considered alone, suggest the possibility of a lower limit. This conclusion would be supported by the Hungarian trials if they were carried out according to GAP. However, the Meeting also took note of the 0.2 mg/kg residue from a treatment according to GAP reported in the 1967 monograph and the fact that most EU GAP allows much shorter PHIs (7 to 20 days) than the 35 to 56 days in the German trials or 31 days in the Hungarian trials. The Meeting agreed to withdraw the previous recommendation of 0.2 mg/kg for wheat on the basis that the available data were insufficient by current standards.

In general the Meeting shared the doubts expressed by a number of countries at the CCPR regarding draft MRLs for dimethoate based on old data which may not meet current standards in several respects, including relevance to current GAP, acceptable analytical methods, adequate reporting (e.g. the inclusion of such details as sample storage periods and conditions, intervals from sampling to analysis, critical supporting studies etc.). These same concerns might also apply to existing CXLs if they were re-examined.

The difficulty is that in most of the controversial cases the data are quite limited by current standards. Disregarding the older studies from which the data may or may not still be valid is likely to leave an even less satisfactory data base. While the JMPR over several years has attempted to review *ad hoc* submissions to address specific concerns, it is clear that the general problem cannot be adequately considered until a comprehensive periodic review of a complete current data base can be conducted. Only then will there be an adequate basis to determine whether any of the current CXLs or remaining draft limits . General..... 2

revised or revoked.

The Meeting noted that the manufacturer no longer supports omethoate in either the CCPR or the European Union, and recommended that any future periodic review of dimethoate should also include a re-evaluation of current Codex MRLs for omethoate with a view to estimating omethoate residues which result from the use of dimethoate (or formothion).

The recommendations for withdrawal and revision of MRLs are shown in Annex I.

4.18 DIQUAT (031)

RESIDUE AND ANALYTICAL ASPECTS

Diquat, previously evaluated for residues by the JMPR in 1970, 1972, 1976, 1977 and 1978, is included in the CCPR periodic review programme.

Diquat is a non-selective contact herbicide and crop desiccant. It is strongly adsorbed to soil and is not taken up by plant roots. When used as a herbicide to control weeds before planting or emergence, between the rows of established crops, or even just after emergence, no residues (<0.05 mg/kg) are found in the harvested crop. Small residues which may be found occasionally are caused by contamination.

The major use of diquat is for pre-harvest desiccation to aid the harvesting of seed and fodder crops. Residues of diquat are found from this application, mainly from direct contact of the spray with the raw agricultural commodity.

New data from supervised residue trials on crops for which MRLs have previously been recommended were available to the Meeting, together with data on two other crops (soya beans and lentils).

Additional data were also received on diquat residues in processed fractions from sorghum and soya beans, in addition to the previously evaluated trials on wheat, barley and oilseed crops. In wheat, residues in the bran (maximum 2.7 mg/kg) are about twice those found in the grain, while residues in white flour (maximum 0.19 mg/kg) are 20-25gradation pathway of diquat in water has been elucidated. TOPPS was found to be the major degradation product. On further irradiation, this compound is degraded to picolinamide and then via picolinic acid to volatile fragments. The monopyridone was formed to only a limited extent.

In plants the main photoproduct TOPPS occurs as a residue, 7-14 days after treatment, at roughly half to one-third the level of diquat. Other products of diquat photodegradation on plants appear to be incorporated into natural plant constituents. The Meeting agreed that the residue should be defined as diquat cation, the position taken in previous JMPR reviews.

The new data on residues from supervised trials, together with the information previously reviewed, were evaluated as follows.

Onion, Bulb. No new data were submitted since the evaluation in 1970. The Meeting agreed to withdraw the recommendation of 0.1 mg/kg because the results were too few to estimate a maximum residue level.

The residue data for beans (dry), lentils, peas (dry) and soya beans are mutually supportive and the residues were evaluated together.

Numerous further results from residue trials (8 for bean, 66 for peas, 64 for lentils and 50 for soya beans) from many countries showed residues from <0.01 to 0.2 mg/kg. The Meeting agreed to replace the recommendation for shelled beans and shelled peas by recommendations for beans (dry), lentils, peas (dry) and soya bean (dry) of 0.2 mg/kg. In soya bean hulls the residues ranged from 0.5 to 2.4 mg/kg.

Potatoes. On the basis of a large number of new residue data the Meeting estimated a maximum residue level of 0.05 mg/kg for potatoes to replace the previous recommendation (0.2 mg/kg).

Sugar beet. No new data have been submitted since the last evaluation in 1972. The Meeting agreed to withdraw the recommendation of 0.1 mg/kg because the two results available were not enough to estimate a maximum residue level.

Other vegetables. The Meeting agreed to withdraw the recommendation (0.05* mg/kg) and substitute recommendations for specific vegetables where information on GAP and sufficient valid residue data are available.

Barley. Since the residue situation is well covered by the many results evaluated by earlier Meetings and by additional newer values, the Meeting agreed to maintain the current recommendation of 5 mg/kg.

Maize. No new data have been provided since residues in maize were evaluated by the 1972 JMPR, but more precise references have now been made available to support the original data. In all cases (30 results) residues in maize seed were below the limit of determination (<0.05 mg/kg). The Meeting estimated a maximum residue level for maize of 0.05* mg/kg as being a practical limit of determination.

Oats. Thirty three results from residue trials carried out in the United Kingdom, Canada and New Zealand in 1963-1973 were submitted. Diquat residues following applications at commercial rates (0.4-0.8 kg ai/ha) were in the range 0.24-1.8 mg/kg, with one higher result (2.2 mg/kg) from a total of 18 results. The mean residue was 0.9 mg/kg. These levels are of the same order as those found on wheat following application at similar rates. The Meeting estimated a maximum residue level of 2 mg/kg for oats.

Rice. Newer residue trials in Japan show residues in paddy rice of 0.02-0.13 mg/kg, but earlier values from trials at commercial rates (0.3-0.6 kg ai/ha) were in the range of <0.05-9 mg/kg. The Meeting estimated a maximum residue level of 10 mg/kg for paddy rice to replace the previous recommendation (5 mg/kg). In processing studies on paddy rice treated at exaggerated application rates, residues of 0.96 mg/kg were found in dehusked rice prepared from paddy rice containing diquat at 13 mg/kg. Residues of 0.16 mg/kg were found in polished rice from paddy rice containing 6.4 mg/kg. The Meeting estimated a maximum residue level of 1 mg/kg for husked rice to replace the previous recommendation (0.2 mg/kg) and agreed to maintain the

current recommendation for polished rice (0.2 mg/kg).

Sorghum. On the basis of earlier residue results and newer data the Meeting agreed to maintain the current recommendation of 2 mg/kg for sorghum.

Wheat. New residue values together with earlier data support the previous MRL. The Meeting agreed to maintain the current recommendations of 2 mg/kg for wheat and wheat wholemeal.

Wheat bran, unprocessed. On the basis of the residues (maximum 2.7 mg/kg) evaluated by the JMPR in 1978 the previous MRL of 5 mg/kg can be supported.

Wheat flour. Wheat milling studies showed that diquat residues in the flour were approximately 20-25% of the residues in the grain. Because the recommendation for wheat is 2 mg/kg, the Meeting estimated a maximum residue level of 0.5 mg/kg.

Cotton seed. No new residue data were available, nor were the original data (14 results) on which the 1972 recommendation for the seed of 1 mg/kg was based submitted for re-evaluation. There was information on only two GAP applications (Spain, Australia) for use as a desiccant in cotton. The Meeting agreed to withdraw the recommendation for cotton seed (1 mg/kg).

Poppy seed. No new residue data were available and the original data were not submitted for re-evaluation. The Meeting agreed to withdraw the recommendation for poppy seed (5 mg/kg).

Rape seed. The previous MRL is supported by newer residue data on the whole seed. The Meeting agreed to maintain the current recommendation of 2 mg/kg for rape seed.

Sunflower seed. Data from Australia, Canada, Chile, France and Israel showed residues in the range <0.05 to 1 mg/kg. The Meeting estimated a maximum residue level of 1 mg/kg for sunflower seed to replace the previous recommendation (0.5 mg/kg).

Vegetable oils. One of the uses of diquat is as a pre-harvest desiccant on a range of oilseed crops. The residues in the extracted oils are consistently undetectable (see the individual commodities rape seed oil, soya bean oil, sunflower seed oil). This is to be expected in view of the ionic nature of diquat. Both the underlying science and the available data support the estimation of a group maximum residue level for crude vegetable oils of 0.05* mg/kg as being a practical limit of determination.

Because no residue information was available for the edible oils of cotton seed, rape seed, sesame seed or sunflower seed, the Meeting agreed to withdraw the respective recommendations, but because residues are not detectable in the crude oils there would be no residues in the edible oils. Similar comments apply to soya bean oil, for which there is no current recommendation.

Meat and edible offal (mammalian). New trials on farm animals (cattle and sheep) showed no measurable residues (<0.02 mg/kg) in tissues when feed containing levels of diquat up to 100 ppm in the diet was fed for 30 days. Maximum residues from alfalfa would be expected up to 95 ppm. The Meeting confirmed the previous maximum residue level estimate of 0.05* mg/kg for meat and edible offal (mammalian), this being a practical limit of determination.

Milks. Diquat residues were not detectable (<0.01 mg/kg) in the milk from cows on feed

containing up to 100 ppm diquat. These new results support the previous MRL of 0.01* mg/kg.

Poultry meat and edible offal. Trials on hens showed no measurable residues in poultry (meat and edible offal) when the feed contained 10 ppm diquat. The Meeting estimated a new maximum residue level for poultry meat and edible offal of 0.05* mg/kg, this being a practical limit of determination.

Eggs. Newer investigations indicate that no residues are measurable (<0.01 mg/kg) in eggs from hens consuming feed containing 10 ppm diquat. The Meeting confirmed the previous maximum residue level estimate for eggs of 0.05* mg/kg, a practical limit of determination.

Animal feeds. Results of desiccation trials carried out on alfalfa and clover showed that the recommended MRLs were compatible with the MRLs for animal commodities.

Alfalfa fodder. Results from 6 supervised trials on alfalfa (whole plant) covered a wide range. On the basis of the highest value of 95 mg/kg 3-5 days after treatment at 0.3 kg ai/ha the Meeting estimated a maximum residue level of 100 mg/kg for alfalfa fodder.

Clover. Residues in clover 4-7 days after treatment at 0.5-0.56 kg ai/ha were 10-35 mg/kg. The Meeting estimated a maximum residue level of 50 mg/kg for clover.

On the basis of further data available on residues from supervised trials and current GAP the Meeting concluded that the residue levels listed in Annex I are suitable for establishing maximum residue limits.

FURTHER WORK OR INFORMATION

Desirable

Additional data on soya bean oil and soya bean meal.

4.19 DISULFOTON (074)

RESIDUE AND ANALYTICAL ASPECTS

Disulfoton was completely re-evaluated by the 1991 JMPR in accordance with what was later to be designated as the CCPR periodic review programme. The ADI was revised, new MRLs were proposed, and others recommended for revision or withdrawal in the context of current GAP. Discussion of the new or revised proposals at the CCPR in 1993 and 1994 prompted comments on various proposals (including that for milk); comments that some data supporting national limits were not included in the re-evaluation; and a proposal that the disulfoton metabolite demeton-S should be excluded from the definition of the residue. Clarification of the GAP for cabbage and sorghum forage (green) was requested.

The Meeting received and reviewed substantial additional data (280 reports); information on GAP from the manufacturer and some countries; comments from The Netherlands on the definition of the residue and written comments from countries in support of their positions at the CCPR on various commodities, including milk.

Barley. Although there appeared to be no outstanding questions from the CCPR on the 1991 JMPR estimate of 0.2 mg/kg for barley grain, some additional US data and comments from the French government proposing a 0.05 mg/kg limit were considered. The French comments were based on the view that residues from trials strictly according to GAP did not exceed 0.02 mg/kg. While residues were up to 0.2 mg/kg after 30 days in the additional data provided, the two foliar applications in the trials did not represent GAP, which permits only one foliar application.

The Meeting agreed that the data summarized in 1991 would support a 0.05 mg/kg limit if the trials involving two EC applications at the recorded 28-37 day PHI were not according to GAP. All other residue were $\leq$0.03 mg/kg. The Meeting re-examined the 1991 data in the light of the current GAP information provided. Since residues were $\leq$ 0.03 mg/kg in all but the trials with 2 EC applications, it is obvious that the 1991 JMPR gave the greatest emphasis to these results. Residues after 28-37 days resulting from 2 EC applications at 1.1 kg ai/ha ranged from 0.01 to 0.14 mg/kg. Therefore, basically what is being questioned is whether these data represent GAP.

The Meeting observed that current GAP allows a single foliar autumn or spring EC application in addition to an at-plant EC application, both at 1.1 kg ai/ha. A 60-day PHI applies to at-plant applications and 30 days to foliar. The 1991 JMPR evaluation does not indicate whether the 2 EC applications were at-plant, foliar or some other. If it can be assumed that an at-plant and a foliar application were made and that the 28-37 day PHI in the trial refers to the foliar application, it would be reasonable to assume that the EC data represent GAP. That was apparently the view that the 1991 JMPR took when they had access to the original reports.

With this assumption, the residues from this application regimen are 0.01(4), 0.02, 0.04, 0.06, 0.09, 0.1(2), and 0.14 mg/kg. These would be consistent with the 0.2 mg/kg estimate of the 1991 JMPR. The Meeting concluded that the results reviewed in 1991 probably reasonably reflect GAP, and confirmed the 1991 estimate.

Beans (dry). Government comments questioned the 1991 JMPR estimate for dry beans of 0.01 mg/kg (limit of determination), preferring 0.02 mg/kg and noting that most residues in the 5 trials were from applications at 1.5 times the GAP application rate. The Meeting noted that the 0.01 mg/kg proposal was not at the limit of determination according to the 1991 monograph, and that according to current GAP, whether an exaggerated rate has been used can depend on the row spacings, and is not entirely defined in terms of kg ai/ha. The 1991 evaluation does not allow this to be determined.

In addition to the 5 supervised trials reviewed by the 1991 JMPR, the maximum residue in one of two additional trials was 0.03 mg/kg compared to <0.01 mg/kg in the other and in the previously reviewed trials. The "double side dress" granular application at GAP rates was interpreted to mean a side dress on each side of the furrow, which is GAP. Although 6 of 7 trials showed residues of <0.01 mg/kg, and although information on sample handling and storage conditions in the new trials is desirable, the Meeting saw no reason that the higher value should not represent GAP and recommended accordingly that the 1991 estimate of 0.01 mg/kg should be increased to 0.05 mg/kg. Additional data reflecting GAP are desirable.

Beans, Common. Maximum residues did not exceed 0.05 mg/kg in snap or green beans from two additional US trials not reviewed by the 1991 JMPR. The Meeting agreed that an argument could be made for a 0.1 mg/kg limit for common beans as proposed in French comments as opposed to the 0.2 mg/kg estimated by the 1991 JMPR, in view of the fact that most of the trials had been conducted at 1.4 times the GAP rate. However, owing to the relatively small number of trials, the Meeting was reluctant to recommend a 0.1 mg/kg limit. If the German 75th percentile approach summarized by the 1990 JMPR is applied to the 59-67 day results (four results at 0.01 mg/kg, one each at 0.04, 0.06, 0.11 and 0.14 mg/kg) a 0.2 mg/kg maximum residue level is suggested. Even adjusting the results to the GAP rate would lead to 0.14 mg/kg. The Meeting confirmed the 1991 JMPR estimate of 0.2 mg/kg for common beans.

Beans, Lima. The Meeting did not consider the data on two Lima bean trials reviewed by the 1991 JMPR (0.02 mg/kg maximum residue) and the one additional trial provided to the present Meeting (<0.01 mg/kg) to be sufficient for estimating a maximum residue level.

Broccoli. The Meeting received 10 additional reports on United States trials in 1972 which were not reviewed by the 1991 JMPR. Residues from possible GAP ranged from 1.6 to 15 mg/kg after 33 days compared to the 0.2 mg/kg level estimated by the 1992 JMPR for a 14-day GAP PHI. However, because (1) the data were for residues in the whole plant as distinct from the flower heads to which the MRL applies, (2) the granular at-plant applications were at exaggerated rates compared to US GAP, and (3) there was some uncertainty as to whether the field at-plant band applications were in accordance with GAP, the data were not considered suitable for estimating a maximum residue level.

The Meeting considered country comments questioning whether the trials reviewed by the 1991 JMPR (residues of 0.01 to 0.11 mg/kg) closely reflected reported GAP and proposing a 0.1 mg/kg limit. The Meeting re-examined data summarized in the 1991 monograph, taking into account country comments and current GAP labels, and concluded that the 1-2 applications indicated as approved in the 1991 review were no longer GAP, which allows only one application per season for broccoli, for either EC or GR applications.

The Meeting noted that residues do not exceed 0.11 mg/kg even from two applications and that application of the 75th percentile approach to estimating MRLs described in the 1990 JMPR Report would suggest a maximum residue level of 0.1 mg/kg, and concluded that residues from GAP would be unlikely to exceed 0.1 mg/kg on the basis of the data available. On the basis of previously reviewed and new information the Meeting recommended that the 1991 estimate of 0.2 mg/kg for broccoli should be lowered to 0.1 mg/kg.

Cabbage. The Meeting considered additional data not reviewed by the 1991 JMPR, clarification of current US GAP (42-day PHI and one application confirmed) and French comments questioning the GAP basis and rationale for the 1991 JMPR estimate of 0.2 mg/kg as a partial replacement of the 0.5 mg/kg CXL for vegetables. Residues were ≤0.05 mg/kg in three of the new reports provided, and did not reflect GAP in 5 others. In 5 others they ranged from 1.4 to 8 mg/kg from at least 1.7 times GAP application rates after 51 days (42-day GAP PHI), but sufficient trial detail was not provided to decide whether these 5 conformed to GAP except in their maximum rate and PHI.

The GAP labels submitted confirmed the suspicion that the 2 applications in the trials

reviewed in 1991 were not according to current GAP, although the 1991 information indicated that two applications were allowed for some uses. The Meeting noted French comments, including the observation that the mean residue was only 0.03 mg/kg, the doubt about the validity of the 0.17 mg/kg value and the view that a statistical analysis of the data supported 0.1 mg/kg. The Meeting did not agree that because 0.17 mg/kg was reported at a 39/43 day PHI and 0.09 mg/kg at 29/32 days in the same trial the data were necessarily invalid, especially for an at-plant application. A similar situation is also evident in another of the trials, although at lower levels.

The Meeting applied the German 75th percentile procedure for estimating maximum levels to the data. That approach would suggest that the 0.2 mg/kg recommended by the 1991 JMPR would be required if the residue of 0.17 mg/kg is included and if it could be assumed that the data represent GAP. However, according to the current GAP information provided, none of the trials reviewed in 1991 reflect GAP, because two applications were used and some treatments exceeded GAP rates. Not only do the 1991 data not reflect GAP, but this appears also to be the case for the data submitted to the present Meeting, because GAP does not include band over-row, over-furrow or over-row post-emergence treatments (only side dress applications are permitted). While few if any results appear to fully reflect GAP, 0.2 mg/kg would not be exceeded even from exaggerated applications. On the basis of new and previously reviewed information, the Meeting confirmed the 1991 JMPR estimate of 0.2 mg/kg.

Cattle milk. The Meeting considered the written proposal of The Netherlands that a 0.01 mg/kg limit could be supported for the milk of cattle (rather than 0.02 mg/kg), which was based on the view that feed would not contain residues at the 20 mg/kg limit proposed for sorghum forage (green) in practice since sorghum forage is unlikely to be fed at 100% of the cattle diet. It was also noted that few of the trials resulted in residues up to 20 mg/kg in green sorghum forage.

The Meeting drew attention to the new level estimated for sorghum forage (green) of 5 mg/kg (see below) and agreed that on this basis a lower feeding level could be used as a basis for estimating a limit for milk. The Meeting also agreed that sorghum forage is not likely often to amount to 100% of the diet, although it could be as much as 75% on occasion. With these considerations, and noting that none of the other feed items for which MRLs are proposed are likely to contain residues exceeding 5 mg/kg, the Meeting agreed that it would be reasonable to use another feeding trial reviewed by the 1991 JMPR as the basis for a limit for milk. With residues up to 0.004 mg/kg from a 7.2 ppm feeding level and 0.012 mg/kg from 18 ppm, and noting that residue measurements are possible down to 0.001 mg/kg, the Meeting agreed that a 0.01 mg/kg maximum residue level for the milk of cattle, goats and sheep should be recommended.

Cauliflower. No new data were available. However, the Meeting considered written comments from the French government that a 0.05 mg/kg limit could be supported as opposed to the 1991 JMPR estimate of 0.2 mg/kg, assuming that the high value of 0.31 mg/kg was an outlier. It also considered current US GAP information, since the trials were in the USA. The Meeting observed that 3 applications had been made compared to the two that are allowed by current GAP. The first application was within GAP and the second and third were at 1 to 1.7 fold rates. Therefore, strictly speaking the trials represent exaggerated use. The Meeting observed that except for the 0.31 mg/kg value, residues were similar after 28-30 and 38-43 days. Combining these data gives a data base of 0.01(11), 0.02, 0.04(2) and 0.31 mg/kg. The Meeting agreed that the residue of 0.31 mg/kg appeared to be an outlier and concluded that 0.05 mg/kg would not be likely to be exceeded from GAP. This is supported by application of the German 75th percentile approach to

estimating MRLs. The Meeting revised the maximum residue level estinated by the 1991 JMPR for cauliflower to 0.05 mg/kg.

Cotton seed. The 1991 JMPR recommended a 0.1 mg/kg limit, based on residues of ≤0.05 mg/kg, considering one 0.43 mg/kg value to be aberrant. In response to concerns expressed at the CCPR that all relevant data had not been submitted, the Meeting reviewed current GAP information and additional data for disulfoton residues in cotton seed, representing several spray regimens. The trials appear to accord with GAP, since the manufacturer informed the Meeting that formulations designated as "SC" in the 1994 submission were actually EC formulations. "SC" had been used as a generic term for spray concentrates. The trials included two with in-furrow + side dress applications with residues of <0.19 mg/kg after 28 days (control 0.19 mg/kg), and several from seed + foliar treatments (<0.06, 0.03, and 0.1 mg/kg after 33-95 days) and foliar treatments (<0.01 to 0.12 mg/kg at 88-111 days). With the exception of the 0.12 mg/kg residue where the control value was 0.04 mg/kg, the control values generally appear to contribute significantly or almost entirely to the reported residues.

In taking the new information into account together with the data reviewed by the 1991 JMPR, it was concluded that there might be a possibility of residues exceeding 0.1 mg/kg, but that there was insufficient evidence to recommend revision of the 1991 estimate of 0.1 mg/kg, which the Meeting therefore confirmed.

Maize. The Meeting received additional data from disulfoton trials in the United States, none of which reflected reported GAP and were therefore considered unsuitable as a basis for revising the 1991 JMPR 0.01 mg/kg estimate.

The Meeting also considered an inquiry from a delegation to the 1994 CCPR as to whether the 0.01 mg/kg proposal for maize grain was at the limit of determination. The Meeting observed that the 1991 JMPR considered the limit of determination for maize (dry grain) to be 0.01 mg/kg and recorded maize grain residues as ≤0.01 mg/kg. Because some residues were observed at the 0.01 mg/kg level, the Meeting concluded that it should not be designated as at the limit of determination.

Oats, wheat. The Meeting considered the 1994 CCPR request to re-examine limits for the green forages and straws of oats and wheat as there appeared to be inconsistencies between the two, as well as additional data not reviewed by the 1991 JMPR. The 1991 JMPR estimated 0.5 and 2 mg/kg respectively for oat and wheat green forages and 0.05 and 10 mg/kg respectively for their straws. No new data on oats were provided. The Meeting re-examined the summarized data and GAP for oats, noting that grain residues did not exceed the 0.01 mg/kg limit of determination, straw residues did not exceed 0.03 mg/kg, and green forage residues were up to 0.25 mg/kg after 30 days. The Meeting confirmed the 1991 JMPR estimates of 0.01 mg/kg (limit of determination) for oat grain, 0.5 mg/kg for oat forage (green) and 0.05 mg/kg for oat straw.

In the case of wheat the 1991 monograph refers to 30 trials with GR and EC formulations, 1-3 applications and PHIs of 27 to 100 days. Residues in Wheat green forage from single GR applications, which are GAP, are reported as <0.01 to 2.4 mg/kg (mean 0.5, s.d. 0.58) in Table 2 of the 1991 monograph. However, in view of information that a 75-day forage grazing restriction applies to the single GR application at planting, the only forage residues tabulated in 1991 which correspond to the GAP reported to the present Meeting range from 0.06 to 1 mg/kg (mean 0.36, s.d. 0.27 at PHIs of ≥66 days).

In addition to the data on wheat forage reviewed by the 1991 JMPR, substantial additional data were provided to the Meeting, although most of it did not reflect GAP, because either multiple granular applications were made (GAP allows 1), SC (=EC) formulations were applied (for EC GAP grazing or cutting for forage is prohibited) or harvest intervals were less than the 75-day grazing/feeding restriction for granular at-plant applications. Green forage residues did not exceed 0.6 mg/kg in the single trial conforming to GAP, which is in line with the maximum 1 mg/kg GAP residue reported in the 1991 monograph. On the basis of current GAP information and relevant data, the Meeting recommended lowering the 1991 estimate of 2 mg/kg for wheat forage (green) to 1 mg/kg.

In the case of wheat straw, the data in the 1991 monograph showed residues ranging between <0.01 and 24 mg/kg (n = 29, mean 1.6, s.d. 4.9). Obviously the 1991 JMPR considered 24 mg/kg to be an outlier, since it recommended a 10 mg/kg limit. All of the residues, except 3 of ≤0.01 mg/kg not included above, were at 27 to 50 days, and most of them at 27-32 days. Residues were ≤0.8 mg/kg, except three results of 8, 10 and 24 mg/kg. Substantial new data were also provided to the Meeting, again mostly for PHIs around 30 days. Residues in 30 samples ranged from <0.01 to 1.5 mg/kg, with a mean of 0.34 mg/kg and s.d. 0.5.

The Meeting noted that few results were available for PHIs greater than 30 days, that a 30-day PHI applies to grain from EC foliar applications, that straw might be fed if grain is harvested within 30 days after EC uses, even with label restrictions on foraging/grazing, and that of approximately 60 results at intervals around or greater than the 30-day PHI (including new results not previously reviewed) residues did not exceed 2 mg/kg (except for values of 8, 10 and 24 mg/kg). Having some reservation about giving no weight at all to the three high values, and taking into account government technical arguments, the Meeting lowered the 1991 estimate of 10 mg/kg for wheat straw to 5 mg/kg.

The Meeting took note of country comments that the residue of 0.11 mg/kg in wheat grain in the 1991 review was an outlier, and observed that all of the 31 results (27-50 day PHIs, mostly 27-32 days) in the 1991 data were ≤0.06 mg/kg (mean 0.02, s.d. 0.02), except the single 0.11 mg/kg value. In 42 results in the substantial data provided to the present Meeting, residues ranged from <0.01 mg/kg to 0.3 mg/kg (mean 0.04, s.d. 0.06) with a relatively continuous distribution of values up to the 0.3 mg/kg residue, but weighted to the lowest values. In both cases most of the data were for PHIs around 30 days for foliar SC (i.e. EC) applications at rates approximating GAP for EC formulations, which includes a 30-day PHI.

A case might be made that the 0.11 mg/kg value in the 1991 data base was an outlier. However, noting that residues were ≤0.2 mg/kg, except one of 0.3 mg/kg, the Meeting concluded that the 1991 JMPR estimate of 0.2 mg/kg for wheat grain could not be lowered. Because a residue occurred at 0.3 mg/kg the Meeting considered recommending an increase to 0.3 mg/kg, but since in the combined 1991 and 1994 data a total of 73 results included only one value exceeding 0.2 mg/kg the Meeting confirmed the 0.2 mg/kg estimate for wheat grain.

Peas, Black eye. Substantial data were received from 1968 US supervised trials on black-eyed peas (green and dry). These "peas" are regulated as beans in the USA. The Meeting was unable to review these data in conjunction with the 1991 JMPR data on beans, because PHI intervals for the additional trials were 28 to 46 days compared to US GAP for beans of 60 days.

Peas, Garden. Although no outstanding questions remained after the 1991 JMPR 0.1 mg/kg estimate for garden peas, limited additional information on peas (0.04 and 0.1 mg/kg in peas and pods respectively) did not require revision of the previous estimate.

Pecans. The Meeting reviewed additional data and current GAP provided in response to concerns expressed at the 1993 CCPR that the 1991 JMPR recommendation to lower the 0.1 mg/kg CXL to 0.01 mg/kg (both limits of determination) did not accommodate GAP soil uses or even the maximum foliar GAP rates. All of the additional data from SC (= EC) formulations (GAP includes either EC or GR) were at 3 to 18 times the reported GAP for foliar ground EC applications of 0.4 kg ai/ha (aerial applications can be 0.8 kg ai/ha, but no aerial data were included). When adjusted to EC GAP rates residues after 26-28 days, compared to the GAP of 30 days for foliar applications, would be up to approximately 0.05 mg/kg. However, control values were often of the order of 0.03 to 0.1 mg/kg.

One of the difficulties, as is often the case for older compounds, is that many of the results were obtained by methods for which limits of determination were not as low as are currently attainable, and there were more old than new data. In this case the additional data do not strictly reflect GAP, but even so in a significant number of cases even control values are above the 0.01 mg/kg level that the method is capable of determining. The 1991 evaluation does not include control values, although the residue in one case is reported as <0.02 mg/kg, presumably a control value.

Although it is clear that new and older methods are capable of determining residues of 0.01 mg/kg, in practice control values can exceed that level. Primarily for this reason the Meeting agreed to withdraw the 1991 JMPR proposal of 0.01 mg/kg, retaining the current 0.1 mg/kg CXL. The Meeting agreed that additional data reflecting the higher aerial foliar applications and soil applications are desirable.

Sorghum forage. The Meeting considered written country comments expressing concern that the 1991 JMPR estimate of 20 mg/kg for sorghum forage (green) was too high for animal safety, and views that the high values leading to that estimate were aberrant. The Meeting also reviewed current GAP information that a 45-day forage/grazing PHI applies, and additional data with maximum residues from GAP applications up to 0.6 mg/kg. It noted maximum residues of 2.1 mg/kg after a GAP 45-day PHI in the 1991 JMPR review (with the exception of one residue of 14.2 mg/kg in a total of 27 values) and residues of <0.01, 3.8, 5.1 and 19 mg/kg after 33-35 days. Noting that a case can be made that the 14.2 mg/kg is an outlier, noting that residues were up to 5 to 19 mg/kg after 33-35 days compared to a 45-day foraging restriction and that other 45-day residues slightly exceeded 2 mg/kg, the Meeting replaced the recommendation of 20 mg/kg for sorghum forage (green) by one of 5 mg/kg.

Sorghum grain. Although no outstanding questions remained on the 1991 JMPR estimate of 0.5 mg/kg for sorghum grain, the Meeting received substantial additional data from trials with granular formulation in which residues did not exceed 0.08 mg/kg from GAP applications and data from trials in accordance with EC GAP but with SC applications, again confirmed as being EC formulations. In these latter residues were relatively evenly distributed up to 0.7 mg/kg. Taking all the data reviewed by the present Meeting and by the 1991 JMPR into account, only 2 of 52 values reflecting GAP exceeded 0.5 mg/kg (0.6 and 0.7 mg/kg from SC applications). While percentage-wise the number of values exceeding the 1991 JMPR 0.5 mg/kg level is low, noting that there is a continuous distribution of GAP residues up to the maximum of 0.7 mg/kg

level, the Meeting recommended increasing the 1991 estimate from 0.5 to mg/kg on sorghum grain to 1 mg/kg.

Tomato. The Meeting considered country comments from Germany and France questioning whether the three relevant US tomato trials (Japanese trials appeared not to include relevant metabolites) were a sufficient basis for a limit, and if so suggesting that the recommended 0.1 mg/kg as partial replacement of the current 0.5 mg/kg CXL for vegetables is not needed since the reported residues after 30 days in the three trials were <0.01(2) and 0.02 mg/kg. On reconsideration of the data base which is small for such a major crop, and taking into account the country comments, the Meeting decided to withdraw the 1991 recommendation.

Definition of the residue. The Meeting considered a written Netherlands government comment proposing deletion of demeton-S (the oxygen analogue of disulfoton) from the definition of the residue which currently includes the sum of disulfoton, demeton-S and their sulphoxides and sulphones, expressed as disulfoton.

The Meeting took note that none of the animal or plant metabolism studies reported in the 1991 JMPR periodic re-evaluation listed demeton-S as a residue, although its sulphoxide and sulphone were so listed. The Meeting also noted that analytical methods can separate and measure the other oxidative metabolites separately or they can be oxidized to the common sulphone. None of the field trials reviewed in the 1991 monograph were presented in such a way as to reveal the levels of the individual compounds. The review leaves a level of uncertainty as to how many of the analyses (if any) included determinations of demeton-S. Therefore, while available evidence suggests that residues of demeton-S are not likely to occur in practice, the data summaries do not allow that to be confirmed with confidence.

As a practical matter, it is probable that many of the current results are based on methods which oxidize residues to the disulfoton oxygen analogue sulphone. This will have taken into account the more toxic metabolites. The fact that there may not have been residues of demeton-S would not appear to be of practical significance. Because of uncertainties remaining on the possible occurrence of residues of demeton-S, the lack of any practical significance in having it included in the definition, the fact that most national MRLs appear to include demeton-S in the residue, and the lack of national monitoring data which include analyses for demeton-S to show whether or not it is a significant component of the residue (suggested at the 1993 CCPR), the Meeting recommended that the definition of the residue should not be changed at present.

Recommendations for MRLs are recorded in Annex 1.

FURTHER WORK OR INFORMATION

Desirable

1. Additional residue data on pecans reflecting the higher aerial foliar application rates, and data from soil applications according to GAP.

2. Additional residue data from trials on dry beans reflecting GAP.

4.20 ETHEPHON (106)

RESIDUE AND ANALYTICAL ASPECTS

The present evaluation is part of the CCPR periodic review programme.

Residue aspects of ethephon were reviewed by the JMPR in 1977, 1978, 1983 and 1985. As an ADI had not been allocated, Guideline Levels were estimated in 1977 and 1978. In view of the time since these estimates, information on current use patterns as well as further residue data and critical supporting studies were required to enable the estimation of maximum residue levels.

Ethephon is a systemic plant growth regulator belonging to the phosphonate family. It is readily absorbed by the plant and releases ethylene which is a natural plant hormone. Ethylene influences directly several physiological processes (e.g. ripening, maturation) and stimulates the endogenous production of ethylene.

Use patterns, usually including one or two treatments at various growing stages of the plants, were reported for a wide range of crops from many countries.

A number of supervised field trials were conducted on several crops in typical geographical regions. Parent ethephon residues were determined in various crop parts and residues of monochloroacetic acid (MCAA), a potential decomposition product of an impurity (the 2-chloroethyl ester) in technical grade ethephon, were also determined in blackberries, grapes, pineapples, tomatoes and cantaloupes. Residues of MCAA were below the limit of determination (<0.01 mg/kg) in all samples.

Residues of ethephon were stable in the treated crops and did not show substantial changes with time, so the PHI usually had little influence on the estimated maximum residue levels.

Apples were treated at rates of 0.5 and 1 kg ai/ha, within the recommended range in the USA, with Ethrel^{R} and harvested from 3 to 13 days after application. Samples taken at day 7 (the PHI corresponding to the lower rate) after treatments with 0.5-0.67 kg ai/ha showed residues varying from 0.37 to 2.32 mg/kg. The highest residues found at longer PHIs (corresponding to the higher rate) were 1.19, 1.76 and 2.04 mg/kg irrespective of the rate. The Meeting concluded that the residue data supported a limit of 5 mg/kg.

Analyses of cherry samples taken 7-8 and 13-14 days after applications in accordance with current use patterns showed residues of 0.69-6.6 mg/kg and <0.01-3.93 mg/kg respectively. The results support the previous estimate of 10 mg/kg.

In a trial conducted in Australia, peaches were treated at rates of 0.2 and 0.4 kg ai/ha and analyzed at harvest two to three weeks after treatment. In the three samples analyzed residues of ethephon were 0.18 and 0.21 mg/kg from 0.2 kg/ha and 0.46 mg/kg from the higher rate. There were no results at the current PHI of 5 days. The Meeting withdrew the previous estimate.

Blackberry samples from trials in the USA in 1974 and 1989 at rates of 1.12-2.8 kg/ha showed residue levels ranging from 8 to 18 mg/kg 1-3 days after application. Thee recommended

rate is 1.27 kg ai/ha. The data are not sufficient to estimate maximum residue level. The Meeting withdrew the previous estimate.

The residues in blueberries from US trials according to Canadian use patterns were 1.4-19 and 2.1-9.1 mg/kg 4 and 39 days after the treatments respectively. The GL recorded previously (20 mg/kg) covers these residues and is now recommended as an MRL.

Samples of cranberries taken 4-7 and 8-14 days after applications at 1.1 kg/ha contained residues of 0.2-2.4 and 0.1-1.1 mg/kg respectively. Residues were below 0.4 mg/kg at 17-21 days after application. No GAP was reported for cranberries. The Meeting withdrew the previous estimate.

Grapes should be treated at least 14 days before harvest. Residues were in the range 0.09-0.82 mg/kg in samples harvested between 14 and 47 days after treatment at 0.56 kg ai/ha. Residues decreased from the range 0.07-2.2 mg/kg with an average of 0.93 mg/kg at day 7 to 0.16-0.47 mg/kg with an average of 0.28 mg/kg at 45 days and <0.01 mg/kg at 91-108 days.

Residues in raisins from grapes treated about 45 days before harvest ranged from 0.21 to 1.49 mg/kg. The maximum concentration factor found from grapes to raisins was 3.5. Raisin waste from grapes harvested 45 days after treatment showed ethephon residue levels of 3.27 to 38 mg/kg with an average of 15.1 mg/kg. In view of the current use patterns the Meeting estimated a maximum residue level of 1 mg/kg in grapes.

Following treatments with 0.38-1 kg ai/ha in Canada, residues in dried figs derived from fruits treated 14-15 days before harvest were in the range 0.32-8.5 mg/kg. The application conditions correspond to US registered uses. Samples taken at 21-41 days contained residues between 0.22 and 2.73 mg/kg and did not show any significant differences at different PHIs. The new residue data support a limit of 10 mg/kg for dried figs. As no residue data were available for fresh figs, the Meeting withdrew the previous estimate.

The concentration of ethephon residues in pineapples following two or three applications did not depend on the rate of the early treatments. When the last treatment was at or below the maximum rate, whole fruit samples taken 7-14 days after the last application contained residues between <0.02 and 1.1 mg/kg with an average of 0.17 mg/kg (9 samples). The residues in 21 pulp samples ranged from 0.06 to 0.33 mg/kg with an average of 0.18 mg/kg. Following two applications at double rates (2.55 + 2.24 kg ai/ha), the maximum residue in the whole fruit was 1.3 mg/kg. On the basis of current US GAP, the Meeting estimated a maximum residue level of 1 mg/kg.

Trials were conducted with four varieties of cucumber at application rate of 0.25 kg ai/ha (one or two treatments) and at PHIs between 28 and 48 days. No residues were found in any of the 9 samples analyzed above the 0.01 mg/kg limit of determination. As the trial conditions do not correspond to reported GAP, the Meeting was not able to estimate a maximum residue level.

Residues in whole cantaloupes from recommended treatments were in the range 0.04-0.4 mg/kg 2-4 days after application. Residues of 0.55 mg/kg in the pulp and 0.69 mg/kg in the peel at day 2 indicate that residues in the whole fruit would be between 0.5 and 1 mg/kg. Residue levels reported in the 1977 evaluation were in the same range when the applications were made at the currently recommended rates. The ratio of the residue in the peel to that in the pulp varied

with the time after application. The peel always contained higher residues. The Meeting estimated a maximum residue level from current use patterns of 1 mg/kg.

As no residue data were reported for other varieties of melon, the Meeting withdrew the previous estimate for melons, except watermelon.

In Peppers treated at 1.12 kg ai/ha, close to the recommended rate, residues ranged from 3.5 to 26.3 mg/kg 5 to 8 days after application. This is similar to the range reported in the 1977 evaluation. In Canadian trials at 0.75 kg ai/ha the residues varied from 0.72 to 1.1 mg/kg 7-8 days after treatment. The new results support the previously recorded GL of 30 mg/kg, which is now recommended as an MRL.

Tomatoes treated with 1.8 kg ai/ha (the maximum recommended rate in the USA is 1.5 kg ai/ha) contained residues in the range 0.09-1.4 mg/kg 3 to 7 days after application. The rate and sampling intervals also cover the current use patterns established in other countries. On the basis of the new results and those reported in the 1977 Evaluations the Meeting estimated a maximum residue level of 2 mg/kg according to current GAP.

In sweet corn treated at 0.56 kg ai/ha, the residues (in kernels plus cobs with husks removed) ranged from <0.02 to 0.62 mg/kg at sampling intervals of 21-39 days, while five of the eight samples analyzed showed residues of less than 0.02 mg/kg 50-79 days after application. The residues were 0.04, 0.05 and 0.14 mg/kg in the other samples. The forage contained residues from 0.15 to 3.95 mg/kg and <0.02 to 1 mg/kg at the shorter and longer sampling intervals respectively. No GAP was reported for sweet corn.

The residues in peas ranged from <0.01 to 0.05 mg/kg and for pea vines from 0.12 to 1.26 mg/kg between 30 and 56 days after application. No GAP was reported.

Residues in mature barley grain ranged from <0.02 to 0.69 mg/kg 35-90 days after application. In one trial 0.78 mg/kg was detected 7 weeks after treatment, but residue levels in the grain at harvest were generally below 0.05 mg/kg. The straw contained residues up to 1.7 mg/kg.

Numerous trials conducted at a rate of 0.56 kg ai/ha, close to the maximum rate registered in the USA, showed residues in mature wheat grain in the range 0.08-0.68 mg/kg at sampling intervals of 34-41 days after application. Residues in the straw varied between 0.95 and 3.23 mg/kg.

Following recommended uses, residues at harvest ranged from <0.01 to 0.3 mg/kg in oat and rye grain and from 0.35 to 1.4 mg/kg in the straw.

In view of the similar use patterns on barley, rye and wheat, the residues were assessed together. It was concluded that the results were mutually supportive and the Meeting estimated maximum residue levels of 1 mg/kg in barley, rye and wheat grain, and 5 mg/kg in the corresponding straws.

As no GAP was reported for oats, no limit could be recommended.

Fifteen of 19 maize grain samples analyzed showed residues of less than 0.02 mg/kg (limit of determination). Residues in the remaining four samples ranged from 0.03 to 0.12 mg/kg.

At harvest, the residues in popcorn kernels were <0.02 mg/kg in 6 samples and 0.19 mg/kg in one sample. Silage and stover contained residues from 0.02 to 2.44 and 0.05 to 1.18 mg/kg respectively. As the trial conditions did not correspond to reported GAP, residue limits could not be recommended.

Rice was treated with 0.36-0.56 kg ai/ha at the tilling stage and sampled at the mature stage 48-69 days later. Residues in the grain were <0.01-0.46 mg/kg. The straw contained residues between 0.04 and 1 mg/kg. No GAP was reported.

A single field trial was conducted on sugar cane with ethephon applied aerially at 2.24 kg ai/ha, about five times the recommended rate. The ethephon residue in cane stalks decreased rapidly from about 4.6 mg/kg immediately after treatment to about 1.3 mg/kg one week later, then more gradually to about 0.2 mg/kg at maturity, 79 days after application. The available information is not sufficient to estimate a maximum residue level.

Residues in hazelnuts (filberts) were in the range 0.03-0.1 mg/kg 28 to 39 days after application at 0.69 kg ai/ha, close to the recommended rate of 0.76 kg/ha. The residues in dried nuts after treatment at 1.87 kg ai/ha were in about the same range. The Meeting was informed that GAP corresponding to the trial conditions was under consideration in the USA. When the recommended use pattern is followed the residues would be below 0.2 mg/kg, which was estimated as a maximum residue level.

Thirteen varieties of walnuts were treated at recommended rates (500 or 750 mg/l) or at an exaggerated rate (1000 mg/l) in California. At PHIs between 7 and 36 days the residues were below 0.3 mg/kg and the average residue was below 0.1 mg/kg. The results support the previously estimated GL of 0.5 mg/kg.

Macadamia nuts were treated once with 500 to 2000 mg/l Ethrel^{R}, 3, 6 or 9 days before harvest or twice, approximately 10 weeks apart, with 750 or 1000 mg/l. None of the 30 samples analyzed showed residues of ethephon above the limit of determination (0.01 mg/kg). The trial conditions cannot be related to the reported use pattern, so a maximum residue level could not be estimated.

Residues in cotton seed treated at about the maximum recommended rate (1.68 kg ai/ha) contained residues from 0.12 to 2.1 mg/kg. Neither the sampling interval (7-14 days) nor the mode of application (ground or aerial) had an observable effect on the residue levels. The results indicate that residues in cotton seed are unlikely to exceed 2 mg/kg when GAP is followed. The Meeting estimated 2 mg/kg as a maximum residue level.

In rape at harvest, residues ranged from undetected to 1.8 mg/kg in the straw and from undetected to 1.2 mg/kg in the seed. As samples were not taken at registered PHIs (30-49 days), a maximum residue level could not be estimated.

Coffee beans were sampled 13 and 30 days after treatment at rates from 120 to 960 mg ai per plant. The residues were between <0.01 and 0.15 mg/kg. The data could not be evaluated because the GAP application rate is expressed in kg ai/ha and the trial data in mg ai/plant. The Meeting agreed to withdraw the previous estimate for coffee beans, 0.1 mg/kg.

No residue data were provided for black currants, lemons, limes, mandarins or onions.

The estimates recorded as GLs by the previous Meetings are therefore withdrawn.

Metabolism studies have been conducted with ^{14}C- and ^{32}P-labelled ethephon on a wide variety of crops, including apples, cherries, cantaloupes, citrus, cucumbers, figs, grapes and raisins, hazelnuts, olives, peaches, pineapples, squash, rubber, tomatoes, tobacco and walnuts. These studies demonstrated that ethylene and phosphoric acid are the only significant metabolites in plants. The latter is taken up into the plant phosphate cycle. No other metabolites were produced in apples, citrus, tomatoes, cucumbers, grapes, olives, walnuts, pineapples, cantaloupes or figs.

Extracts of cherry leaves, but not of fruit, contained unidentified radioactive material accounting for about 5% of the applied ^{14}C in addition to ethephon and ethylene. Similarly an unidentified "metabolite" accounting for about 2% of the applied ^{14}C was found in the extracts from treated squash plants.

In peaches autoradiography indicated a product which was identified as an adduct of ethephon with sugars in the fruit. It was concluded that the binding of ethephon to sugars was involved in the translocation of the compound and was not a metabolic reaction. A similar adduct of ethephon with glucose was produced (to the extent of less than 4% of the applied ethephon) when excised rubber bark was incubated with [^{14}C]ethephon. It was identified as â-D-glucopyranose-1-(2-chloroethyl) phosphonate, a conjugate of 2-chloroethylphosphonic acid.

The excretion of ethephon and the levels of its residues in products of animal origin were studied in cows, goats and poultry.

Ten dairy cows were fed twice a day for 28 days at rates of 0, 1, 5 or 20 ppm in the feed. Milk samples were collected at the morning and evening milkings on days 0, 1, 2, 4, 7, 14, 21 and 28 (the treatment period) and on days 29, 30, 32 and 35 in the withdrawal period. No residues were detected in any milk samples after 28 days feeding.

In another experiment dairy cows were administered ethephon at levels equivalent to 15, 50 or 150 ppm in the feed for 28 days. No ethephon residues (<0.05 mg/kg) were detected in any of the milk samples from the 15 and 50 ppm groups. Of the fifteen samples analyzed during days 19 and 27 from the 150 ppm group, residues in ten were below 0.05 mg/kg while the other samples contained 0.14, 0.1, 0.14, 0.12 and 0.11 mg/kg. The tissues analyzed were muscle, heart, fat, liver and kidney. The liver of one of the three animals treated at 150 ppm contained 0.2 mg/kg ethephon but residues were not detectable in any other samples (<0.1 mg/kg in muscle and <0.2 mg/kg in heart, fat, liver and kidney).

Two lactating goats were dosed with [^{14}C]ethephon at a level equivalent to 10 ppm in the diet for 7 days. Urine, faeces, milk and blood samples were collected daily. Volatiles were collected for 24 hours on the seventh day of the study. Approximately 16 hours after the last dose the animals were slaughtered and tissues collected. Analysis for total radiocarbon showed that a major proportion (31%) of the administered dose was lost as volatiles (ethylene 29%, CO_2 2%). Urine, faeces and gut contained 19.1%, 6.6% and 0.8% respectively. Average radiocarbon levels in whole milk increased for 3.5 days and then reached a plateau (0.38-0.42 mg/kg ethephon equivalents) between 3.5 and 7 days. The total milk collected over the seven-day period contained 3.3% of the administered radioactivity. Kidney and liver had the highest residue levels, at 1.18 and 1.2 mg/kg ethephon equivalents respectively, while fat, heart and muscle contained

0.5, 0.16 and 0.1 mg/kg.

Two groups of Leghorn laying hens, each consisting of 6 birds, were dosed once a day by gelatin capsule for five consecutive days with [^{14}C]ethephon at a level equivalent to 53 ppm in the feed. Ten hens were slaughtered approximately 22-23 hours after the last dose, and muscle (composite of leg and breast) and fat samples, the kidneys and the liver were collected for analysis. All samples were analysed for their radioactive contents. Approximately 26-30% of the administered radioactivity was recovered in the excreta, and about 58% was recovered as ethylene. The $^{14}CO_2$ trap, eggs and tissues accounted for less than 1% of the total radioactivity administered. The ^{14}C (as ethephon equivalents) in the eggs on days 1 to 5 was about 0.002, 0.022, 0.082, 0.183 and 0.179 mg/kg. The yolk contained approximately 80-90% of the residue of which 72.4% could be extracted with a hexane-methanol mixture. The average total ^{14}C residues (mg/kg) were 0.3 in liver, 0.2 in kidney, 0.02 in muscle and 0.15 in fat. Phosphonic acid was not identified in any of the samples.

In view of the residue levels in feed grains and plant by-products (e.g apple pomace, cotton seed meal, pineapple bran, sugar cane molasses, stover etc), the maximum ethephon residue in composite cattle or goat feed is unlikely to exceed 2 mg/kg. Even less would be expected in poultry feed. Consequently animal tissues, milk and eggs should not contain any ethephon residues above the limit of determination of current analytical methods. The Meeting estimated the LODs as maximum residue levels.

The effect of processing on residues was studied in apples, cranberries, grapes, peppers, tomatoes, sugar cane, cotton seed, olives and wheat.

Fresh whole apples containing an average residue of 0.37 mg/kg yielded dried pomace containing an average of 0.73 mg/kg, showing a concentration factor of about 2.

Several sets of cranberry samples were processed into cranberry sauce by a method which approximated commercial practice. Processing reduced the residue level in cranberries sampled 0 and 7-10 days after treatment by average factors of 6.9 and 1.5 in freshly frozen puree, and of 11.5 and 2.15 in cranberry gel, respectively.

The highest concentration factors from grapes to raisins found in a processing study were between 3.5 and 5.3. Residues in wine were at about the same level as in the corresponding grape samples or somewhat lower.

The ethephon residue was reduced by about 79% and 98%, calculated on a dry weight basis, when sweet and hot peppers were commercially dehydrated.

The average residues (mg/kg) found in processed fractions of fresh tomato containing 0.73 mg/kg ethephon were as follows: wet pomace 0.38, dry pomace 1.39, canned fresh juice 0.25, canned puree 0.44, canned paste 0.55, canned juice from concentrated puree 0.29.

Sugar cane was treated at three to four times the proposed label rate to obtain measurable residues during processing. The average ethephon residues (mg/kg) found in two studies were: mature cane 0.13, 029; raw sugar 0.06, 0.28; molasses 0.69, 2.17; mixed juice 0.14, 0.37; syrup 0.37, 0.93. There was a substantial loss of ethephon during the clarification step.

As the application rate was four times the recommended maximum rate only the concentration factors can be used to estimate the residue levels in processed sugar and by-products.

Ginned cotton seed was processed and the fractions analyzed. Ethephon residues (mg/kg) were <0.01-0.32 in ginned cotton seed, <0.01-0.03 in cotton seed hulls, <0.01-0.19 in cotton seed meal, <0.01-0.02 in crude oil, <0.01-0.06 in refined oil and <0.03 in soapstock. Since the initial residues in the cotton seed were much lower than the estimated maximum residue level and the apparent ethephon residues were higher in oil from untreated than from treated plants, the reported studies do not provide sufficient data to estimate residue levels in crude or refined oil.

Apparent monochloroacetic acid residues were extremely low and at the same level in the control and treated samples, showing that no additional monochloroacetic acid was derived from the ethephon application.

It is unlikely that residues would ever be found in alkali-refined oil or in soapstock because ethephon is extremely unstable in bases.

Residue levels in olive oil prepared from seeds harvested 6-7 days after treatment varied from <0.01 to 0.012 mg/kg.

Treated wheat grain contained 0.17 mg/kg ethephon. The wheat bran, wheat shorts and germ, and wheat grain dust derived from it contained 0.23, 0.25 and 0.10 mg/kg ethephon respectively. No quantifiable residues were found in the other fractions (middlings, low grade flour and patent flour). The maximum concentration factor from processing was 1.5 times (in wheat shorts and germ). The residues in the wheat were too low compared with the likely maximum residue level to obtain a realistic estimate of maximum residues in the processed fractions.

Storage stability tests with ethephon and monochloroacetic acid (MCAA) were carried out with several crops. The results showed that ethephon is stable at about -20°C or at room temperature after freeze-drying in or on spiked apples, blackberries, cherries, grapes, pineapples, peppers and tomatoes for at least two years. Studies are being conducted on wheat, cotton seed and cantaloupes. Until a new method is available, walnut samples should be analyzed within three months of harvest. Samples of grapes, pineapples, tomatoes and cotton seeds spiked with MCAA showed a loss of 3-24% after one year under frozen storage conditions.

The principle of the analytical method for the determination of residues has not changed since the early 70s. It consists in extraction with methanol, pH adjustment, precipitation of interfering materials, esterification and final quantification by gas chromatography using a flame-photometric detector or an alkali flame-thermionic detector in the phosphorus mode. The limits of determination are between 0.01 and 0.05 mg/kg for all crops, 0.05 mg/kg for milk, 0.1 mg/kg for muscle and 0.2 mg/kg for other animal tissues. Recoveries range from 70 to 120%.

The Meeting agreed to maintain the definition of the residue as ethephon because the parent compound amounts to >95% of the residue and the analytical method used for determining the residues in supervised trials measures the parent compound.

The Meeting estimated the maximum residue levels shown in Annex I. As an ADI has

now been established they are recommended for use as MRLs.

4.21 ETHION (034)

RESIDUE AND ANALYTICAL ASPECTS

Ethion, previously evaluated for residues by the JMPR in 1968, 1969, 1972, 1975 and 1983, is included in the CCPR periodic review programme.

Ethion is used as an insecticide and acaricide in pre-harvest application on a variety of crops, especially citrus, to control aphids, scales, mites, leaf miners and leaf hoppers. It is formulated as WP, EC or GR and applied between one and four times at a rate of 0.36-2.3 kg ai/ha. Residue data from supervised trials on apples, pears, plums, grapes, citrus, cucumbers, melons and summer squash have been submitted to the Meeting.

Ethion is essentially non-systemic. Metabolism studies on citrus using radiolabelled ethion have shown the degradation of the parent compound to occur on leaf and fruit surfaces. The oxygen analogue metabolites, ethion mono-oxon and ethion dioxon, were identified products (up to 11% and 4% of the total residue respectively). A metabolism study in goats with labelled ethion showed incorporation of significant levels of radiocarbon into casein and lactose, indicating degradation and reincorporation into natural products, and low to negligible levels of the parent chemical in milk. A study on laying hens using the radiolabelled compound showed residues of ethion and its oxygen analogue metabolites to be less than 0.01 mg/kg in eggs and tissue.

Methods of residue analysis in plants involved solvent extraction with acetone followed by dichloromethane/water partition and silica gel Sep-Pak clean-up of the dichloromethane extract. Quantification was accomplished by gas chromatography on a 530 m capillary methyl silicone column connected to a nitrogen-phosphorus detector. For the analysis of milk, cow and poultry tissues and eggs the sample was blended with acetone (acetonitrile for fat), and transferred to hexane. This was followed by acetonitrile partition, clean-up on a polyethylene alumina column, aqueous dilution and dichloromethane partition. For liver, a florisil column was used in place of the polyethylene alumina column. Quantification was by gas chromatography with a packed methyl silicone column connected to a flame-photometric detector. The limits of determination were 0.005 mg/kg in milk and cattle meat, 0.01 mg/kg in eggs and poultry tissue, 0.05 mg/kg in cucurbits, 0.1 mg/kg in apples and pears and 0.5 mg/kg in dry apple pomace.

There was insufficient information on GAP and residues from supervised trials made available to the Meeting for the following commodities covered by Codex CXLs: almonds, apricots, cherries, chestnuts, common beans, cotton seed, egg plant, garlic, hazelnuts, maize, nectarines, onions, peaches, pecans, peppers, sweet peppers, strawberries, tea, tomatoes, walnuts, winter squash, and the meat and edible offals of pigs and sheep. The Meeting therefore proposed withdrawal of the relevant MRLs. Residues in other commodities were evaluated as follows.

Citrus fruits. Ethion residues in citrus fruits are quite persistent and small differences in the PHI have little effect on residue levels. Decreases are probably mostly accounted for by growth dilution.

Numerous US trials according to GAP (3 applications at 3.4 kg ai/ha, with a PHI of 0 days for grapefruit, oranges, tangerines and tangelos and of 15 days for lemons and limes) showed residues which exceeded the present CXL of 2 mg/kg. There were 11 residues in grapefruit over the range 0.62-2.8 mg/kg, 12 in lemons and limes at 1.1-2.9 mg/kg, 6 in oranges at 0.42-3.4 mg/kg and three results each for tangerines and tangelos with a minimum of 1.9 mg/kg and a maximum of 2.7 mg/kg. On the basis of these data the Meeting estimated a maximum residue level of 5 mg/kg for citrus fruits to replace the previous recommendation (2 mg/kg).

The residue in the whole fruit was concentrated primarily in orange oil (11 times) and dry pulp (4.3 times). The residue was reduced in syrup (0.25 times that in the fruits) and finisher pulp (0.02 times). No residues of ethion or its oxygen analogues were found in orange juice (<0.02 mg/kg).

Pome fruits. Results of 9 US trials (6 on apples, 3 on pears) at a maximum rate of 3.4 kg ai/ha, with a 28-day PHI and 3 applications, showed that the present MRL of 2 mg/kg for apples and pears does not suffice since the minimum residue was 0.72 mg/kg and the maximum 3.8 mg/kg. There were no data from trials according to current GAP. The Meeting agreed to withdraw the previous recommendation for apples and pears.

No residues were transferred from apples to cider, but the residue was concentrated in wet and dry pomace, 4.1 and 13 times respectively.

Plums and prunes. The two trials available did not suffice for an evaluation. The Meeting agreed to withdraw the recommendation for plums (including prunes) of 2 mg/kg.

Grapes. Residues in some samples from 9 supervised US trials with two applications of 2.24 kg ai/ha and a PHI of 30 days exceeded the present MRL of 2 mg/kg, with a range of 0.47-4.4 mg/kg. There were no data from trials according to current GAP. The Meeting agreed to withdraw the previous recommendation.

Raisins. Average total residues in raisins and raisin waste showed maximum concentration factors of 2.7 and 9.9 times respectively. The evaluation of processing studies using an application rate of 2.2 kg ai/ha showed large variations of residues in raisins (minimum 0.69 mg/kg, maximum 7.2 mg/kg). The Meeting could not recommend an MRL for raisins because it had withdrawn the previous recommendation for grapes.

Cucurbits. There were 4 values available for cucumbers and melons, and 5 for summer squash, from US trials based on 3 applications, a 7-day PHI and a application rate of 1.1 kg ai/ha.

Residues in cucumbers ranged from 0.03 to 0.42 mg/kg. Summer squash residues were lower (minimum 0.02 mg/kg, maximum 0.05 mg/kg). In melons the few results were below the previous MRL of 2 mg/kg (minimum O.17 mg/kg, maximum 0.58 mg/kg).

Because of the lack of US GAP the Meeting agreed to withdraw the recommendations for

MRLs for cucumbers (0.5 mg/kg), summer squash (0.5 mg/kg) and melons (2 mg/kg).

Meat and edible offal of cattle. Analysis of samples of liver and kidney showed no detectable ethion (<0.005 mg/kg at feeding levels of 5, 10 and 20 ppm). No ethion was detected in muscle at the 5 and 10 ppm feeding levels, while a maximum of 0.008 mg/kg (0.04% transfer) was found at 20 ppm. Fat from cattle fed at all levels contained ethion and showed a minimum of 0.1 mg/kg and a maximum of 0.22 mg/kg (1.1% transfer) at the 20 ppm feeding level.

Milk. Ethion residues in milk appeared rapidly, peaked in 4 to 8 days, and remained relatively constant thereafter. The highest ethion residue found in milk at the 20 ppm feeding level was 0.034 mg/kg (0.17% transfer) and occurred after 4 days.

Meat and edible offal of poultry. White Leghorn hens were fed unlabelled ethion at 10 ppm in their daily feed ration for nine weeks. Tissue samples (gizzard, liver, muscle and fat) taken after nine weeks of feeding were analyzed. No ethion residue (<0.01 mg/kg) was found in any of samples analyzed.

Eggs. Egg samples collected from days 54 to 60 of the feeding study were analyzed. No ethion was detected (<0.01 mg/kg).

In the absence of MRLs for animal feed items (and in the case of cattle meat and milks information on veterinary uses) the Meeting agreed to withdraw the previous recommendations for eggs, milks, and the meat and edible offal of cattle, goats, horses, pigs, poultry and sheep.

The Meeting noted that the oxygen analogue metabolites were usually only a minor part of the residue. The animal transfer study on lactating cows provided evidence that ethion tends to partition into the fat. The Meeting therefore agreed that the residue should continue to be defined as ethion (fat-soluble).

On the basis of the residue data from supervised trials the Meeting concluded that the residue levels listed in Annex I are suitable for establishing maximum residue limits.

4.22 FENPROPIMORPH (188)

±-*cis*-4-[3-(4-*tert*-butylphenyl)-2-methylpropyl]-2,6-dimethylmorpholine

Fenpropimorph is a morpholine fungicide with systemic activity, interfering with sterol biosynthesis. It was considered for the first time by the present Meeting.

TOXICOLOGY

After oral administration to rats, goats and chickens, fenpropimorph was rapidly absorbed, distributed and excreted. In rats and goats, enterohepatic circulation plays an important role. The half-life in plasma and blood varied from 16 to 24 h. In all three species, the levels of the residues

in tissues were relatively low. No accumulation was detected in organs or tissues; only minor amounts appeared in milk and eggs. The excretion pattern (rate and route) was not significantly influenced by the administration route, number of exposures, species, sex or dose.

Fenpropimorph was extensively metabolized in all three species studied (rat, goat and chicken) and a small proportion of the parent compound was found only in chickens. The first metabolic steps involve oxidation of the side chains of the phenyl and morpholine rings. Further metabolism occurs, as indicated by the detection of many (mostly unidentified) metabolites. After administration of the morpholine-labelled compound to rats $^{14}CO_2$ was expired, indicating degradation of the morpholine ring.

Fenpropimorph is slightly to moderately toxic to rats after acute oral exposure. WHO has classified fenpropimorph as being unlikely to present an acute hazard in normal use.

In a four-week toxicity study, rats were given dietary doses of 0, 100, 250, 625 or 1600 ppm fenpropimorph. Increased liver weights and reduced haemoglobin were observed in all dose groups. No NOAEL could be defined. In a three-month toxicity study, rats were exposed to fenpropimorph in the diet at levels of 0, 6.25, 12.5 or 25 ppm. On the basis of increased liver weights at doses ≥12.5 ppm the NOAEL was 6.25 ppm, equal to 0.38 mg/kg bw per day.

Dogs were fed diets containing 0, 50, 100, 200 or 400 ppm fenpropimorph for 13 weeks, or 0, 25, 100 or 400 ppm for 12 months. At the highest dose, the serum activities of alkaline phosphatase and both aspartate and alanine aminotransferases were increased and some slight effects on organ weights were seen. The NOAEL was 200 ppm, equivalent to 5 mg/kg bw per day in the 13-week study and 100 ppm, equal to 3.2 mg/kg bw per day, in the 12 month study .

In a carcinogenicity study, fenpropimorph was administered in the diet to mice at 0, 5, 30, 150 or 1000 ppm for 95 weeks (followed by a recovery period). At the highest level, the main effects were decreased body-weight gain, decreased haemoglobin in males and increased relative liver weights. In females, erythrocyte cholinesterase activity was decreased by 26% at 150 ppm and 29% at 1000 ppm. No effect was found on brain cholinesterase, and there was no evidence of carcinogenicity. The NOAEL was 30 ppm, equal to 3.0 mg/kg bw per day.

In a two-year toxicity/carcinogenicity study, rats were fed doses of 0, 5, 10, 50 or 250 ppm fenpropimorph in the diet. The effects seen at 50 ppm and above were decreased brain cholinesterase activity and increased relative liver weights in males, and enlarged hepatocytes in animals of both sexes. There was no evidence of carcinogenicity. The NOAEL was 10 ppm, equal to 0.3 mg/kg bw per day.

A two-generation reproductive toxicity study was performed in which rats received dietary doses of 0, 6.25, 12.5 or 25 ppm fenpropimorph. Several marginal effects were observed in the highest dose group only. In the F_1 generation, an increased number of stillborn pups was observed, and the pups had decreased body weight and retarded unfolding of the auricle. In F_2 pups, development of the fur and opening of the eyes was retarded. The NOAEL in this study was 12.5 ppm, equivalent to 0.6 mg/kg bw per day.

In order to investigate peri- and post-natal effects, pregnant rats were exposed by gavage to fenpropimorph at doses of 0, 2.5, 10, 40 or 160 mg/kg bw per day from day 15 of gestation to day 21 of lactation. At the highest dose, many toxic effects were observed in dams and pups,

including unsatisfactory general state and pup care, decreased body weight, increased number of dead fetuses, increased pup mortality and diminished physical and behavioural development. At 40 mg/kg bw per day the body weights of dams, pup mortality and gripping reflex (female pups) were affected. The NOAEL for maternal and developmental toxicity was 10 mg/kg bw per day.

Rats were exposed by gavage to fenpropimorph at doses of 0, 2.5, 10, 40 or 160 mg/kg bw per day on days 6-15 of gestation. Maternal toxicity, as evidenced by reduced body-weight gain, vaginal bleeding and an increased number of dead implants (only at 160 mg/kg bw per day), was observed at doses ≥40 mg/kg bw per day. At the highest dose, the weight and length of the fetuses were reduced, and irreversible structural changes, such as cleft palate and inferior brachygnathia, were observed. The NOAEL was 10 mg/kg bw per day for maternal toxicity and 40 mg/kg bw per day for embryo-fetotoxicity and teratogenicity.

Two teratogenicity studies were performed with rabbits treated orally. In the first study (with doses of 0, 2.4, 12, 36 or 60 mg/kg bw per day during days 6-18 of gestation), severe maternal toxicity was observed at 60 mg/kg bw per day; 11 dams died. Only one fetus with several anomalies survived at this dose. At 36 mg/kg bw per day, most of the effects were less severe and occurred at lower incidence; six fetuses had pseudoankylosis. The NOAEL was 12 mg/kg bw per day for both maternal and embryo-/fetotoxicity.

In the second study, rabbits were exposed by gavage to fenpropimorph at doses of 0, 7.5, 15 or 30 mg/kg bw per day on days 7-19 of gestation. Maternal and embryo-fetotoxicity were observed only at 30 mg/kg bw per day. An increased total number of malformations and anomalies was also observed at this dose. The main irreversible structural changes were cleft palate and shortened fore- and hind limbs. The NOAEL was 15 mg/kg bw per day for maternal toxicity, embryo-/fetotoxicity and teratogenicity.

Fenpropimorph has been adequately tested in a range of *in-vitro* and *in-vivo* assays. The Meeting concluded that it was not genotoxic.

No sign of delayed neuropathy was observed in chickens treated with fenpropimorph.

An ADI of 0-0.003 mg/kg bw was established on the basis of the NOAEL of 10 ppm, equal to 0.3 mg/kg bw per day, in the two-year toxicity/carcinogenicity study in rats, using a safety factor of 100.

A toxicological monograph was prepared summarizing the data that were reviewed at the present Meeting.

TOXICOLOGICAL EVALUATION

Levels that cause no toxic effect

Mouse: 30 ppm, equal to 3.0 mg/kg bw per day (95-week carcinogenicity study)

Rat: 10 ppm, equal to 0.3 mg/kg bw per day (two-year toxicity/carcinogenicity study)
12.5 ppm, equivalent to 0.6 mg/kg bw per day (two-generation reproductive toxicity

study)
10 mg/kg bw per day (maternal toxicity in teratogenicity study)
40 mg/kg bw per day (embryo-/fetotoxicity and teratogenicity in teratogenicity study)

Dog: 100 ppm, equal to 3.2 mg/kg bw per day (one-year toxicity study)

Rabbit: 15 mg/kg bw per day (maternal and embryo-/fetotoxicity and teratogenicity in teratogenicity study)

Estimate of acceptable daily intake for humans

0-0.003 mg/kg bw

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

Further observations in humans.

4.23 FENTIN (040)

RESIDUE AND ANALYTICAL ASPECTS

Fentin residue data were evaluated in 1970 and 1972 and then re-evaluated in 1991. The 1991 Meeting required residue data from supervised trials according to current GAP on crops for which the use of fentin compounds is still registered, including cacao beans, carrots, celeriac, celery, coffee beans, peanuts and pecans, to be accompanied by current information on GAP in the countries concerned.

The manufacturer submitted residue data on pecans, and informed the CCPR that the use on other commodities would not be supported. Consequently, the CXLs for these commodities were recommended for withdrawal by the 1993 CCPR.

The US registered use pattern allows up to 10 treatments on pecans with a maximum application rate of 4.2 kg ai/ha in the season. The last application should be just before shuck split. A trial was reported from Georgia, USA. The test plots, consisting of a row of 6 trees for ground treatment and 5 trees in two rows for aerial application, were located in an orchard with 30-year-old trees planted at about 18 m square. An untreated control plot of 2 x 2 trees was located between the treated plots. The distance between the control and aerially treated plots was about 54 m. Triphenyltin hydroxide in a flowable formulation was applied 11 times to both plots at 0.42 kg ai/ha at 14-day intervals. The total amount of pesticide applied was 4.6 kg ai/ha. Duplicate samples were taken from each plot at 48 and 56 days after the final application. The total organotin residues were determined by atomic absorption spectrometry. The limit of determination expressed as tin was 0.005 mg/kg. The conversion factors are 3.09 and 2.96 to calculate triphenyltin hydroxide and fentin, respectively. The recovery was 79%.

The levels of total tin in or on pecans treated by ground or air application and in the untreated control samples were at or below the limit of determination (≤0.005 mg/kg) with the exception of one sample (0.008 mg/kg) taken 48 days after the last aerial treatment. This residue corresponds to 0.024 mg fentin/kg or 0.03 mg triphenyltin hydroxide/kg.

The Meeting noted that in one replicate sample a detectable residue was present indicating that the previous assumption that there were no residues was not valid. The Meeting further concluded that the residue data from two trials conducted at one site in one year were insufficient to estimate a maximum residue level, and consequently withdrew the previous recommendation of 0.05* mg/kg.

4.24 FOLPET (041)

RESIDUE AND ANALYTICAL ASPECTS

Folpet was first evaluated in 1969, and most recently re-evaluated in 1993. The 1993 JMPR was informed that data from cucumber trials would become available in the future from Turkey, Israel and Cyprus. The 1993 Meeting extended the TADI for folpet to 1995.

New information on GAP and data on cucumber trials from Cyprus, Hungary, Israel and Turkey were made available to the Meeting.

The official PHI for cucumbers in Israel is 14 days, but data were available from one trial for samples harvested 10 days after the final application, and from the other trial at 7 days. The highest residues at day 10 were 0.05 mg/kg of folpet and 0.2 mg/kg of phthalimide.

The cucumber trial from Turkey could not be evaluated against Turkish GAP because spray concentration is prescribed in the GAP, and the application in the trial was described in terms of kg ai/ha.

In the Hungarian trial after 14 days (the Hungarian PHI) residues were below the limit of determination (0.05 mg/kg).

In Cyprus the official PHI is 0 days, when the highest folpet residue recorded was 0.36 mg/kg (range 0.12-0.36 mg/kg). This is consistent with residues on day 0 in the Turkish trial (range 0.07-0.28 mg/kg). The majority of the folpet residues in the Hungarian trial at short intervals after treatment were also in the same range, but folpet residues in cucumbers from one plot harvested 2 days after treatment were 0.74 mg/kg.

The Meeting estimated a maximum residue level of 0.5 mg/kg for folpet in cucumbers.

Residue data on apples and lettuce were also made available to the Meeting, but were only in summary form and could not be evaluated.

FURTHER WORK OR INFORMATION

Desirable (repeated from 1993)

Full details and results of the French trials on apples and lettuce now awaiting final reports, together with full details of the relevant French GAP.

4.25 GLUFOSINATE-AMMONIUM (175)

RESIDUE AND ANALYTICAL ASPECTS

Glufosinate-ammonium is used as a post-emergence directed spray for controlling grasses and broad-leaved weeds in a range of agricultural and horticultural crops and as a desiccant on agricultural crops. It was first reviewed by the 1991 JMPR and further information was promised for review by the 1994 JMPR at the 1993 CCPR (ALINORM 93/24 A, para 196), where it was stated that the manufacturer would provide supplementary residue data on fruits and oil seed to support the proposed MRLs. Germany would submit residue data on berries. Canada would provide residue data on lentils and information on GAP for rape seed. There were reservations on the proposed MRLs for rape seed and sunflower seed by France and Germany respectively. Clarification of the availability of citrus processing studies was requested. It was stated that the manufacturer no longer supported the use as a desiccant on soya beans.

The 1991 JMPR had requested an analytical method for determining residues in plants containing vegetable oils, and in meat, milk and eggs.

The present Meeting received summarized information on GAP from Australia, Canada, Germany, The Netherlands and Norway. The manufacturer provided summaries of good agricultural practice for pesticide uses from Belgium, Brazil, France, Germany, The Netherlands and Italy, and an overview of the registration of glufosinate-ammonium world-wide. The manufacturer provided new and supplementary residue data and summary reports on residues in potatoes, currants, sunflower, banana, rape seed, citrus (including processed fractions), kiwifruit and soya beans. A new analytical method and storage stability data were also provided. Explanatory notes on residue trials on currants and sunflower were received from Germany. France provided explanatory notes on residue data on rape seed and sunflower.

The analytical determination of glufosinate-ammonium and the relevant metabolite 3-[hydroxy(methyl)phosphinoyl]propionic acid in rape, soya beans, sunflower (seeds and oil), meat, fat, kidney, liver, milk and eggs is carried out after extraction with water (or a 1:1 mixture of n-propanol and water for milk and fat), clean-up by liquid-liquid partition and anion exchange chromatography, and derivatization with trimethyl orthoacetate. The derivatives are cleaned up on a mini silica gel column and are determined by gas chromatography using a phosphorus-specific flame-photometric detector. The recoveries from untreated control samples fortified with glufosinate-ammonium or the metabolite ranged from 64 to 116% at levels of 0.05 to 10 mg/kg for plant material, and from 70 to 120% for eggs fortified at 0.05-0.25 mg/kg, milk at 0.02-0.1 mg/kg, meat at 0.05-0.25 mg/kg, and liver and kidney at 0.1-0.5 mg/kg. The limit of determination was 0.02 mg/kg for milk, 0.05 mg/kg for plant materials, fats, oils, eggs and meat and 0.1 mg/kg for kidney and liver.

Analytical storage stability studies carried out on almonds, apples, maize, oranges and soya bean seeds indicated that both the parent and the metabolite residues remained stable under frozen conditions for 24 months.

Processing studies carried out on oranges showed that the parent residues are not concentrated in processed commodities, although the metabolite was concentrated in dried peel, dried pulp and molasses (concentration factors 1.6 and 1.9). Trials on potatoes showed the same residue levels in the peelings and the peeled potatoes. The residues were evenly distributed in the tubers and did not decrease during cooking. Processing studies on wheat showed that the milling process leads to an appreciable lowering of the residue in flour and in products baked with it. The residue levels in the bran fractions may be up to twice as high as those in the unprocessed grain. Investigations on rape and sunflower seed showed an increase of the residues in oil cake (concentration factors 2-3) and a reduction in the oil.

The Meeting reviewed the new information on residues in the context of that previously reviewed. When glufosinate-ammonium is applied for weed control residues in the harvested commodities are mostly very low. When it is used as a desiccant, the commodity is directly contaminated and shows residues at harvest. No uptake of the active ingredient via the roots was found, although the metabolite is occasionally taken up via the roots to a small extent.

Citrus fruits. Glufosinate-ammonium is registered for weed control in Brazil, Japan, New Zealand and Spain with application rates from 0.4 (Brazil) to 2 kg ai/ha (Japan and New Zealand). The trials reviewed by the 1991 JMPR from Brazil, Italy, South Africa and the USA, were not according to GAP (of Brazil) and the whole fruit was not analysed. The Meeting received data on residues in the whole fruit of grapefruit (6 trials), lemons (4), limes (2) and oranges (10) from US supervised trials carried out in 1988/89. Glufosinate-ammonium was applied three times at 1.7 kg ai/ha (the proposed label rate for the USA) and at 3.4 kg ai/ha, and samples were taken 8 to 15 days after treatment. No residues of the active ingredient above the limit of determination (0.02 or 0.05 mg/kg) could be detected in any sample. The residues of the metabolite in samples treated at the proposed application rate ranged from <0.05 to 0.14 mg/kg and at the double rate from <0.05 to 0.6 mg/kg. The application rate in the US trials approximates the GAP of Japan, New Zealand and Spain. The Meeting considered that the additional data supported the previous recommendation of 0.1 mg/kg, although the (lower) application rate is not yet official GAP in the USA.

Pome and stone fruits. After the use of the herbicide for weed control the parent and metabolite

residues in apples and pears in German trials were below the limit of determination (<0.05 mg/kg). The Meeting agreed to maintain the current recommendation of 0.05* mg/kg for pome and stone fruits as being a practical limit of determination.

Berries. The Meeting re-evaluated the German residue trials (reported but not tabulated in the 1991 monograph) on blackberries, gooseberries, raspberries, strawberries and grapes, which it considered to be mutually supportive. The Meeting agreed to include grapes in the group "berries and other small fruits (except currants)" at the level of the previous recommendation of 0.1 mg/kg for berries and other small fruits.

Currants. The re-evaluation of four German supervised trials according to GAP on black currants (13 values) showed parent residues at or near the limit of determination (<0.02-0.03 mg/kg), but the residues of the metabolite were <0.02 (6), 0.05 (2), 0.07, 0.12 (3) and 0.48 mg/kg. The Meeting estimated a maximum residue level of 0.5 mg/kg for currants, black, red, white.

Banana. Glufosinate-ammonium is registered for weed control on bananas in Australia, Brazil, Cameroon, Colombia, France and the Philippines with application rates from 0.4 (Brazil) to 1.5 kg ai/ha (Philippines). The present JMPR evaluated residue trials from Brazil and the Philippines. The Meeting received new data on residues from supervised trials (1987-90) carried out in Mexico (3 trials), Costa Rica (2), Colombia (6) and Ecuador (2) which could be evaluated on the basis of Colombian GAP. Glufosinate-ammonium was applied six times a year at application rates from 0.6 to 2 kg ai/ha. Samples were taken between 4 and 155 days after treatment, depending on the ripeness of the banana clusters. There was no apparent correlation between the measured residues and the length of the PHI, nor between the residue level and the total number of applications. The residue data indicate that the active ingredient is not normally found either in banana peel or pulp (<0.05 mg/kg). The metabolite can be taken up via the roots: the highest residues of the metabolite in one sample were 0.13 mg/kg in the pulp and 0.06 mg/kg in the peel. When the relative weights of the peel and pulp are taken into account, this is equivalent to a maximum combined residue in whole banana fruit of 0.12 mg/kg. The Meeting estimated a maximum residue level of 0.2 mg/kg for banana to replace the previous recommendation (0.05* mg/kg).

Kiwifruit. The herbicide is registered for weed control in kiwifruit in Italy (0.2-0.35 kg ai/ha) and New Zealand (1-2 kg ai/ha, 28-day PHI), and the 1991 JMPR evaluated supervised trials carried out in these countries. The 1994 Meeting received data from ten US trials carried out in California and South Carolina in accordance with proposed GAP (application rates from 1 to 2 kg ai/ha and a 14-day PHI). Residues of the parent compound in or on kiwifruit harvested 14 days after the last of three applications were all below the limit of determination (<0.05 mg/kg). The concentrations of the metabolite ranged from <0.05 to 0.37 mg/kg. If this proposed use in the USA becomes registered these results would suggest an MRL of 0.5 mg/kg.

Bulb onion. The use of glufosinate-ammonium for pre-emergence treatment is registered in Canada and Germany. Six German supervised trials according to GAP (0.6-0.8 kg ai/ha) were available. In all samples the residues of the parent compound were below the limit of determination; residues of the metabolite were up to 0.03 mg/kg. The Meeting estimated a maximum residue level for onion, bulb, of 0.05 mg/kg.

Corn salad. The use of glufosinate-ammonium for pre-emergence treatment in lettuce is registered in Brazil, Canada and Germany. In four German supervised trials on corn salad (lamb's

lettuce) according to GAP (0.6 kg ai/ha), the residues of the parent compound and the metabolite were below the limit of determination in all samples. As this is a minor crop the Meeting considered the available data adequate to estimated a maximum residue level for corn salad of 0.05* mg/kg as being a practical limit of determination.

Common bean (pods and/or immature seeds). Glufosinate-ammonium is registered in Germany for the post-emergence treatment of dwarf French beans, spraying between rows with a shield. Eight German supervised trials according to GAP (1 kg ai/ha) were available. The residues of the parent compound and the metabolite in all samples (whole pods) were below the limit of determination. The Meeting estimated a maximum residue level for common bean (pods and/or immature seeds) of 0.05* mg/kg as being a practical limit of determination.

Broad bean (dry), Common bean (dry). Supervised trials with glufosinate-ammonium as a desiccant, with an application rate of 0.6 kg ai/ha, were carried out in Germany in the years 1984-1987, and were evaluated on the basis of German GAP (0.5 kg ai/ha, 14-day PHI). Nine trials on broad beans and five on common beans were available. The residue levels of the parent compound 10-14 days after treatment ranged from <0.05 to 0.89 mg/kg in the seeds of broad beans and from <0.05 to 1.5 mg/kg in common beans. No residues of the metabolite could be found in any samples. The Meeting estimated a maximum residue level of 2 mg/kg for both broad bean (dry) and common bean (dry) as the data were considered to be mutually supportive.

Peas (dry). Supervised trials with glufosinate-ammonium at a desiccant, at an application rate of 0.6 kg ai/ha, were carried out in Germany (6 trials) in the years 1984-1988 and in Denmark (1 trial) in 1988, and were evaluated on the basis of German GAP for field peas (0.5 kg ai/ha, 14-day PHI). In the German trials the residue levels of the parent compound ranged from 0.48 to 2.2 mg/kg and of the metabolite from <0.05 to 0.11 mg/kg in seeds 10-14 days after treatment. In the Danish trial the residues of the parent compound were 0.1 and 0.25 mg/kg and those of the metabolite were below the limit of determination (<0.05 mg/kg). The Meeting estimated a maximum residue level of 3 mg/kg for peas (dry).

Soya bean (dry). The Meeting noted that the use of glufosinate-ammonium as a desiccant on soya beans was no longer supported by the manufacturer. The Meeting therefore evaluated only the residue data from the use for weed control, registered in Brazil and Japan with application rates from 0.5 to 0.93 kg ai/ha. Residue data were received from a total of 56 US supervised trials under conditions of minimum tillage or no-tillage with application rates from 0.52 to 3.2 kg ai/ha. No residues of the parent compound could be determined in the seeds, and the metabolite was quantifiable in only five of the 56 samples, at levels of 0.03, 0.03, 0.04, 0.05 and 0.1 mg/kg The Meeting estimated a maximum residue level of 0.1 mg/kg for soya bean (dry) to replace the previous recommendation (2 mg/kg).

Carrot. The use of glufosinate-ammonium for pre-emergence treatment is registered in Canada and Germany. Eight German supervised trials according to GAP (0.6 kg ai/ha) were available. The residues of the parent compound and the metabolite were below the limit of determination in all samples. The Meeting estimated a maximum residue level for carrot of 0.05* mg/kg as being a practical limit of determination.

Potato. Glufosinate-ammonium is used for pre-emergence weed control in European countries and Japan, and as a desiccant in Belgium, Brazil, Canada, Denmark, Germany, The Netherlands and the UK with application rates from 0.4 to 0.6 kg ai/ha and a PHI from 7 days (Brazil) to 14

days (Belgium, Germany). Only the use as a desiccant leads to quantifiable residues in the tubers. A total of 48 supervised trials of the use as a desiccant were received (34 in Germany, 6 in France, 8 in the UK). In 12 German trials according to GAP (0.6 kg ai/ha) the residue levels of the parent compound in the tubers ranged from <0.05 to 0.17 mg/kg 14 days after treatment. The metabolite could not be determined in the tubers (<0.05 mg/kg). The Meeting agreed to maintain the current recommendation of 0.5 mg/kg for potato.

Sugar beet. The use of glufosinate-ammonium for pre-emergence weed control is registered in Austria and Germany. Eight German supervised trials according to GAP (1 kg ai/ha) were available. The residues of the parent compound and the metabolite were below the limit of determination (<0.05 mg/kg) in all beet samples. The Meeting estimated a maximum residue level of 0.05* mg/kg for sugar beet, as being a practical limit of determination, and 0.1 mg/kg for sugar beet leaves or tops.

Asparagus. The use of glufosinate-ammonium for weed control is registered in Canada, Germany, Italy and Japan with application rates from 0.4 to 0.75 kg ai/ha. Six German supervised trials according to GAP (0.6 kg ai/ha) were available. The residues of the parent compound and the metabolite were below the limit of determination (<0.05 mg/kg) in all samples. The Meeting estimated a maximum residue level for asparagus of 0.05* mg/kg as being a practical limit of determination.

Maize. Glufosinate-ammonium is registered for weed control in Austria, Brazil and Germany with application rates from 0.3 to 1 kg ai/ha. A total of 14 German supervised trials were received: three trials with a single direct treatment at sowing, six trials with an inter-row weed control treatment (at 30-50 cm plant height) in addition to the direct sowing application and five trials with only inter-row weed control. No residues are to be expected in food or feed crops at harvest from direct sowing applications. After inter-row weed control (11 trials), the residues of the active ingredient in maize were <0.05 mg/kg except in one sample which contained 0.07 mg/kg. No residues of the metabolite were detectable (<0.05 mg/kg) in any sample (of shoot, cob or grain) at any sampling time. The Meeting estimated a maximum residue level of 0.1 mg/kg for maize to replace the previous recommendation (0.05* mg/kg).

Wheat. Glufosinate-ammonium is registered in Brazil and Japan for weed control with minimum tillage or direct drilling up to the time shortly before emergence. Two trials were available from Brazil and one from Germany with that use (application rates 0.6-1.2 kg ai/ha). The residues of the parent compound and the metabolite were below the limit of determination (<0.05 mg/kg) in all samples of grain and straw. A further 15 supervised trials (3 in the UK, 12 in Germany) using glufosinate-ammonium as a desiccant were available. Three British and six German trials approximated proposed GAP in the UK. The residues of the active ingredient ranged from <0.05 to 0.21 mg/kg and of the metabolite from <0.05 to 0.14 mg/kg (PHI 10-33 days). If the proposed use in the UK becomes registered these results would suggest an MRL of 0.5 mg/kg for wheat.

Rape seed. Glufosinate-ammonium is used as a desiccant in Canada (0.3-0.41 kg ai/ha, 5-day PHI), Germany (0.5 kg ai/ha, 14-day PHI) and the UK (0.4-0.6 kg ai/ha). Eighteen residue trials were carried out in Canada during the period 1988 to 1990 with 0.3 to 0.4 kg ai/ha according to the label recommendation. The residues of the active ingredient in the seed ranged from 0.05 to 4.2 mg/kg; they were under 1 mg/kg in 13 of the 18 trials and higher than 3 mg/kg in only three. There was no discernible correlation between the residue and the PHI. Residues of the metabolite were lower and ranged from <0.05 mg/kg to 0.64 mg/kg. The residues in 14 European trials (11

from Germany and 3 from the UK) were significantly lower than the Canadian levels. The British trials were with a higher application rate (0.8 kg ai/ha) than registered. The residues in the seeds were 0.1-0.15 mg/kg of the parent compound and 0.05-0.17 mg/kg of the metabolite. Eight of the German trials were according to GAP (0.6 kg ai/ha, 14-day PHI). The residues in the seed were <0.2 to 0.49 mg/kg of the parent and <0.2 to 0.28 mg/kg of the metabolite. The Meeting estimated a maximum residue level of 5 mg/kg for rape seed to replace the previous recommendation (1 mg/kg).

Sunflower seed. Glufosinate-ammonium is registered for use as a desiccant in Germany (0.5 kg ai/ha, 14-day PHI) and Hungary (0.4-0.5 kg ai/ha). The Meeting re-evaluated the data on residues received in 1991 from France (10 trials), Germany (6), Hungary (3) and Italy (4). The three Hungarian trials were not considered, as the metabolite was not determined. The French and Italian, and one of the German, trials were at higher application rates (0.75-1.0 kg ai/ha) than German GAP and only five trials from Germany at 0.6 kg ai/ha with a 14-day PHI could be evaluated on the basis of German GAP. The residues of the active ingredient in the seed ranged from <0.05 to 1.5 mg/kg and of the metabolite from 0.05 to 0.82 mg/kg. The Meeting estimated a maximum residue level of 5 mg/kg for sunflower seed to replace the previous recommendation (2 mg/kg).

Primary animal feed commodities

Maize forage. Glufosinate-ammonium is registered for weed control in Austria, Brazil and Germany with application rates from 0.3 to 1 kg ai/ha. A total of 14 German supervised trials were received: three with only one direct sowing treatment, six with treatment for inter-row weed control (at 30-50 cm plant height) in addition to the application during sowing, and five trials with applications for inter-row weed control only. After direct sowing treatments, no residues are to be expected in food- or feedstuffs at harvest. After inter-row weed control (11 trials), the residues of the parent compound ranged from <0.05 to 0.09 mg/kg both in whole green plants after a 22-70 PHI and in plants without cobs after 71 to 105 days. No residues of the metabolite (<0.05 mg/kg) were present in any sample at any sampling time. The Meeting estimated a maximum residue level of 0.2 mg/kg for maize forage.

Wheat straw and fodder, dry. Glufosinate-ammonium is registered only in Brazil and Japan for weed control in connection with minimum tillage or direct drilling up to the time shortly before emergence. Two trials in Brazil and one in Germany with that use were available (application rates 0.6-1.2 kg ai/ha). The residues of the parent compound and the metabolite were below the limit of determination (0.05 mg/kg) in all samples. Glufosinate-ammonium is temporarily registered in the UK for use as a desiccant. Three British trials with treatment at 0.8 kg ai/ha and six German trials at 1 kg ai/ha were available. After a 14-day PHI the residues of the parent compound ranged from 0.65 to 14 mg/kg and of the metabolite from 0.23 to 4.3 mg/kg. If the proposed use in the UK becomes fully registered these results would suggest a maximum residue level of 20 mg/kg for wheat straw and fodder, dry.

Processed foods of plant origin

Wheat bran. Three processing studies carried out on wheat showed an increase of the parent residues in coarse bran (concentration factor from grain to bran 1.2-2.3). The residue in fine bran was increased in one trial but decreased in the other two.

Wheat flour. Three processing studies carried out on wheat showed a reduction of the residues in the flour. Residues in the flour were above the limit of determination in only one trial (grain 0.59 mg/kg; flour 0.09 mg/kg) with a ratio of flour to grain residue of 0.15.

Rape seed oil, crude; sunflower seed oil, crude. Two processing studies on rape seed and three on sunflower seed showed a concentration of the residues in oil cake (concentration factor 2-3) and a reduction in the oils. The Meeting estimated a maximum residue level for rape seed oil, crude and sunflower seed oil, crude, of 0.05* mg/kg as being a practical limit of determination.

By-products used for animal feed

Citrus pulp, dry. Processing studies on oranges demonstrated that the parent residues are not concentrated in processed commodities. The metabolite was concentrated in dried peel, dried pulp and molasses however (concentration factors 1.6, 1.6 and 1.9 respectively).

Recommendations for new or revised MRLs are recorded in Annex 1.

4.26 GLYPHOSATE (158)

RESIDUE AND ANALYTICAL ASPECTS

Glyphosate was first evaluated by the 1986 JMPR and subsequently in 1987 and 1988.

The Meeting received a proposal to revise the MRLs for soya bean and soya bean fodder on the grounds that the present Codex MRL for soya beans (5 mg/kg) is inadequate to cover the residues that result from the use of glyphosate as a desiccant, which involves application close to harvest.

At the 26th (1994) Session of the CCPR it was suggested (ALINORM 95/24, para 261) that the proposed MRL in unprocessed wheat bran (40 mg/kg) was too high and should be reconsidered by the JMPR. The 26th Session amended the draft MRL to 20 mg/kg pending the JMPR review.

Several residue studies with in-crop applications of glyphosate to soya beans were submitted to the Meeting for review of the MRLs for soya beans and soya bean fodder according to the new use pattern as a pre-harvest desiccant.

The use of glyphosate for in-crop weed control in soya beans varies greatly depending on the nature of the weeds (annual or perennial), extent of infestation, stage of crop growth and application equipment used.

More recently the pre-harvest application of glyphosate as a desiccant has been approved both in Canada and the USA. Two separate studies have investigated the residue levels of glyphosate and its metabolite aminomethylphosphonic acid (AMPA) in soya bean grain.

The first study was conducted at four supervised trial sites in Canada. For all treatment

rates (0.45, 0.9 and 1.8 kg ai/ha) the combined residue levels of glyphosate and AMPA were less than 0.1 mg/kg.

In the second study where ten test sites were selected in the USA, glyphosate and AMPA residues ranged from 0.12 to 3.0 and <0.05 to 0.39 mg/kg respectively.

Data from supervised trials on soya bean crops in the USA were submitted to the Meeting. They demonstrated that when a sequential application of glyphosate in the crop is combined with a pre-harvest application, the glyphosate and AMPA residues in the beans vary considerably, depending on the application rate and the timing of the application.

In these studies the maximum residue levels of glyphosate and AMPA in soya beans following the application of glyphosate at the maximum label use rate as a desiccant according to good agricultural practices were 16.9 and 1.8 mg/kg respectively. In soya bean hay, the maximum residues of glyphosate and AMPA were 202 and 1.7 mg/kg.

The Meeting estimated maximum residue levels of 20 mg/kg for soya bean (dry) and 200 mg/kg for soya bean fodder to replace the previous recommendations (5 and 20 mg/kg respectively).

Glyphosate residues in pigs, poultry and cattle were evaluated by the 1986 JMPR. When administered to animals glyphosate is rapidly excreted without degradation.

Residues in cattle, pig and poultry meat, eggs and milk were negligible after the animals were fed with a diet containing 100 ppm glyphosate and AMPA. The highest residues were found in pig liver and kidney (up to 0.16 and 0.91 mg/kg respectively) and cattle kidney (up to 1.4 mg/kg).

Residue levels of glyphosate in wheat treated according to the proposed label directions for the pre-harvest use of glyphosate were within the Codex MRL (5 mg/kg).

The Meeting received details of a processing study on wheat to determine the fate of glyphosate and AMPA residues during milling. In two trials with incurred residues of glyphosate and AMPA the concentration factor for residues in the production of unprocessed wheat bran from grain ranged from 1.8 to 2.5 and averaged about 2.0.

On the basis of studies evaluated by the JMPR in 1987 and the new study described above, the Meeting confirmed that a concentration factor of 4.0 was adequate and therefore estimated a maximum residue level of 20 mg/kg for unprocessed wheat bran to replace the recommendation of the 1988 Meeting (40 mg/kg).

Residues were determined by HPLC with fluorescence detection after post-column derivatization with *o*-phthalaldehyde. The method has been validated from 0.05 to 250 mg/kg for both glyphosate and AMPA in various crop samples.

Revised recommendations are recorded in Annex 1.

4.27 HEPTACHLOR (043)

RESIDUE AND ANALYTICAL ASPECTS

Heptachlor was evaluated by the 1993 JMPR on the basis of monitoring data supplied by The Netherlands, Sweden and the USA in response to a request for more information by the 1991 JMPR when existing ERLs for carrots, tomatoes and other vegetables were converted to temporary limits. Monitoring data had been provided to the 1991 JMPR by Canada, the USA and Sweden.

The 1993 JMPR noted the low incidence of heptachlor in carrots, sugar beets, tomatoes and other vegetables and recommended the withdrawal of the ERLs for these commodities.

The Meeting noted that the 1993 JMPR did not include a statement about realistic limits of determination for monitoring heptachlor, as has been done for other environmental contaminants. The Meeting agreed that for the general monitoring of heptachlor and its metabolite, a suitable limit of determination for the total residue would be 0.01 mg/kg.

4.28 HEXYTHIAZOX (176)

RESIDUE AND ANALYTICAL ASPECTS

Hexythiazox was reviewed by the 1991 JMPR, which estimated maximum residue levels for apple, cherries, citrus fruits, common bean (pods and/or immature seeds), cucumber, currants, grapes, peach, pear, plums (including prunes), strawberry and tomato. At the 25th (1993) Session of the CCPR several delegations expressed concern regarding the GAP information and residue data considered by the 1991 JMPR (ALINORM 93/24A para 197).

The Meeting received the requested clarification of the information on GAP and additional supervised trials data for apples, plums, black currants and French beans.

At the 1993 CCPR several delegations had expressed reservations regarding the recommended MRLs for citrus fruits, pear, cherries, grapes, strawberry, tomato and cucumber, but no new residue data were received.

Apple. The 1991 JMPR estimated a maximum residue level of 0.5 mg/kg, based on nine trials according to GAP: two in Japan with residues of 0.12 and 0.22 mg/kg at a 7-day PHI; one in The Netherlands (0.03 mg/kg, 28-day PHI); two in New Zealand (0.04 and 0.06 mg/kg, 37-day PHI);

two in South Africa (0.08 and 0.09 mg/kg, 30-day PHI) and two in Germany (<0.05 and 0.16 mg/kg, 28-day PHI). The result of a newly reported trial from Poland supported the residue results reported in the 1991 monograph.

The Meeting concluded that the large difference in the application rates and recommended PHIs between Japan and Korea (0.2-0.3 kg ai/ha, 7-day PHI) on the one hand and New Zealand and the European States (0.04-0.1 kg ai/ha, 14-42-day PHI) on the other leads to different residue levels. The Meeting agreed to maintain the current recommendation of 0.5 mg/kg for apple.

Plums. The 1991 Meeting recommended a 0.2 mg/kg MRL based on one New Zealand trial and two German trials according to GAP (0.04-0.06 kg ai/ha, 28-day PHI) and supported by four South African trials on prunes which were evaluated on the basis of New Zealand GAP (0.06-0.1 kg ai/ha, 28-day PHI). The residue values ranged from 0.01 mg/kg to 0.06 mg/kg. As with apples, the GAP authorized in Japan, 0.13-0.2 kg ai/ha and a 7-day PHI, would be expected to lead to higher residues. The residue data from the new Japanese supervised trials (residue in one trial according to GAP 0.48 mg/kg), suggest that a higher MRL is required, but the data were not sufficient to support a revision of the current recommendation (0.2 mg/kg).

Currants. The 1991 Meeting recommended an MRL of 0.2 mg/kg for red and white currants. The two trials on black currants from Poland provided to the present Meeting were not enough to recommend an MRL for black currants.

Common bean (pods and/or immature seeds). The 1991 JMPR recommended an MRL of 0.5 mg/kg. The two new trials provided by The Netherlands, one indoor and one outdoor, were at higher application rates than are allowed by Dutch GAP. The results suggest that a lower limit is required, but the data were not sufficient to support a revision of the current recommendation (0.5 mg/kg).

4.29 IMAZALIL (110)

RESIDUE AND ANALYTICAL ASPECTS

The 1988 CCPR agreed to delete the proposed MRL of 5 mg/kg for melons in view of the lack of registered uses. However, the Meeting was informed that there are now registered uses in Israel, South Africa and Spain, and received information on use patterns, residue data from supervised trials in Spain, and analytical methods for melons.

Melons, except watermelon. There are two types of application in the post-harvest use of imazalil on melons, one with an aqueous solution and the other a wax containing the technical material.

A wax treatment at 0.2 kg ai/hl, which is approved in Israel and Spain, gave a mean residue of 0.59 mg/kg and the range 0.31-0.84 mg/kg.

Aqueous applications consist in a drench at 0.038 kg ai/hl (Spain), a spray up to 0.1 kg ai/hl (South Africa) and a dip at 0.05 kg ai/hl (South Africa), while residue trials were carried out

with drenches at 0.038 kg ai/hl and 0.075 kg ai/hl.

The Meeting concluded that the three types of aqueous treatment are essentially equivalent from a residue aspect because in any aqueous treatment once the whole surface of the fruit is covered with the solution the surplus will run off.

The Meeting also concluded that the results of drenching at 0.075 kg ai/hl in the Spanish trials could be extrapolated to the spray treatment at 0.1 kg ai/hl which is GAP in South Africa, since the residues from drench trials with two different dose rates were in proportion to the dose.

The mean residue from a drench trial at 0.075 kg ai/hl was 1.1 mg/kg, with the range 0.65-1.47 mg/kg. The highest residue from a spray treatment at 0.1 kg ai/hl would therefore be expected to be 2 mg/kg (1.47 x 0.1/0.075 = 1.96).

The residues of imazalil in melon pulp in all the trials were from <0.05 to 0.15 mg/kg.

The analytical methods for melons are suitable for regulatory purposes.

The Meeting estimated a maximum residue level of 2 mg/kg for melons, except watermelon.

4.30 IPRODIONE (111)

RESIDUE AND ANALYTICAL ASPECTS

Iprodione, used as a fungicide for a variety of crops, was reviewed in the CCPR periodic review programme. It is applied by pre- or post-harvest foliar spray, dipping of plants or roots, and as a seed treatment. It is formulated as WP or SC, and for foliar spraying it is applied between one and five times at a rate of 0.25-1.5 kg ai/ha. In the post-harvest treatment of fruits and vegetables it is used at spray concentrations of 0.075-0.5 kg ai/hl and for seed treatment at rates up to 2.5 g/kg seed. Residue data have been received from supervised trials on citrus, pome and stone fruits, berries, grapes, bananas, kiwifruit, vegetables (brassica, bulb, leafy, legume, root and tuber, stalk and stem vegetables, cucumbers, tomatoes and peppers), cereals, nuts and seeds.

Metabolism studies in plants have shown that iprodione is degraded to *N*-(3,5-dichlorophenyl)-3-isopropyl-2,4-dioxoimidazolidine-1-carboxamide (RP30228), which is the only significant metabolite in certain crops, and also to the desisopropyl derivative (RP32490), a relatively minor metabolite.

The parent compound is generally the main component of the total residue resulting from foliar application. Except in potatoes, certain rice fractions (especially straw) and peanut hay, residues of metabolites are undetectable.

Iprodione is metabolized extensively in goats, chickens and dairy cows. Excretion in urine and faeces is extensive and rapid. Iprodione does not accumulate in the milk, eggs or tissues. Residues of iprodione and its metabolites decrease rapidly when the dose is withdrawn.

Metabolism is similar in goats, chickens and dairy cattle.

Iprodione has low water solubility, is not volatile and is expected to dissipate rapidly in water under natural field conditions. Under laboratory conditions it shows no significant degradation at pH 3, a half-life of 20 days at pH 6 and complete degradation in less than 24 hours at pH 9.

Iprodione has low mobility in various soil types and does not accumulate in soil: its half-life generally varies, in the laboratory, between 20 and 80 days. Light has been shown to accelerate degradation under aerobic conditions. Field trials showed that there was a progressive increase in the rate of degradation with successive treatments.

Processing studies on black currants, grapes, tomatoes, potatoes, maize, wheat, peanuts and hops showed a reduction of the residues in juice, beer, flour and potato flakes and chips, but a concentration in dry pomace and raisins.

Methods of analysis are based on GLC with an EC detector after solvent extraction of the substrate and clean-up by Florisil column chromatography. The limit of determination in most crop and animal samples is between 0.01 and 0.1 mg/kg. The methods determine the parent compound, and the two metabolites if required.

The residue data from supervised trials are on the parent compound only and were evaluated as follows.

Citrus fruits. Data were available from New Zealand, Japan and Israel, but there was no information on GAP. As there were only two trials with dip treatments (0.05-0.075 kg ai/hl, in Italy), the data were also rather limited. No MRL could be recommended.

Pome fruits. Trials on apples with spray treatments in Japan were not in line with GAP. Only three results could be evaluated for pears from spray treatments (Italy, 4-7 treatments, application rate 1.35 kg ai/ha, PHI 20 to 21 days). The residues were 0.51-3.6 mg/kg. These results are not sufficient to recommend an MRL, particularly as according to GAP there should be only 2-3 treatments.

Post-harvest dipping trials (one treatment, 0.05-0.075 kg ai/hl) carried out in France and Italy on apples could be used to estimate a maximum residue level. As there was no decrease in residues during storage, ten results from storage periods between 0 and 222 days could be evaluated (minimum residue 0.61 mg/kg, maximum 2.4 mg/kg). The Meeting agreed to replace the recommendation for apples and pears (10 mg/kg Po), by a recommendation for pome fruits of 5 mg/kg Po.

Apricots. There were only two trials from France, and samples were not taken within the recommended PHI. An MRL could not be recommended.

Cherries. There were five values from Canadian spray trials. There were 6-8 treatments at rates of 0.7-0.875 kg ai/ha with a one-day PHI (residues 1.1-6.5 mg/kg). The Meeting considered the data from cherries and from other stone fruits to be mutually supportive and estimated a maximum residue level of 10 mg/kg for cherries.

Peaches. There were nine values from Canadian trials, based on 2-5 pre-harvest spray treatments at rates of 0.75-1.0 kg ai/ha with a PHI of 0-1 day, similar to Canadian GAP. Residues were 2.2-7.6 mg/kg. In one trial the residues on days 4, 7 and 14 after treatment (9, 10 and 8.5 mg/kg respectively) were higher than on day 0 (7.6 mg/kg). There were no new data on post-harvest treatments. The Meeting estimated a maximum residue level of 10 mg/kg for peaches to replace the previous recommendation (10 mg/kg Po).

Data from France and Australia on nectarines were made available to the Meeting, but there is no GAP in France. A single value from Australia was not sufficient to recommend an MRL.

Plums. Iprodione is registered in France, New Zealand and the USA. For pre-harvest spraying there are 2-3 treatments, a rate of 0.037-0.075 kg ai/hl and a PHI of 0-3 days. There were no residue data from these countries that could be evaluated. Data from South Africa were made available, but there was no GAP. The Meeting agreed to withdraw the recommendation for an MRL for plums (including prunes) of 10 mg/kg.

Gooseberry; Currants, Black, Red, White. The trials on currants and gooseberries carried out in the UK and The Netherlands were not in conformity with GAP, with one exception. The residues considerably exceeded the MRL recommended in 1977, the maximum being 20 mg/kg. The Meeting agreed to recommend withdrawal of the MRL for currants (5 mg/kg).

Blackberries and raspberries. Residue data from four trials on blackberries in the USA in 1986 were provided. The US GAP is included in the GAP for caneberries, which specifies a maximum of 4 applications. Five applications were used in the trials, but this was not regarded as significantly different from 4 in its effect on residues. The residues covered a wide range, from 5.8 to 22 mg/kg, reflecting the typical variation of residues in berry fruits. The Meeting noted that trials in Canada on raspberries with a similar use pattern gave similar residues. The Meeting estimated a maximum residue level of 30 mg/kg for iprodione in blackberries.

In raspberry trials there were four results from the UK which corresponded to GAP: 4-5 treatments, 0.75 kg ai/ha and a PHI of 7 to 8 days. The residues were 0.92-5.4 mg/kg. The Meeting also evaluated Canadian raspberry data (residues 4.6 to 31 mg/kg) according to US GAP and used US blackberry data in support. The Meeting estimated a maximum residue level of 30 mg/kg for raspberries to replace the previous recommendation (5 mg/kg).

Strawberries. There were many results from world-wide strawberry trials. The five US trials with 22 results (minimum residue 0.5 mg/kg, maximum 9.1 mg/kg) were based on 1-5 treatments at 1.1 kg ai/ha with a 0-day PHI. From Belgium there were 4 residues from trials according to GAP (1.9-6.0 mg/kg). In Germany (6 results), residues 10-12 days after the last of 3 treatments at 0.94-1,25 kg ai/ha were lower at 0.13-4.5 mg/kg. The UK provided 7 results from trials according to GAP (0.75 kg ai/ha, 1-day PHI) with residues of 1.9-4.8 mg/kg. There were 6 results from the similar Canadian GAP (1.1 kg ai/ha, 1-day PHI) (minimum residue 0.97 mg/kg, maximum 6 mg/kg) and two results each from New Zealand (3 treatments, 0.7 kg ai/ha, 1-day PHI) and Spain (2-3 treatments, 0.75 kg ai/ha, 3-day PHI) with values from 1.6 to 3.9 mg/kg. The Meeting agreed to maintain the current recommendation of 10 mg/kg for strawberries.

Grapes. Extensive data on grapes were available from France, Chile, Portugal, Spain, Italy, Germany, Morocco, Canada and the USA. The official application rates (mostly 0.75-1.0 kg

ai/ha) and number of applications (mostly 3 or 4) were similar from country to country, but the official PHI varied from 0 days (USA) to 28 days (Germany and Italy). Iprodione residues were quite persistent, and sometimes higher at longer intervals than at the official PHI. Numerous residues were in the 1-5 mg/kg range, with three in the 6-10 mg/kg range and three at 10-11 mg/kg. The Meeting agreed to maintain the current recommendation of 10 mg/kg for grapes.

Bananas. In Spain, iprodione is registered as a post-harvest treatment (1 application, 0.03 kg ai/hl, no PHI). Three residue values from trials according to GAP were available (pulp <0.1 mg/kg, peel 4-7 mg/kg, whole fruit 1.7-3.4 mg/kg). Only three values from one country were not sufficient to recommend an MRL.

Kiwifruit. The suggested MRL is based on 13 values from New Zealand 3-5 applications at 0.75 kg ai/ha and a 1-day PHI (minimum residue 0.28 mg/kg, maximum 4.5 mg/kg). The residues determined in six samples of peeled fruit were between 0.14 and 0.91 mg/kg. The Meeting agreed to maintain the current recommendation of 5 mg/kg for kiwifruit. No GAP was available for post-harvest treatment.

Fennel. The data from one supervised trial were insufficient to recommend an MRL.

Garlic. Data from two trials were available, but their validity could not be confirmed. The Meeting agreed to withdraw the recommendation for garlic (0.1 mg/kg).

Bulb onions. There were six results from Canada (2-5 spray treatments, 0.75-1 kg ai/ha, a 13 to 19-day PHI) which approximated GAP, giving residues of 0.05-0.18 mg/kg. The 5 values from two US trials according to GAP ranged from <0.05 mg/kg to 0.11 mg/kg. The Meeting estimated a maximum residue level of 0.2 mg/kg for onions to replace the previous recommendation (0.1 mg/kg).

Broccoli. Eight values from 4 trials in the USA (1.1 kg ai/ha, 2 treatments) showed iprodione residues between 4.1 and 22 mg/kg. The Meeting estimated a maximum residue level of 25 mg/kg for iprodione in broccoli.

Cauliflower. Trials from Canada could not be evaluated because no Canadian GAP was available. Some French trials were within the application conditions of GAP, but the intervals after treatment were much longer than the official PHI of 15 days. The data could not be used to estimate a maximum residue level.

Head cabbages. Trials from Canada, Germany and the UK were not in conformity with GAP. An MRL could not be recommended.

Chinese cabbage. Trials from Canada, Germany, Denmark and the USA were generally not in accord with GAP. An MRL could not be recommended.

Kohlrabi. There was only one residue value from a treatment according to GAP, from The Netherlands. An MRL could not be recommended.

Cantaloupe. Although there were two trials from France, there was no information on French GAP. An MRL could not be recommended.

Cucumbers. Residue data were available from 7 trials which did not closely reflect GAP. An evaluation of a total of 10 results from France (4 treatments, 0.075 kg ai/hl, a 5-day PHI), the UK (4 treatments, 1.1 kg ai/hl, a 2-day PHI), Denmark (2 to 4 treatments, 0.05 to 0.075 kg ai/hl, PHI 2 to 4 days) and Canada (3 to 9 treatments, 0.05 kg ai/hl, 1-day PHI) showed residues of <0.1-1.8 mg/kg). The Meeting therefore estimated a maximum residue level of 2 mg/kg to replace the previous recommendation (5 mg/kg).

Sweet peppers. Seven US trials based on 8 applications and a 0-day PHI were not in line with GAP (up to 4 treatments, PHI of 3-14 days). The Meeting agreed to withdraw the recommendation for sweet peppers (5 mg/kg).

Tomatoes. Outdoor trials from the USA could not be evaluated because no US GAP was available. The conditions of application in indoor trials in Denmark, Canada and the UK (1 to 7 treatments, 0.05 kg ai/hl, a 0- or 1-day PHI) approximated GAP, but a total of 6 results was not sufficient to support an MRL for a major crop. The Meeting agreed to withdraw the previous recommendation for tomato (5 mg/kg).

Witloof chicory (sprouts). The MRL of 1 mg/kg for witloof chicory recommended in 1977 has been supported by trials in France (1987-1992). There was a total of 20 results which could be evaluated, with residues of 0.03-1 mg/kg. The Meeting agreed to maintain the current recommendation of 1 mg/kg.

Lettuce, Head and Leaf. Numerous trial results were available from many countries. Data on head lettuce were from six German greenhouse trials based on 3 treatments, 0.5 kg ai/ha and a 21-day PHI, two outdoor UK trials (2-6 treatments, 0.25 kg ai/ha, a 7-day PHI), two trials from The Netherlands (2 applications, 0.75 kg ai/ha, 10-42-day PHI, indoor) and one French trial (3 treatments, 0.75 kg ai/ha, 23-day PHI, indoor). The total of 24 residues from <0.02 to 9.2 mg/kg were within the range of the previous MRL. The Meeting agreed to maintain the current recommendation of 10 mg/kg for head lettuce.

Data from US trials on leaf lettuce (3 treatments, 1.1 kg ai/ha, 14-day PHI) were made available to the Meeting. The 18 residue values ranged from 0.16 to 22 mg/kg. The Meeting estimated a maximum residue level for leaf lettuce of 25 mg/kg.

Dandelions. Iprodione is authorized for use in France, but there was only one residue trial which was not in line with GAP. An MRL could not be recommended.

Common beans (pods and/or immature seeds). Trials on succulent beans (snap and lima beans) from Canada and the USA approximated GAP. Residue data from 4 Canadian trials (1-2 treatments, 0.75 kg ai/ha) and 15 US trials (2 treatments, 1.1 kg ai/ha) were provided. In a total of 19 values residues were from <0.05 to 1.3 mg/kg. The Meeting estimated a maximum residue level of 2 mg/kg for common bean (pods and/or immature seeds).

Beans (dry). An evaluation of 14 results from trials in Canada and Japan on white and kidney beans showed that after 14-76 days the residues were lower than 0.1 mg/kg. The Meeting estimated a maximum residue level for dry beans of 0.1 mg/kg to replace the previous recommendation (0.2 mg/kg).

Peas. The description of the analyzed commodity in the submitted trials could not be verified and

the data were considered inadequate for the estimation of a maximum residue level.

Carrots. There were two residue trials according to GAP from The Netherlands covering pre-storage treatment (1 post-harvest spray, 30.4 g ai/t). As the residues do not decrease during storage but even increase because of the water loss, residues at days 0, 63 and 130 were considered for evaluation. Residues were 4.1-7.9 mg/kg.

Results from pre-harvest trials using foliar sprays were available from the USA with rates of application (1.3 to 2.25 kg ai/ha) and numbers of treatments (8 to 13) which were somewhat higher than GAP (4 treatments, 0.56 to 1.12 kg ai/ha). The residues, 0.49-3.1 mg/kg, were substantially below those from the post-harvest treatments. The data were consistent among the various post-harvest trials and the Meeting recommended an MRL of 10 mg/kg. The residues from pre-harvest treatments were lower and would be covered by the proposal for post-harvest treatment.

Radishes. Only three residues from GAP treatments were available, from The Netherlands (1 treatment, 2 kg ai/ha, a 12-day PHI). The residues were 1.8-2.2 mg/kg from a single trial. An MRL could not be recommended.

Potatoes. Four results from US trials after foliar spraying (4 treatments, 1.1 to 2.2 kg ai/ha, 14-day PHI) were in conformity with GAP. The residues in the tubers were below the limit of detection (<0.05 mg/kg). As there were only two trials and potatoes are a major crop no MRL is recommended. Post-harvest uses are registered only for seed potatoes; there is no GAP for the post-harvest treatment of potatoes for consumption.

Sugar beet. Iprodione is an authorized product for seed treatment in France and Greece. After seed treatment in UK trials (1.5 kg ai/tonne of seed), there were no residues above the limit of detection (<0.1 mg/kg). An MRL of 0.1* mg/kg is recommended.

Swedes and turnips. Only one trial from the UK corresponded to GAP. The data are not sufficient to estimate a maximum residue level.

Celery. Iprodione is authorized in Australia, but there were only residue values up to 69 mg/kg from US trials which did not correspond to GAP. An MRL could not be recommended.

Cumin Seed. A single trial was inadequate to recommend an MRL.

Barley. Thirteen residue values from UK trials in accordance with GAP (2-3 treatments, 0.5 kg ai/ha, PHI 41-65 days) were <0.1-1.5 mg/kg. After seed treatment according to German GAP, the residues in the grain were less than 0.05 mg/kg. The Meeting estimated a maximum residue level of 2 mg/kg for barley.

Oats. A single trial of a seed treatment was inadequate to recommend an MRL.

Wheat. As with barley, the trials were in the UK (3 treatments, 0.5 kg ai/ha, a PHI of 42 to 74 days). The residues in grain (5 trials, 8 results) were all ≤0.1 mg/kg. The data were considered inadequate to estimate a maximum residue level for a major crop.

Maize. There were trials in Italy and the USA, but as there was no information on GAP an MRL

could not be recommended.

Rice. USA GAP for the use of iprodione on rice permits 2 treatments and a rate of 0.56 kg ai/ha, with the last application not later than when the heading is 75% complete. There were 18 results on husked rice after PHIs of 28 to 58 days. Residues were 0.09-7.1 mg/kg. The Meeting estimated a maximum residue level of 10 mg/kg for rice, husked, to replace the previous recommendation (3 mg/kg).

Almonds. USA GAP for the use of iprodione on almonds permits 4 treatments and a rate of 0.56 mg/kg ai/ha, with the last application within 5 weeks from petal fall. Four trials could be evaluated, which showed that the residues were mainly on the hulls. Those in the nuts were <0.1-0.18 mg/kg. The Meeting estimated a maximum residue level of 0.2 mg/kg for almonds. This would be compatible with residues of 2 mg/kg in almond hulls.

Rape, oilseed. Data from UK trials (residues 0.12-0.43 mg/kg from 1 to 2 treatments at 0.5 kg ai/ha with a 21-day PHI) could be used to recommend an MRL. The Meeting estimated a maximum residue level of 0.5 mg/kg for rape seed.

Sunflower seed. The use of iprodione on sunflower is registered in France. There were five values from France (2 to 3 treatments, 0.4 to 0.7 kg ai/ha, PHI 61-85 days) and 1 value from Italy (2 treatments, 0.75 kg ai/ha, 41-day PHI) that could be used. Residues were <0.04-0.36 mg/kg. The Meeting estimated a maximum residue level of 0.5 mg/kg for sunflower seed.

Coffee. Although iprodione was applied to coffee in two trials, there was no information on GAP. The data were insufficient to recommend an MRL.

Milk, cow tissues. Dairy cattle were treated once daily for 29 days with iprodione at levels corresponding to 5, 15, 50 and 200 ppm in the feed. Milk samples were collected on treatment days 8, 17 and 28 and tissue samples at slaughter. At the 5 ppm feeding level there were no detectable residues of iprodione or its metabolites in milk (<0.01 mg/kg) or tissues (<0.05 mg/kg). At the 15 and 50 ppm feeding levels the total residues in milk were 0.026-0.052 mg/l) and in tissues <0.05-0.76 mg/kg. In the absence of detailed information on metabolism the Meeting was unable to recommend MRLs for milk or tissues.

Poultry. Three groups of hens were treated for 28 days by capsule with iprodione at nominal levels of 2, 20 and 100 ppm in the diet or 0.15, 1.5 and 7.5 mg/kg body weight. The total residues in eggs reached a plateau after day 7 of the treatment at 0.1 mg/kg, 0.64 mg/kg and 1.9 mg/kg at the three feeding levels. They had decreased to undetectable levels (<0.01 mg/kg) by day 9 for the 2 and 20 ppm feeding levels and day 12 in the 100 ppm group.

The total residues in liver, muscle, kidney and fat from the 2 ppm feeding level at day 28 were 0.53, <0.05, 0.23 and 0.15 mg/kg respectively, and had decreased to undetectable levels (<0.05 mg/kg) by day 14 of withdrawal at all three feeding levels. In the absence of detailed information on metabolism the Meeting was unable to recommend MRLs for poultry meat or eggs.

Animal feeds. Results of trials on bean fodder and the straw and fodder of cereal grains were available.

Bean forage. Residue data from 13 supervised US trials on snap and Lima bean forage covered a wide range. On the basis of the highest value of 75 mg/kg the Meeting could support a maximum residue level of 100 mg/kg for bean forage (green).

Straw and fodder (dry) of cereal grains. Residue data from supervised trials in the UK on the straw of barley (11 values) and wheat (4 values) were provided. Residues ranged from 0.63 to 5.5 mg/kg. Residues in the grains were of the order of 0.1 mg/kg (wheat) to 1.5 mg/kg (barley). The Meeting agreed the data could support a maximum residue level of 5 mg/kg for the straw and fodder (dry) of cereal grains.

On the basis of the residue data from supervised trials the Meeting concluded that the residue levels listed in Annex I are suitable for establishing MRLs.

4.31 METHAMIDOPHOS (100)

[See also acephate (4.2)]

RESIDUE AND ANALYTICAL ASPECTS

Methamidophos is a widely used organophosphorus insecticide with systemic properties; its residues may also occur as a metabolite of acephate. It was first evaluated in 1976, with further reviews of residue aspects in 1979, 1981, 1984, 1989 and 1990. Extensive new residue data were reviewed by the 1990 JMPR, together with updated information on current GAP and national MRLs. At the 24th Session of the CCPR (1992), the proposed MRLs for some commodities were held at Step 7B pending comment from several countries for various reasons (ALINORM 93/24, para: 119-123); the commodities were broccoli, head cabbages, cauliflower, celery, citrus fruits, cotton seed, egg plant, melons except watermelon, peaches, potatoes and tomatoes. Information on GAP, results of residue trials and national MRLs have been received from manufacturers and additional data and comments have been submitted by several countries. The relevant data on these crops published in the earlier Evaluations have been reassessed. The present review is mainly concerned with the above mentioned crops but some data on residues in hops, kale, pome fruits, rice, soya beans and yard-long beans are also included.

Information on minor modifications that had been made to the method of residue analysis was made available. These were aimed at consolidating the extraction procedures and improving the recovery and reproducibility. Information was also provided that illustrated the validity of a method for the determination of residues of methamidophos in pome fruits, potatoes and rice, and of a GLC method that was suitable for beets, green vegetables, grains, husks and potatoes.

Since residues of methamidophos can also arise from the use of acephate, the uses of both pesticides have to be taken into account. Extensive information on the use patterns of the two pesticides on the Step 7B crops referred to above was made available from various sources, together with information on GAP for some additional crops.

A review of the data on residues of methamidophos arising from the use of acephate on citrus fruits and brassica crops that had been published in the Evaluations of earlier JMPRs showed that very few results had been obtained under current GAP conditions. Fortunately, some

had been resubmitted this year and these could be evaluated. Results of the relevant supervised trials are summarized on a commodity basis below.

Citrus fruits. Data on residues from the use of methamidophos on citrus fruits in Egypt and the USA, reported by the 1981 JMPR, were not supported by GAP information. In trials in Spain in 1988 residues were up to 0.85 mg/kg at day 0 but declined to 0.05 mg/kg by day 60; the Spanish GAP PHI, however, is 28 days. Trials with acephate on mandarin oranges in Japan at GAP rates were reported by the 1990 JMPR, showing up to 0.09 mg/kg of methamidophos at 30 days PHI but 0.15 mg/kg at 45 days. Further trials on mandarin and summer oranges in Japan in 1992-93 gave residues ranging from 0.03 to 0.33 mg/kg in the whole fruit at 30 days; the majority of the residue was in the peel. The Meeting agreed to withdraw the current recommendation of 0.5 mg/kg for citrus fruits.

Pome fruits. Trials of methamidophos on apples in Italy in 1992, according to Italian GAP, gave residues up to 0.33 mg/kg at 21 days PHI. In similar trials in France in 1992 residues were somewhat lower, reaching 0.1 mg/kg at 21 days. Pears treated with methamidophos in France in 1992 showed up to 0.2 mg/kg at 21 days, declining from 1 mg/kg at day 0. No data were available on residues arising from the use of acephate on pome fruit. Although the data under GAP conditions were rather limited (7 trials) the Meeting agreed to recommend an MRL of 0.5 mg/kg for pome fruits.

Peach. Trials with methamidophos on peaches reported by the 1976 JMPR were not according to GAP. Summary data from trials on peaches in Spain showed up to 0.26 mg/kg at 21 days; however, this was a double-dose treatment and Spanish GAP requires a 28-day PHI. No data were available on residues arising from the use of acephate on peaches. The Meeting agreed to withdraw the previous recommendation for peach (1 mg/kg).

Broccoli. The trials with methamidophos on broccoli reported by the 1976 and 1981 Meetings were not according to GAP. Two trials in Brazil, recorded by the 1990 JMPR, showed no residues above the limit of determination. Trials of acephate on broccoli were carried out in five countries in which this use is not registered, and thus GAP was not observed. The Meeting agreed to withdraw the previous recommendation for broccoli (1 mg/kg).

Cabbages, Head. Summary data reported by the 1976 JMPR from the treatment of cabbages in the USA and Germany gave residues of methamidophos up to 0.11 mg/kg at 7 days and 0.07 mg/kg at 14 days but the applications were not according to the quoted GAP. Data on residues in cabbages treated in Australia were reviewed at the 1981 JMPR. Residues were 0.02-0.07 mg/kg at 13-14 days and <0.02 mg/kg at 20-21 days PHI; the stated PHI in Australia was 35 days. Data reported to the 1990 JMPR showed that residues of methamidophos were generally below 0.01 mg/kg in the USA at the recommended PHI of 35 days, apart from one apparently anomalous study giving 0.76 and 1.1 mg/kg; all trials included 6 applications at 1.1 kg ai/ha instead of the maximum of 4 allowed under GAP. Residue data from the use of acephate on cabbages in New Zealand were reviewed by the 1984 JMPR from two trials that were according to their GAP and gave 0.17 and 0.2 mg/kg at 7 and 10 days PHI, respectively. No other valid data on residues in cabbages from acephate uses were available. The Meeting agreed to withdraw the previous recommendation for head cabbages (1 mg/kg).

Cauliflower. Trials on cauliflower in Germany and the USA reported at the 1976 JMPR showed residues of methamidophos in the heads up to 0.45 mg/kg at 14 days, 0.23 mg/kg at 21 days and

0.12 mg/kg at 28 days; leaves showed up to 6.28, 1.11 and 0.62 mg/kg, respectively, at the same time intervals. Data reported by the 1981 JMPR from trials in Australia and Germany showed residues in cauliflower heads of 0.02 mg/kg or less at 20-21 days PHI; the GAP PHI is 28 days in Australia and 21 days in Germany. The information available to the 1990 JMPR was very variable. Two trials in Brazil showed <0.01 mg/kg at PHIs from 14 to 28 days. Results from trials in the USA in 1973 gave up to 0.48 mg/kg in the flowerheads at 15 days and 0.21 mg/kg at 21 days (the residues in the leaves were higher) but none of these results were obtained at the GAP PHI of 28 days. No valid data were presented on residues of methamidophos from the use of acephate on cauliflowers. In the absence of adequate data either to support the existing recommendation or to suggest a new one, the Meeting agreed to withdraw the previous recommendation for cauliflower (1 mg/kg).

Melons, except Watermelon. Only one of the trials reported by the 1990 JMPR (from Mexico in 1973) was according to the then appropriate recommended GAP; residues were below 0.1 mg/kg from day 0 to day 14. All US trials in 1982 involved an excessive application rate (1.5 times the maximum); at 14 days PHI residues ranged from 0.19 to 0.56 mg/kg. No data were available on residues of methamidophos from trials according to current GAP or resulting from the use of acephate on melons. The Meeting agreed to withdraw the previous recommendation for melons, except watermelon (0.5 mg/kg).

Egg plant. The 1976 JMPR recorded residues in the range 0.02 to 0.10 mg/kg for PHIs of 0 to 7 days after applications of methamidophos to egg plants in Mexico; the treatments were outside current Mexican GAP rates. The data reported to the 1984 JMPR showed very variable residues, with maxima of 1.9 mg/kg at 3 days and 0.65 mg/kg at 7 days, using up to 15 applications; but, again, these treatments were not in accordance with GAP. The 1990 JMPR reported results from the USA which were then, but are not now, according to US GAP, showing residues up to 0.17 mg/kg at 3 days and up to 0.12 mg/kg at 7 days PHI. No data were available on residues of methamidophos resulting from the use of acephate on egg plants. The Meeting agreed to withdraw the previous recommendation (1 mg/kg).

Tomato. Only one result from the residue trials reported by the 1976 JMPR had been obtained under the quoted recommended use (GAP) conditions. Trials data from New Zealand and South Africa were available to the 1981 JMPR. Although it is stated that it could not be determined whether nationally approved GAP had been followed, the highest residue was 0.53 mg/kg at 4 hours PHI; at 7 days residues were <0.01 to 0.3 mg/kg. Trials data from Spain and Brazil were recorded at the 1990 JMPR. In the Spanish glasshouse trials, residues were 0.18-0.25 mg/kg at 3 days, 0.27-0.35 mg/kg at 7 days and 0.20-0.34 mg/kg at 14 days. Results from Brazil were all under 0.01 mg/kg from 3 or 2 days PHI. However, neither treatment was in accord with the stated GAP. Summary data were provided from two trials of methamidophos on tomatoes in Thailand in 1993. Crops were sprayed at either the maximum rate or at double rate; in either case residues were about 0.1 mg/kg at 25 days PHI. The PHI for most crops in Thailand is 21 days but no information was available as to whether this use is registered.

Data on residues of methamidophos from the use of acephate on tomatoes, as presented in the 1976 JMPR Evaluations, are inadequate to relate the residues to the appropriate GAP. For the 1990 JMPR, data were produced from 5 trials of the use of acephate on tomatoes in France in 1988, with residues of 0.31 and 0.43 mg/kg of methamidophos at 21 days after the last of two applications; other results were below 0.1 mg/kg at 21 days. This use is not currently registered in France.

Data from 4 trials of acephate on tomatoes which were carried out according to the relevant GAP in Japan in 1984 and 1985 and from one trial in South Africa in 1973 were provided to the present Meeting. In the Japanese trials, at the recommended PHI of 3 days, residues of methamidophos were between 0.03 and 0.08 mg/kg. Residues in the South African trials were 0.03 and 0.07 mg/kg at 3 days. Several trials were also carried out in Canada, which has no registered uses of acephate on food crops (maximum residues 0.15 mg/kg at 3 days and 0.21 mg/kg at 21 days).

For such a major crop, adequate residue data obtained under GAP conditions were limited and not sufficient either to support the existing recommendation or to suggest a new one. The Meeting agreed to withdraw the previous recommendation (1 mg/kg).

Kale. Data from one trial at two levels in Brazil were assessed at the 1990 JMPR. After 4 applications at 0.6 kg ai/ha, 1 mg/kg was found on the day of the last application but residues were below 0.01 mg/kg after 14 to 28 days. When a double-dose treatment was given, residues were also below 0.01 mg/kg at 21 days PHI. Six trials were carried out in Thailand over three growing seasons using four applications at either the maximum recommended rate of 1.2 kg ai/ha or double this amount, at intervals of 5 to 6 days. Residues declined rapidly, from 30-50 mg/kg at day 0 to less than 0.05 mg/kg at the usual Thailand PHI of 21 days. Although it is stated that GAP was observed in the trials, no information was available on whether the use is registered in Thailand. No maximum residue level could be estimated.

Yard-long beans. Data on six trials carried out in Thailand over three growing seasons on yard-long beans were provided. Four applications were made at either the maximum recommended rate of 1.2 kg ai/ha or double this amount, at intervals of 5 to 6 days. The residues found in the succulent pods with beans (without peduncle) declined rapidly, from 11 to 26 mg/kg at day 0 to less than 0.02 mg/kg at 14 days; no further sampling was done as the residues had then reached the limit of determination. The usual PHI in Thailand is 21 days for most crops; although the report states that GAP was observed in the trials, no information was available on whether the use is registered in Thailand. No maximum residue level could be estimated.

Potato. Residues from trials of methamidophos on potatoes reported by the 1976 JMPR did not exceed 0.11 mg/kg at 7 days PHI but the summary data are limited and the number of applications was twice the number allowed by GAP. Data reported at the 1981 JMPR were confined to one trial in New Zealand at double the GAP application rate; residues were 0.07 and 0.19 mg/kg at 7 days and <0.01 and 0.03 mg/kg at 14 days. At the 1982 JMPR no data were detailed, but it was stated in the 1982 evaluation, which was published with the 1989 Evaluations, that "In 23 experiments in which potatoes were treated repeatedly with methamidophos in accordance with GAP, all residues were below the existing MRL of 0.1 mg/kg". At the 1990 JMPR data were presented from Brazil, Spain and the USA, all results being below 0.01 mg/kg. Four trials of methamidophos on potatoes were carried out in Germany in 1988, using 7 applications at 0.6 kg ai/ha. All residues were below the limit of determination (0.01 mg/kg) from day 0 to day 21; the PHI in Germany is 14 days.

Summary data reported by the 1976 JMPR showed that residues of methamidophos in the peel and pulp of potatoes treated with 1 to 2 kg ai/ha of acephate were 0.03-0.06 mg/kg and 0.02-0.04 mg/kg, respectively, 3 and 14 days after application. Very limited data summarized by the 1984 JMPR showed no residues of methamidophos above 0.05 mg/kg following treatment of

potatoes in New Zealand with acephate at 0.42 to 0.84 kg ai/ha.

The Meeting estimated a maximum residue level of 0.05 mg/kg for potato to replace the previous recommendation of 0.1 mg/kg.

Celery. Limited data on residues of methamidophos in celery were recorded by the 1976 JMPR. At 21 days PHI, residues were up to 1.55 mg/kg in the stalks, 0.08-6.0 mg/kg in the tops and 0.02-0.20 in the whole plant; treatments were close to US GAP. Residue data from the USA, as reported by the 1990 JMPR, showed a similarly large variation. At the recommended PHI of 21 days, residues ranged from <0.01 to 1.27 mg/kg in the stalks and from 0.02 to 3.14 mg/kg in the whole plant. No data were available on residues of methamidophos resulting from the use of acephate on celery. From the review of existing data, the Meeting agreed to confirm the recommendation for celery (1 mg/kg).

Rice. In 4 trials in Thailand in 1992/93, rice was treated twice with methamidophos at 0.6 kg ai/ha. The residues were about the limit of determination (0.01 mg/kg) in polished grain, straw, glume and bran at 50 to 61 days PHI after being 27 mg/kg in the green plant at day 0. Methamidophos is not registered for use on rice in Thailand, although acephate can be used. This use on rice is at a rate similar to the GAP for methamidophos on rice in Malaysia and several Central and South American countries. No maximum residue level could be estimated.

Cotton seed. Data from treated cotton were summarized very briefly in the 1976 Evaluations. Residues in cotton seed were up to 0.06 mg/kg at 21 to 26 days after treatment with methamidophos at 0.26-2.24 kg ai/ha. As the data also covered rape seed treatments, the results could not be interpreted with any degree of assurance. In the report of the 1982 JMPR, although no data were given, it was stated that the residue data provided from supervised trials supported the existing MRL for cotton seed. Residue data on cotton seed, cotton forage (green) and cotton bolls were reported by the 1990 JMPR. Residues on cotton seed ranged from 0.1 to 1.6 mg/kg at 7 days and from 0.02 to 0.21 mg/kg at 28 days. No data were given at the USA recommended PHI of 50 days and 5 applications were made instead of the allowed maximum of 2. Data were made available from trials of methamidophos on cotton in the USA in 1973 using 5, 6 or 7 applications of 1.1 or 2.2 kg ai/ha. Six days after the last of 7 treatments the highest residue in the fuzzy seeds was 0.05 mg/kg, all other treatments giving 0.01 mg/kg or less.

The data in the Evaluations of the 1976 JMPR for residues of methamidophos derived from the use of acephate on cotton list only the "..maximum levels found in a series of experiments". No evidence of the extent of the trials or of the range of residues found is included. Fortunately, full results of all of these trials have been provided for the present Meeting, although only in tabular format. Of the 159 results quoted, 6 were from 6 to 8 applications of acephate at 0.88 kg ai/ha, 124 from 4 to 15 applications at 1.1 kg ai/ha and 29 from 4 to 8 applications at 2.2 kg ai/ha; PHIs ranged from 6 to 69 days. Residues were below the limit of determination of 0.01 mg/kg in 129 of the samples examined; there were 8 results at 0.01 mg/kg, 15 at 0.02 mg/kg and one each at 0.03, 0.07, 0.09, 0.13, 0.14, 0.23 and 0.26 mg/kg. All of the last four results over 0.1 mg/kg were from one trial in which the residues of acephate were also unusually high, being in the range 0.61 to 1.4 mg/kg as against the normal findings of less than 0.1 mg/kg with occasional excursions up to 0.4 mg/kg. Information was provided that, although no maximum number of applications was prescribed, it was extremely unlikely that more than 5 per season would ever be used under the USA label directions for insect control and current GAP. Therefore, disregarding the four apparently anomalous results which all involved eight applications and two of which at

double the maximum rate, it is clear that at 21 days PHI residues of methamidophos will generally be well below the proposed Step 7B MRL of 0.1 mg/kg. The Meeting agreed to maintain the current recommendation of 0.1 mg/kg for cotton seed.

Soya bean. Summary data were provided from a trial of methamidophos on soya beans in Thailand in 1993; residues from 3 applications at 0.25 or 0.5 kg ai/ha after 7 days were <0.01 and 0.01 mg/kg, respectively. These are well within the current CXL of 0.05 mg/kg.

Hops. Residues in dry hops 59 days after treatment in Poland with methamidophos at 0.75 kg ai/ha were 0.04 mg/kg, but it was not clear whether this treatment was according to Polish GAP. German GAP has 1.8-3.6 kg ai/ha and a 42-day PHI. The residues are well within the present CXL for hops, dry, of 5 mg/kg.

Data were provided on the effects of various forms of processing on the residues of methamidophos in several commodities. Residues in crude and refined oils from treated cotton seed, soya beans and corn were below the limit of determination (0.01 mg/kg); nor could residues be detected in mint oil. Canning green beans caused residue losses up to 55 % of the original value and no residues could be detected in dried pinto beans.

Information was also provided on residues of methamidophos occurring in food in commerce and in market basket studies. Residue data showed the distribution of methamidophos between the peel and pulp of treated mandarin and summer oranges. Residues of methamidophos in the pulp of mandarins did not exceed 0.10 mg/kg, while 0.14 mg/kg was on the peel; the maximum level in the whole fruit was 0.11 mg/kg. In four trials with 50% acephate wettable powder on oranges, residues of methamidophos on the peel reached 0.68 and 0.97 mg/kg while the respective pulps contained 0.03 and 0.05 mg/kg at 30 days PHI; the maximum in the whole fruit was 0.33 mg/kg.

Methamidophos residues in crops treated with acephate at the maximum label rates were monitored from harvest through typical commercial processes to the consumer. Bell peppers showed the least loss, 3 to 17%, from the farm gate to the consumer. In Brussels sprouts, residues decreased by about 33% after sorting, while blanching plus freezing lost a further 34%. Cauliflower residues were reduced by about 60% after trimming and processing. In lettuce, levels were reduced by 10% by removing wrapper and outer leaves. Snap bean levels decreased by about 64% during handling from the field to the market shelf and by canning.

Eight market basket surveys were carried out quarterly in 1984 and 1985, each involving the collection of samples from three different geographical locations within the USA. From 26 to 62 commodities were collected in each of the surveys, the edible portions of each commodity from each location being combined and stored frozen until analysed. Residues of methamidophos were found in only 7 of the 62 commodities sampled, namely cantaloupe (0.1 mg/kg), celery (0.04 mg/kg), cucumbers (0.06 mg/kg), lettuce (0.02 mg/kg), sweet green peppers (0.26 mg/kg), tomatoes (0.17 mg/kg), and canned snap beans (0.01 mg/kg). Methamidophos was not consistently found in any commodity in every survey.

Residues of methamidophos were found in only five groups in the 1992 Australian Market Basket Survey, 24 or 32 samples in each group. The residues (mg/kg) were lettuce max. 0.27, mean 0.014; spring rolls max 0.1, mean 0.040; chicken nuggets max 0.03, mean 0.005; pears max. 0.003, mean 0.0012; oranges max trace, mean 0.0002.

From the same market basket study, the daily intakes by various age/sex groups were calculated to be, as ìg/kg bw for an average energy intake, adult male, 0.0403; adult female, 0.0226; boy 12 years, 0.0655; girl 12 years, 0.0450; child 2 years, 0.0747; infant 9 months, 0.0028. Results for the 95% decile energy intake were about 1.8 times greater.

The changes shown in Annex 1 are recommended.

4.32 METHIDATHION (051)

RESIDUE AND ANALYTICAL ASPECTS

Although the JMPR was not requested to re-examine the 1992 confirmation of the 0.5 mg/kg CXL for apples, based on a 14-day PHI, a country reported its revised GAP (a longer PHI and fewer applications) and proposed that the data reviewed by the 1992 JMPR would support a lower limit of 0.2 mg/kg. While the commenting country's revised GAP would not be sufficient to revise the CXL because other countries' GAP permits a 14-day PHI, the residues reported to the 1992 Meeting which were according to GAP with various PHIs did not exceed 0.18 mg/kg after 14 days. However, since residues approached 0.5 mg/kg in trials previously reviewed by the JMPR which were in accordance with GAP the Meeting recommended that the CXL should be retained.

The Meeting re-examined the estimate by the 1992 JMPR in its periodic review of 1 mg/kg for cotton seed on the basis of new information on current GAP and written comments from one country, based on a statistical analysis of the data, supporting 0.5 mg/kg. On the basis of the new GAP information the Meeting concluded that four of the studies examined by the 1992 JMPR were based on treatments with 1.5 to 1.7 times the maximum approved seasonal application. These studies included the highest values of 0.34 and 0.68 mg/kg, leaving a maximum value of 0.27 mg/kg for the remaining results. If adjusted to the GAP rate residues would still be up to approximately 0.5 mg/kg.

The Meeting agreed that on a purely statistical basis a case might be made for a lower limit. However, because of the relatively limited number of results and the lack of a clear reason not to believe the results valid, the Meeting confirmed the 1992 estimate.

The Meeting also considered a country comment questioning the proposal of 2 mg/kg for crude oil, twice the level proposed for the seed, and noted that the 1992 JMPR had reviewed data from two cotton seed processing studies. Residues of 0.02 and 0.04 mg/kg in the seed had resulted respectively in 0.06 and 0.07 mg/kg in the crude oil, an average concentration factor of 2.4. The 2 mg/kg estimated by the 1992 JMPR is therefore consistent with the application of this concentration factor to the proposed MRL of 1 mg/kg. While the Meeting agreed that better processing studies with cotton seed containing residues higher than 0.04 mg/kg would be desirable, the estimate was based on the available data. The Meeting confirmed the 1992 recommendation of 2 mg/kg as an MRL for cotton seed oil, crude.

The Meeting was asked whether the residues supporting the 1992 estimate of 0.05 mg/kg

for cucumbers were from glasshouse or outdoor uses. The 1992 JMPR monograph listed glasshouse uses, but the trials data did not indicate whether the trials were outdoor or glasshouse. In the absence of additional information, the Meeting was unable to recommend changing the current proposal.

The Meeting reviewed information on GAP from Spain, France and Chile for nectarines and peaches and written comments from Chile concerning the 1992 periodic review recommendation to withdraw the 0.2 mg/kg CXLs for apricots and nectarines while retaining the CXL at the same level for peaches. The comments noted that pests and uses are very similar for nectarines and peaches.

The Meeting agreed that the information on GAP indicated that the uses on the two fruits were similar, and noted that it was usually willing to combine data on nectarines and peaches when GAP is the same for both, and almost always when there is a good data base for one but not for the other. Although none of the results reviewed by the 1992 JMPR were from trials which closely matched GAP, the Meeting agreed that a credible case could be made for interpreting German peach trials reviewed by the 1992 JMPR in the context of French GAP application rates.

With maximum residues up to 0.7 mg/kg after 14 days and 0.3 mg/kg after 21-24 or 28 days, the Meeting concluded that the current 0.2 mg/kg CXL could reasonably be supported only at PHIs of 28 days or more, although the reported PHI according to French GAP is 14 days. While the PHI in Chile is 28 days, no data were available from that country (or neighbouring countries with similar GAP). The data suggest that 0.2 mg/kg could be a little low even at 28 days.

The Meeting recommended that the CXL of 0.2 mg/kg for nectarines should be retained for the time being (as previously recommended for peaches), but on the basis of a PHI of 28 instead of 14 days. It confirmed the 1992 recommendation to withdraw the CXL of 0.2 mg/kg for apricots.

4.33 MONOCROTOPHOS (054)

RESIDUE AND ANALYTICAL ASPECTS

Monocrotophos was re-evaluated by the JMPR under the CCPR periodic review programme for residues in 1991 and toxicologically in 1993.

The 1991 JMPR requested information on GAP for rice in the countries in which residue trials have been carried out.

At the 1993 CCPR, several countries indicated that the information considered by the JMPR did not reflect their current agricultural practices. It was decided not to advance any MRL then at Step 3 or to propose the deletion of the existing CXLs at that Session, but to await a full re-evaluation by the JMPR in 1994 based on updated GAP and residue data to be provided by national governments.

The 1993 CCPR also requested the manufacturer to provide an analytical method with a lower limit of determination than current methods.

The Meeting received only limited information on national GAP for monocrotophos. It noted some differences between this new information and that submitted to the 1991 JMPR, but they were not so serious as to require changes in existing CXLs, except in the case of soya beans.

Egg plant, chilli peppers, tea. Comments were made at the 25th Session of the CCPR (ALINORM 95/24, paras 136-138) on the proposed MRLs for egg plant, chilli peppers and tea. No new information was provided, and the Meeting made no new recommendations.

Soya beans. The 1991 Meeting was aware that some residues in trials from Australia exceeded the existing MRL for soya beans, but concluded that the application rates in these trials, 0.4 and 0.45 kg ai/ha, were considerably higher than the recommended rate of 0.28 kg ai/ha. The highest application rate in current Australian GAP is 0.36 kg ai/hl however, and therefore close to the rates used in the trials.

The Meeting reconsidered the data on residues in soya beans as given in the 1991 Evaluations, taking note that there was now appropriate GAP in Australia, but concluded that the information was not sufficiently clearly expressed for a revised recommendation to be made.

Rice. The manufacturer submitted information on GAP in India and Thailand in response to a request of the 1991 JMPR, but this did not accord with the GAP with which the residue data submitted to the 1991 JMPR were linked.

The Meeting was informed by the manufacturer that new supervised trials have been planned for rice. The trials would be designed to analyze rice in husk, husked rice, polished rice and bran.

Analytical methods. The manufacturer did not provide an analytical method with a limit of determination lower than the existing limit of 0.02 mg/kg, arguing that since the 1993 JMPR had increased the ADI to its former value of 0.0006 mg/kg bw the development of a residue method with a lower limit of determination was not necessary.

4.34 PARATHION-METHYL (059)

RESIDUE AND ANALYTICAL ASPECTS

Parathion-methyl was initially scheduled for evaluation in the CCPR periodic review programme in 1991 but was postponed, awaiting a comprehensive set of US studies and clarification of US GAP. Information was made available to the Meeting from national governments (Australia, Germany, The Netherlands, Thailand and the USA) and two manufacturers.

Metabolism studies on a lactating goat and laying hens were made available for review. The goat was dosed with the equivalent of 6 ppm parathion-methyl in the feed for 3 days. In the goat neither parathion-methyl nor paraoxon-methyl were present in extracts of milk, kidney,

liver, muscle or fat. Identified metabolites were mostly formed by loss of a methyl group or reduction of the nitro group.

In the hens, dosed for 1 or 3 days with the equivalent of 6 ppm parathion-methyl in the feed, parathion-methyl was identified in the kidney, gizzard, heart and fat. Metabolites with the nitro group reduced to amino were present in the liver. Nitrophenol and its sulphate were identified in the eggs. Nitrophenol was found in all tissues except muscle.

Very little ^{14}C was translocated to the tubers when radiolabelled parathion-methyl ([^{14}C]phenyl) was applied to potato plants. Nitrophenol was the major metabolite. Parathion-methyl was identified as a minor component of the residue, constituting 4% and 0.6% of the total ^{14}C residue in the tubers 5 and 21 days after treatment.

Nitrophenol and parathion-methyl were the major components identified in cotton seed from a plant treated with radiolabelled parathion-methyl ([^{14}C]phenyl). Parathion-methyl was the major component in cotton leaves. Paraoxon-methyl was not detected.

Nitrophenol and parathion-methyl were the major identified components of the residue in lettuce treated with radiolabelled parathion-methyl.

Residue analysis for parathion-methyl, paraoxon-methyl and nitrophenol relied on extraction of plant material with acidic methanol, followed by solvent partition clean-up. Parathion-methyl and paraoxon-methyl were then determined by GLC, with detection by an FPD in the phosphorus mode. Nitrophenol levels were measured by HPLC. The validated LOD for most substrates for the three compounds was 0.05 mg/kg.

Information on frozen storage stability was made available to the Meeting on many commodities: bean seed and pod, dry bean seed, bluegrass hay, cabbage, celery, clover forage, hops, lettuce, maize, maize fodder, maize forage, mustard greens, onions, succulent pea forage, pea straw, dry peas, succulent pea pods and seed, soya bean seed, sunflower, turnip roots, turnip tops, wheat, wheat forage, and wheat straw. Parathion-methyl was stable under the storage conditions; paraoxon-methyl was mostly stable, but losses could occur in the long-term storage of lettuce, hops and sunflower seeds.

Residue trials on apples and pears according to the German use pattern showed that parathion-methyl residues were not detected (<0.05 mg/kg) at the official PHI (28 days) and even at 14 days. However, a total of 2 trials on apples and 2 on pears was insufficient for the Meeting to estimate maximum residue levels.

Four trials according to GAP on 4 varieties of grapes in Germany in 1990 produced no detectable residues (<0.01 mg/kg) at the official PHI (35 days), but also at 28 days. The trials from Thailand could not be evaluated because information on relevant GAP was not available. The Meeting was unable to estimate a maximum residue level because the number of trials was too limited for a major crop.

Trial data for green onions and bulb onions were made available, but the application rate in all trials but one was double the GAP rate in the USA. The Meeting was unable to make recommendations for green or bulb onions.

Trials on cabbage and broccoli were considered together. US GAP for broccoli is the same as for cabbage.

Parathion-methyl residues were not detected in cabbage with or without wrapper leaves in a series of US trials according to GAP. The Meeting noted the analytical problems experienced in four trials from California where the LOD for parathion-methyl in samples including wrapper leaves was 0.5 mg/kg. In these trials oxydemeton-methyl had been applied to the crop as part of the normal insect control regime, and caused interference in the GLC analysis for parathion-methyl. US GAP requires a 21-days PHI for a final application rate of 1.1-1.7 kg ai/ha, and 7 days if the final application rate is 0.56 kg ai/ha.

Residues were not detected (<0.05 mg/kg) in 10 broccoli trials in accordance with US GAP. In two other trials residues of 0.05, 0.06 and 0.10 mg/kg were reported. The Meeting noted that paraoxon-methyl levels were of the same order as parathion-methyl levels in one broccoli trial.

The Meeting estimated maximum residue levels for cabbage and broccoli of 0.2 mg/kg parathion-methyl.

Sweet corn trials could not be evaluated because no GAP for sweet corn was available.

In reviewing the data on head lettuce, leaf lettuce and turnip greens, the Meeting noted that residue levels on the crops from most of the trials were below the LOD (0.05 mg/kg). However, trials in California on each of these crops produced much higher residues (1-2 mg/kg).

In 7 US trials on head lettuce, residues were not detected (<0.05 mg/kg) on lettuce with or without wrapper leaves when parathion-methyl was used according to GAP. In an eighth trial (from California) residues around 1 mg/kg were reported. Parathion-methyl was not detected (<0.05 mg/kg) in 5 of the 8 US trials on leaf lettuce. In 2 trials residues of 0.11 and 0.23 mg/kg were reported, and in the remaining trial (from California), 1.6 mg/kg. The Meeting was informed that all of the California trials, on both leaf and head lettuce, produced samples that were of small size and not of commercial quality. The interval between the final application and harvest was in December 1988 when prevailing conditions were cold and dry, which may explain the lack of normal growth. The Meeting decided to disregard the lettuce trials in California, because the lettuces were not representative of the commodity in commercial trade. There remained 5 valid trials on head lettuce and 6 on leaf lettuce.

The Meeting estimated a maximum residue level of 0.05* mg/kg for head lettuce and 0.5 mg/kg for leaf lettuce.

In 10 of the 14 trials on mustard greens parathion-methyl residues were not detected (<0.05 mg/kg). The highest residue was 0.51 mg/kg. US GAP requires a 21-day PHI if the final application rate is 1.1-1.7 kg ai/ha, and 7 days if the final application rate is 0.56 kg ai/ha. The Meeting estimated a maximum residue level of 0.5 mg/kg for mustard greens.

Parathion-methyl was not detected (<0.05 mg/kg) in 6 US trials on turnip greens according to GAP, but in a seventh trial (from California) residues of 1.8 mg/kg were reported. In 7 trials with a modified use pattern (final application 0.56 kg ai/ha with 7-day PHI) which is not GAP, residues from one Californian trial were 3.8 mg/kg, substantially higher than in the other 6

trials (<0.05 mg/kg to 0.91 mg/kg), supporting the validity of the residue found in the Californian trial which was according to GAP. The Meeting agreed that this residue was not an outlier and estimated a maximum residue level of 2 mg/kg for turnip greens.

In 8 of the US trials on spinach parathion-methyl was not detected (<0.05 mg/kg). In 5 of the remaining trials residues ranged from 0.05 to 0.09 mg/kg, and in the final one 0.30 mg/kg was recorded. US GAP requires a 21-day PHI for a final application rate of 1.1 kg ai/ha, and 15 days if the final application rate is 0.56 kg ai/ha. The Meeting estimated a maximum residue level of 0.5 mg/kg for spinach.

Snap beans and lima beans were considered together as they provided mutual support. Parathion-methyl was not detected (<0.05 mg/kg) in snap beans (whole pods) in 9 US trials according to GAP, nor in succulent whole pods of lima beans in 4 US trials. The Meeting estimated maximum residue levels for common beans and lima beans of 0.05* mg/kg as being a practical limit of determination.

In a series of US trials on dry beans residues were not detected (<0.05 mg/kg) 15 days after the application of parathion-methyl at 1.7 kg ai/ha. US GAP requires a 21-day PHI, but because residues were undetectable the Meeting was able to evaluate the data. The Meeting estimated a maximum residue level for dry beans of 0.05* mg/kg as being a practical limit of determination.

Parathion-methyl residues in dry peas ranged from not detected (<0.05 mg/kg) to 0.18 mg/kg in 8 US trials according to GAP. US GAP requires a 15-day PHI if the final application rate is 1.1 kg ai/ha, and 7 days if it is 0.56 kg ai/ha. The Meeting estimated a maximum residue level of 0.2 mg/kg for dry peas.

Residues were not detected (<0.05 mg/kg) in 5 of the 8 US trials on peas in pod. In the two Delaware trials residues of 0.21 and 0.68 mg/kg were recorded. The Meeting estimated a maximum residue level of 1 mg/kg for garden peas (young pods).

Data from 10 trials on soya beans in the USA could not be evaluated because the trial conditions did not match US GAP.

Residue levels between 0.2 and 0.8 mg/kg were consistently produced in a series of US trials on carrots. The Meeting estimated a maximum residue level of 1 mg/kg for carrots.

Even with exaggerated application rates parathion-methyl residues were not detected (<0.05 mg/kg) in potatoes in a series of US trials in 5 States. The Meeting estimated a maximum residue level for potatoes of 0.05* mg/kg as being a practical limit of determination.

In sugar beet also, exaggerated application rates of parathion-methyl did not produce detectable residues. The Meeting estimated a maximum residue level for sugar beet of 0.05* mg/kg as being a practical limit of determination.

In all 7 US trials on turnips where parathion-methyl was used according to GAP residues were not detected (<0.05 mg/kg). The Meeting estimated a maximum residue level for turnips of 0.05* mg/kg as being a practical limit of determination.

The application of parathion-methyl at 1.1 kg ai/ha to artichokes resulted in residues 7 days after the final application of 0.8 to 1.6 mg/kg in the 4 US trials. The Meeting estimated a maximum residue level of 2 mg/kg for artichokes.

Residue data were available for celery with and without foliage. Residue levels on celery stalks were somewhat lower than on the whole plant but the MRL is estimated on the commodity including foliage. In the 12 trials a number of residue values were reported in the 4-5 mg/kg range. The Meeting estimated a maximum residue level of 5 mg/kg for celery.

Supervised trials on maize from the USA could not be evaluated because the application rate in the trials was twice that permitted in US GAP.

Parathion-methyl residues in rice ranged from 0.2 to 2.3 mg/kg in 6 US trials where parathion-methyl was applied according to US GAP. Paraoxon-methyl residues in the same trials were in the range 0.08 to 0.23 mg/kg. The Meeting estimated a maximum residue level of 3 mg/kg for rice.

No information on GAP was available to evaluate supervised trials on sorghum from the USA.

Parathion-methyl residues in wheat ranged from undetectable (<0.05 mg/kg) to 5.1 mg/kg in a large series of supervised trials in the wheat-growing states of the USA. In the trials according to GAP many residues were undetectable, but more were in the 0.2-0.5 mg/kg range. Paraoxon-methyl residues were undetectable (<0.05 mg/kg) in most of the samples but ranged up to 0.49 mg/kg, which was found in the sample with the highest parathion-methyl residue. The Meeting estimated a maximum residue level of 5 mg/kg for wheat.

The highest residues in cotton seed were 1.2 and 1.4 mg/kg when parathion-methyl was used on cotton according to US GAP, but residues in cotton seed from 2 trials were undetectable (<0.05 mg/kg). The residues from one cotton variety in California appeared to be quite at variance with the residues from another variety in Texas. The Meeting considered that a total of four trials according to GAP were insufficient to make a recommendation.

Only 2 trials were available for the use of parathion-methyl on sunflower; residues in the sunflower seed were not detected (<0.05 mg/kg) as expected because of the long PHI, 30 days. However, the Meeting considered that 2 trials were insufficient to make a recommendation.

Residue data for green hops and dry hops were made available to the Meeting from a series of trials on parathion-methyl in 3 States of the USA. Parathion-methyl residues in green hops in trials according to GAP ranged up to 0.18 mg/kg, while in the dry hops the highest residues were 0.42, 0.49 and 0.99 mg/kg. The highest paraoxon-methyl residues in green and dry hops were 0.15 and 0.35 mg/kg respectively. The Meeting estimated a maximum residue level of 1 mg/kg for dry hops. The current CXL for dry hops, 0.05* mg/kg, was recommended for withdrawal by the 1992 JMPR.

Parathion-methyl residues were not detected (<0.05 mg/kg) in alfalfa seed in 4 US trials according to GAP. No MRL recommendation was made because alfalfa seed is not a listed Codex commodity.

Of the 7 supervised trials on clover forage according to US GAP, 5 appeared to be of one population with residues in the range <0.05 to 0.23 mg/kg while residues from the other two trials were in the range 2.5 to 6.5 mg/kg. All trials appeared to be valid. The Meeting estimated a maximum residue level of 10 mg/kg for clover.

The Meeting was provided with data from 6 supervised trials on bean forage according to US GAP. Parathion-methyl residue levels ranged from <0.05 to 0.66 mg/kg. Data for bean hay could not be evaluated because the interval between the final application and harvest was 15 days whereas the official PHI is 21 days for a 1.7 kg ai/ha application. The Meeting estimated a maximum residue level of 1 mg/kg for bean forage.

Extensive data were provided on parathion-methyl residues on pea forage from trials on dried peas and succulent peas. Residues were measured at 10, 15, 20 and 25 days after the final application, and in a number of cases residues were similar after these different intervals. The 112 valid results cover a very wide range, from <0.05 to 58 mg/kg.

The data appeared to consist of more than one population with 63 values up to 0.5 mg/kg and 43 values above 2 mg/kg. the Meeting noted that there had been contamination of some samples from the Delaware trials, which had provided the highest values. Further, although the PHIs for beans and peas are different, residues on forage should generally be similar for the same application rates, but residues on the pea forage were much higher. The Meeting noted that the US tolerance for garden pea forage is 1 mg/kg, and was reluctant to proceed with a recommendation before an explanation for the divergent data and the reasons for the US tolerance were sought. The data on pea straw and pea vines would also be considered when this further information could be reviewed.

Supervised trials on maize fodder and forage could not be evaluated because the application rate in the trials was higher than US GAP. Similarly, trials on sweet corn fodder and forage could not be evaluated because there is no current GAP for sweet corn and the application rates in the trial exceeded GAP application rates for maize.

In one trial on rice straw residues were recorded at 7.5 mg/kg, while in the other 3 trials residues were only up to 0.2 mg/kg. The Meeting estimated a maximum residue level of 10 mg/kg for rice straw and fodder. The estimate is supported by the estimate for wheat straw and fodder.

The results of trials on sorghum forage, fodder, hay and silage could not be evaluated because no GAP was available.

The highest parathion-methyl residues in wheat forage (6 US trials according to GAP), wheat hay (6 US trials according to GAP) and wheat straw (17 US trials according to GAP) were 1.5, 1.2 and 11 mg/kg respectively. Wheat forage is the part of the wheat plant above the ground. It has a typical moisture content of 75%. Wheat hay is produced by allowing the cut forage to dry for several days in the field after cutting and has a typical moisture content of 12%. Wheat straw (typical moisture 12%) is the remaining part of the wheat plant after the grain has been removed (threshed). The Meeting estimated a maximum residue level of 10 mg/kg for wheat straw and fodder.

Bluegrass hay, Bermuda grass hay and fescue hay were considered together. Residue data

from 5 US trials on each under the same use conditions covered the same general range. The highest reported parathion-methyl residues in the three were 1.0, 1.6 and 2.5 mg/kg respectively. The Meeting estimated a maximum residue level of 5 mg/kg for the hay or fodder of grasses.

Parathion-methyl residues were undetectable (<0.05 mg/kg) in sugar beet fodder 60 days after the final application in 6 US trials. The Meeting estimated a maximum residue level for sugar beet leaves or tops of 0.05* mg/kg as being a practical limit of determination.

The metabolism studies on a lactating goat and laying hens suggest that parathion-methyl residues in animal tissues, milk and eggs will be low compared with residues in animal feed. The metabolism studies were not adequate to recommend MRLs for residues of parathion-methyl in animal commodities derived from residues in animal feeds. Animal transfer studies are needed before MRLs for animal commodities can be recommended.

Processing studies on maize, cotton seed, potatoes, sugar beet, snap beans, soya beans, rice and wheat were made available to the Meeting. In potatoes, sugar beet and snap beans, even exaggerated application rates did not produce detectable residues in the raw agricultural commodities. Parathion-methyl residues tended to be concentrated in the bran and oil fractions of processed commodities. Residue levels in flour and polished rice were less than in the raw grains. Processing did not apparently convert parathion-methyl to paraoxon-methyl.

Parathion-methyl levels were reduced by a factor of 4-5 in the production of brown rice (husked rice) from harvested rice grain. Much of the residue was retained by the rice hulls. Paraoxon-methyl levels in the brown rice were reduced below the LOD (0.05 mg/kg). Parathion-methyl levels were reduced further in the production of polished rice. On the basis of the residue reduction factor from the processing study and the estimated maximum residue level of 3 mg/kg for rice, the Meeting estimated a maximum residue level of 1 mg/kg for husked rice.

In wheat milling, parathion-methyl levels in bran were 1.9-2.4 times the level in the wheat, while levels in flour were close to 0.3 times the wheat levels. On the basis of the residue concentration factor for bran and the estimated maximum residue level of 5 mg/kg for wheat, the Meeting estimated a maximum residue level of 10 mg/kg for wheat bran.

The Meeting agreed that the residue should continue to be defined as parathion-methyl only. Paraoxon-methyl is usually a minor part of the residue and in many cases is not detectable. Paraoxon-methyl residue levels can be similar to parathion-methyl levels but usually only when residues are very low. Paraoxon-methyl need not be determined for monitoring pesticide use practices, but should preferably be determined when total diet studies are conducted.

Nitrophenol residues appear to be more persistent than those of parathion-methyl, and often exceed the parathion-methyl levels. Nitrophenol is not useful for monitoring use practices because it also arises from parathion.

FURTHER WORK OR INFORMATION

Desirable

Animal transfer studies.

4.35 PHORATE (112)

TOXICOLOGY

Phorate, an organophosphorus insecticide which inhibits cholinesterase, was first reviewed by the Joint Meeting in 1977. A temporary ADI of 0-0.0002 mg/kg bw was established in 1982. In 1985, after review of a study of delayed neurotoxicity in chickens, an ADI of 0-0.0002 mg/kg bw was allocated.

The limited data available indicate that phorate when given orally to rats is not readily eliminated, with less than 40% of the administered radioactivity recovered within six days after dosing. Urinary metabolites were identified as *0,0*-diethyl *O*-hydrogen phosphorothioate, diethyl hydrogen phosphate and *0,0*-diethyl *O*-hydrogen phosphorodithioate.

Phorate demonstrated severe acute toxicity in mice, rats and rabbits after administration by various routes. WHO has classified phorate as extremely hazardous.

In a 13-week toxicity study with phorate in mice at dietary levels of 0, 1, 3 or 6 ppm the NOAEL was 1 ppm, equal to 0.18 mg/kg bw per day, on the basis of inhibition of brain cholinesterase activity at dietary levels of 3 ppm and above.

In rats that received phorate in the diet at 0, 0.22, 0.66, 2, 6, 12 or 18 ppm for 13 weeks the NOAEL was 2 ppm, equivalent to 0.1 mg/kg bw per day, on the basis of brain cholinesterase inhibition. At 6 ppm cholinesterase inhibition was associated with tremors and hyperexcitability, and at 12 and 18 ppm with death.

Several studies have been performed with phorate in dogs. A one-year toxicity study in which phorate was administered orally by capsule at 0, 0.005, 0.01, 0.05 or 0.25 mg/kg bw per day gave an NOAEL of 0.05 mg/kg bw per day, as determined by decreased body weights, significant inhibition of erythrocyte and brain cholinesterase activity and clinical signs consistent with cholinergic toxicity at the high dose of 0.25 mg/kg bw per day. A preliminary 14-day range-finding study, a six-week dietary study and 15-week oral capsule study supported the findings reported in the one-year study.

Mice and rats were treated with phorate at dietary levels of 0, 1, 3 or 6 ppm for 18 and 24 months, respectively. In the mouse carcinogenicity study the NOAEL was 3 ppm, equivalent to 0.45 mg/kg bw per day, on the basis of decreased body weights and increased incidences of tremors, hyperactivity and excessive salivation at 6 ppm. Cholinesterase activity was not measured in this study. In the rat toxicity/carcinogenicity study the NOAEL was 1 ppm, equal to 0.05 mg/kg bw per day, on the basis of significant inhibition of brain cholinesterase at 3 ppm and above. There was no apparent effect on erythrocyte cholinesterase activity. Phorate was not

carcinogenic when fed to mice or rats at dietary levels up to 6 ppm.

A two-generation reproductive toxicity study in rats with phorate at dietary levels of 0, 1, 2, 4 or 6 ppm showed no adverse effect on reproductive parameters. The NOAEL was 2 ppm, equal to 0.17 mg/kg bw per day, on the basis of decreased brain cholinesterase activity, tremors, decreased parental and pup body weights and decreased pup survival at 4 ppm and above. In a three-generation reproductive toxicity study in mice fed dietary levels of 0, 0.6, 1.5 or 3.0 ppm the NOAEL was 1.5 ppm, equivalent to 0.23 mg/kg bw per day, on the basis of slightly lower lactation indices at 3 ppm.

Two teratogenicity studies were conducted with phorate in rats at dose levels of 0, 0.125, 0.25 or 0.5 mg/kg bw per day and 0, 0.1, 0.2, 0.3 or 0.4 mg/kg bw per day. The NOAEL for maternal and developmental toxicity was 0.3 mg/kg bw per day on the basis of severe maternal toxicity culminating in death, decreased fetal body weights and delays in fetal skeletal ossification at 0.4 mg/kg bw per day. There was no evidence of teratogenic potential at doses as high as 0.4 mg/kg bw per day. At the maternally lethal dose of 0.5 mg/kg bw per day, there was an increased incidence of fetuses with enlarged hearts. In rabbits treated with doses of 0, 0.15, 0.5, 0.9 or 1.2 mg/kg bw per day, maternal mortality and decreased body weight were observed at doses of 0.5 mg/kg bw per day and above, resulting in an NOAEL of 0.15 mg/kg bw per day. In the absence of embryo- or fetotoxicity, the NOAEL for developmental toxicity was the highest dose level of 1.2 mg/kg bw per day. Phorate was not teratogenic in rabbits.

Phorate has been adequately tested for genotoxicity in a battery of *in-vitro* and *in-vivo* assays. The Meeting concluded that phorate was not genotoxic.

No clinical or histopathological signs of delayed neurotoxicity were seen in chickens.

Ninety-day dietary toxicity studies were conducted in rats with the cholinesterase-inhibiting sulphoxide and sulphone metabolites of phorate. A comparison of phorate and its metabolites revealed that the latter are marginally more potent inhibitors of brain cholinesterase in the female rat. Brain cholinesterase activity was inhibited in animals of both sexes after administration of phorate at a dietary level of 6 ppm, but no significant inhibition was apparent at 2 ppm in either sex. The sulphoxide and sulphone metabolites of phorate inhibited brain cholinesterase only in females treated at the highest dietary level of 2 ppm. There were no significant differences between the erythrocyte cholinesterase-inhibiting activities of the metabolites and the parent compound, phorate.

An ADI was allocated on the basis of an NOAEL of 0.05 mg/kg bw per day in the one-year toxicity study in dogs and the two-year feeding study in rats. The effect noted in both species was inhibition of brain cholinesterase activity, which in the dog was associated with clinical signs consistent with cholinergic toxicity. A safety factor of 100 was applied.

A toxicological monograph was prepared summarizing the data received since the previous evaluation and incorporating relevant sections from the previous monograph and monograph addenda.

TOXICOLOGICAL EVALUATION

Levels that cause no toxic effect

Mouse: 1 ppm, equal to 0.18 mg/kg bw per day (13-week toxicity study)

Rat: 1 ppm, equal to 0.05 mg/kg bw per day (two-year toxicity/carcinogenicity study)

Rabbit: 0.15 mg/kg bw per day (teratogenicity study)

Dog: 0.05 mg/kg bw per day (one-year toxicity study)

Estimate of acceptable daily intake for humans

0-0.0005 mg/kg bw

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

1. Adequate studies on absorption, distribution, excretion and metabolism in the rat. Studies known to exist may address this need, in whole or in part. In order to maintain the ADI, these data should be submitted in 1995, in time for review in 1996.

2. Observations in humans.

4.36 PHOSALONE (060)

RESIDUE AND ANALYTICAL ASPECTS

Phosalone, a phosphorodithioate acaricide and insecticide, was evaluated in 1972, 1975 and 1976. Re-evaluation under the periodic review programme was scheduled for the 1993 JMPR. The JMPR periodic review of the toxicology was conducted in 1993, resulting in the ADI being lowered from 0.006 mg/kg bw to 0.001 mg/kg bw. The scheduled residue review was postponed until 1994 because data could not be provided in time for review by the 1993 Meeting.

The present periodic review was conducted on the basis of data from the manufacturer as well as information on GAP from Canada, Germany, The Netherlands and Spain and limited residue data from Germany and The Netherlands. In response to an inquiry, the manufacturer informed the Meeting that no information was available on the stability of stored analytical samples, the effects of processing, or the residues in the edible portions of foods.

Metabolism in animals is characterized by rapid elimination of phosalone and its metabolites in the urine and faeces, mainly in urine. While a high percentage of the residue has not been identified in most tissues, the available data indicate oxidation to phosalone oxygen analogue, cleavage of phosalone to yield *O,O*-diethyldithiophosphoric acid (and of the oxon to

give the corresponding thiolic acid) and both phosalone and its oxon to 2-oxo-3-mercaptomethyl-6-chlorobenzoxazole (the mercapto metabolite). Diethylthionophosphoric acid may be formed by direct oxidation of the dithiophosphoric acid and/or by hydrolysis of the oxon to the thiolic acid and immediate isomerization to the thiono acid.

The rapid elimination of ^{14}C in the urine and faeces of cows is consistent with findings in the rat and elimination via the urine in the later goat and pig metabolism studies. Although it was reported that essentially all the ^{14}C was eliminated in the urine, faeces and milk, no tissues were analyzed. The fact that residues were found in milk suggested the possibility of low tissue residues. That would be consistent with the trace residues found in rat tissues and in the goat metabolism study. No reference was made to residues of the phosphorus-containing metabolites and their disposition.

The fact that higher residues were found in skimmed milk than in cream suggests that the main residues in milk were not phosalone or its oxygen analogue, since the octanol/water partition coefficient of phosalone indicates that it is fat-soluble. The residue partition in milk was confirmed in later goat metabolism studies.

In a metabolism study in goats 5 doses of [^{14}C]phosalone were given, each at about twice the level of the single dose in the two studies on cows. The specific activity in the goat study was comparable to the higher of the specific activities in the cow studies. The higher doses facilitated the identification and measurement of tissue and milk residues. For example, the total milk residues in the goat study were 5 times those in the cow studies.

About 80-97% of the total ^{14}C was organo-extractable. 59% of ^{14}C residue in the liver was identified, but only 6-36% in the other tissues and only 5.1% in the milk. The sulphide and sulphoxide metabolites accounted for approximately 30 and 21% of the total radioactivity in the liver. In fat, although only 18.4% was identified, approximately equivalent amounts of phosalone and the sulphide metabolite were reported and only slightly less of the sulphoxide. In muscle the sulphoxide was the major identified residue followed by the sulphide, and in milk the sulphoxide was the major compound identified.

The high percentage of ^{14}C excreted in the urine is consistent with that found in other animals. No reference was made to the fate of the phosphorus portion of the molecule nor to attempts, except by acid hydrolysis, at the further separation and identification of the unidentified residues (e.g. enzymatic hydrolysis). In several separative analytical steps significant levels of ^{14}C were counted in discarded fractions. No evidence was presented to support the suggestion that unidentified residues were water-soluble conjugates which would be reduced to undetectable levels by the end of a withdrawal period. It can be concluded that the fate of phosalone in goats has been partially elucidated.

The study of phosalone disposition in pigs after applications to the skin was too short to draw conclusions about the long-term storage potential. The limited exposure area would also not be sufficient to show the total potential exposure. It was sufficient to show that absorption through the skin is relatively slow.

The fate of phosalone residues in plants was investigated in potatoes, sorghum and apples. Although the available information suggests that plant metabolism is similar to that proposed for animals (formation of phosalone oxon, the aglycone, aglycone conjugates and

chloroaminophenol), plant samples were not analyzed for other metabolites found in animals (mercapto, sulphide, sulphoxide, sulphone or phenoxazone).

No evidence was provided in a potato translocation study to support the suggestion that ^{14}C was incorporated into normal plant constituents. The available information was not presented in such a way as to allow an independent conclusion on the nature of the reported residues (phosalone and its oxon). The overall evidence suggests little if any translocation from the surface 14 days after application, although residues became less extractable with time.

Sorghum metabolism studies showed decreasing residues of phosalone and increasing levels of identified and unidentified metabolites from the day of application to the harvest of mature plants. No significant translocation of residues was observed. There appears to be little likelihood of grain residues arising from early spray treatments (before flowering), but residues may occur from treatments at or after the flowering stage. The identified metabolites comprised phosalone, its oxon, the glycoside, aglycone and aminophenol. In foliage, grain and glume (seed head less grain) phosalone was the major identified residue, although after later stage applications the aglycone was a close second. These metabolites accounted at most for 53, 22 and 23% of the total residues in the foliage, grain and glumes respectively.

Over 90% of the residues in the grain from early applications and about half of that from applications at flowering was bound. There appear to have been no attempts to identify the substantial bound residues in this or other plant parts. Two major unidentified metabolites, phenolic in character, accounted for approximately 13% of the residue in foliage, grain and glumes. The remaining extractable residue (11% of the total) consisted of approximately 18 compounds, no one of which was more than 1% of the total residue. A follow-up report on the nature of the water-soluble metabolites in sorghum could not be reviewed as the even-numbered pages were omitted and photographs of TLC plates were not legible. The study should be submitted again for the next rescheduled review of phosalone.

While a significant account of information has been provided on the fate of residues in sorghum, approximately 50 to 75% of the residue has not been identified and, even of the named compounds, only the identities of phosalone and its oxon have been confirmed by more definitive methods such as GC-MS. The levels of the two major unidentified metabolites appear to be similar to those of phosalone and its oxon. Analytical standards of other potential metabolites, some of which have been identified in animal metabolism studies, appear not to have been used in the sorghum investigations. It can be concluded that the metabolism of phosalone in sorghum has been partially elucidated.

Up to 50% of the [^{14}C]phosalone applied to apple trees (apples plus leaves) was lost after 24 days, although the fate of the lost compound was not determined. No rainfall occurred during the test period. About 97% of the radioactivity associated with the apples was found in or on the peel and approximately 90% of that was extractable with methanol. About 90-94% of the peel residue was shown to be unchanged phosalone. Other products on the apples were not identified, although analyses of apple leaves revealed the presence of low levels of phosalone oxon (<3% of the leaf rinse or extract) and the aglycone 6-chlorobenzoxazolone (<5% of the leaf rinse or extract).

While CXLs have previously been established for a variety of fruits (citrus, pome fruit, stone fruit, small fruits and berries), vegetables (fruiting, tuber, root, leafy, brassica) and nuts, the

fate of residues has only been partially elucidated in apples, sorghum and potatoes. The Meeting recommended that in any future studies to supplement the available information in support of continued or new phosalone limits, consideration should be given to determining the fate of residues in other types of crops such as a fruiting vegetable and/or leafy vegetables.

The fate of residues in soil shows similarities to that in plants and animals. A notable difference is the detection of low levels of the disulphide metabolite, $(C_2H_5O)_2PS\text{-}S\text{-}SP(OC_2H_5)_2$ in soil. The half-life of phosalone in soil is typically of the order of 2 days, but depends on the conditions. None of the usual leaching studies were conducted under field conditions nor were results of typical adsorption/desorption experiments available.

Numerous analytical methods have been developed for the determination of phosalone, its oxon and other metabolites in a variety of substrates including plant and animal products, soil and water. Most methods are based on extraction with polar organic solvents, liquid-liquid organic solvent partition and separation and clean-up on Florisil. Hydrolysis and derivatization are used for some metabolites. Most methods for plants emphasize the measurement of phosalone and its oxygen analogue and those for animal products include methods for the total sulphone metabolites and total chlorobenzoxazalone water-soluble metabolites in milk and tissues and for the free aglycone, free chloroaminophenol and free mercapto metabolite in milk. Determination is generally by GLC with EC and/or thermionic detection.

Generally the reported limits of "detection" for phosalone were 0.01-0.02 mg/kg for most crops (0.03-0.05 mg/kg for oily crops), and were usually higher for the oxon. The reports of analytical methods for plants and of general methods of analysis did not include sufficient information to permit an independent estimate of the limits of determination, but they could be independently estimated for those analytical methods for the parent and metabolites in animal matrices which were used in the animal feeding trials. These were validated by radiometric techniques and should be suitable for enforcement purposes.

Reasonable limits of determination would be 0.005 mg/kg for phosalone in milk and 0.02-0.05 mg/kg in animal tissues, 0.02 mg/kg for the oxon in milk, 0.1 mg/kg for the oxon in tissues and for the free aglycone, aminophenol and the mercapto metabolite in milk, 0.05-0.1 mg/kg for total sulphones in milk and tissues, and 0.01-0.02 mg/kg for total benzoxazolone metabolites in milk and 0.02-0.05 mg/kg in tissues.

Data on residue trials were available for a variety of crops, but most of the substantial, relatively old, US data were only summaries and therefore of limited use. Phosalone is no longer registered for food uses in the United States. The remaining data were in many cased also quite old and often not in English, although in most cases English summaries from the individual reports were provided. Often the analytical procedures used were not specified and few representative chromatograms were provided, although control values and percentage recoveries often were. Frequently data summaries gave averaged results from biological and chemical assay methods. Where distinguishable, the monograph includes only the chemical results, as these would be more relevant to current standards and enforcement methods.

Fruits

Apples. Data were available from approximately 150 supervised trials in 10 countries, although mainly only summaries from trials before 1980, many of them in the 1960s. Some of the results

were presented only as averages of analyses by GLC and biological methods. Because of the lack of detail and lack of confidence in the older results, the Meeting concluded that over two thirds of the data were not suitable for consideration (although all are summarized in the monograph). In particular, data from trials in Canada, Denmark, South Africa, Switzerland, the USA, and more than half of those in France were given little consideration. Even in other, generally more recent, studies sample chromatograms, control values, details of the analytical methods, and information on sampling-to-analysis intervals or storage conditions were provided in only a few cases. Often even if the information was supplied it was not in English, and no information was available on the storage stability of analytical samples or on processing.

In considering MRLs the Meeting placed most emphasis on the more recent French and German supervised trials, although the data could be closely matched to GAP only for 8 German trials with WP formulations which resulted in maximum residues of 1.3 mg/kg. The highest residues from approximately 20 French trials which approximated GAP for EC and WP formulations were 1.9 mg/kg for an SC formulation and 3.8 mg/kg for an emulsifiable solution formulation. No relevant French GAP was reported for formulations other than WP and EC, although the application rates in the French SC trials approximated SC GAP in The Netherlands.

The available data suggest that the CXL of 5 mg/kg for apples would not be exceeded. However, because critical supporting information (e.g. interval from sampling to analysis, storage stability data etc.) for the German and French trials was generally lacking, the Meeting could not with confidence confirm this limit and recommended its withdrawal. Future consideration would require critical supporting information and preferably additional, more recent, data from trials according to GAP.

Pears. The data were summaries of trials in the 1960s, almost none of which were according to reported GAP. Many of the analyses were by colorimetric or biological methods. The Meeting concluded that the data were not suitable for estimating a maximum residue level and recommended withdrawal of the 2 mg/kg CXL for pears.

Summary data on apricots without relevant GAP gave an insufficient basis for recommending an MRL.

Cherries. Data were available from supervised trials in four countries and residues did not exceed 6.3 mg/kg in trials which approximated GAP. However, because data from Canada, France and the USA were from pre-1971 trials and mostly summaries with few details of the trials, analyses, or sample handling and storage, the Meeting did not consider them suitable for recommending or confirming MRLs by current standards. Residues in the French trials were determined by colorimetric or biological methods. While more detail was available for some of the 1973-75 German trials (maximum residue 1.1 mg/kg from trials according to GAP), important supporting information (e.g. interval from sampling to analysis, stability of stored samples) was often lacking. The Meeting recommended withdrawal of the current 10 mg/kg CXL.

Data were available from supervised trials on peaches in 4 countries, although older data from the United States and Canada (and some of the French data) had too few details to serve as a basis for recommending MRLs. Summary data for apricots and nectarines were not suitable for supporting the data on peaches.

A total of about 5 supervised peach trials from two countries reasonably reflect GAP and are acceptably documented. Residues in the better documented, more recent, French trials which approximated GAP did not exceed 3 mg/kg. Residues did not exceed 0.13 mg/kg in the Italian trial which was also relatively well described. Although the storage conditions for the analytical samples were adequate in the French and Italian trials (for periods of 8-9 months and 2-3 months respectively) no storage stability data were provided, and sample chromatograms were available only for the Italian trial. While the available data suggest that the 5 mg/kg CXL for peaches may not be exceeded, the Meeting did not consider that the adequately reported results were sufficient to support a limit and recommended its withdrawal. Future consideration would require additional well-documented data from trials according to GAP, with information on intervals and storage conditions from sampling to analysis and on the storage stability of analytical samples.

Although data were available from over 30 supervised trials on plums in five countries, all but the most recent (two 1977 German trials) were mostly summaries with few details of critical supporting information such as sample chromatograms, method validation, plot sizes, sampling to analysis intervals, and stability on storage. Information on sample handling and storage conditions was provided in only a few cases. Much of this supporting information was lacking even for the German trials, although analytical storage conditions were described. While the substantial quantity of data (maximum residue 4.1 mg/kg from an application according to GAP) suggests that the CXL of 5 mg/kg would not be exceeded by treatments according to current GAP, because of the shortcomings in the data the Meeting could not confirm it and recommended that the CXL should be withdrawn.

While data on grapes were available from 55 supervised trials in 7 countries, the data from South Africa and Italy could not be related to reported GAP. Most of the remaining data were summary reports from trials in 1970 or earlier. Generally there is a lack of detailed information, although in a few cases the analytical storage conditions were described. Critical information such as intervals from sampling to analysis, storage stability data, control values and details of analytical methods (control values, sample chromatograms) was generally missing, although in most cases laboratory storage conditions were provided. With a few exceptions, studies did not include information on plot sizes. There was no information on residues in processed products.

Summary data from trials in France (1964) and Switzerland (1966) in accordance with reported GAP indicate maximum residues of 0.4 and 4.2 mg/kg respectively, but residues were determined by outdated colorimetric methods. Because most application rates were exaggerated, only one of the 25 US trials could be related to Canadian GAP: the trial was in 1964 and showed a maximum residue of 2.6 mg/kg. Canadian trials in 1970 in accordance with GAP yielded a maximum residue of 5 mg/kg. Three of four German trials in 1974 or 1975 approximated GAP, with a maximum residue of 1.6 mg/kg.

The available data suggest that the CXL of 5 mg/kg for grapes would not be exceeded from current uses. However, because most of the data were from old summary reports and generally lacked the detail required by current standards, the Meeting could not with confidence confirm the CXL and recommended that it should be withdrawn.

Limited summary data were available on citrus fruits from supervised trials in 1966-69 on oranges (5 trials), lemons (2) and grapefruit (1) in the United States. Information on GAP was available for Spain, Thailand and Japan but it could not be compared with most of the trials data.

The summary data were not accompanied by trial details, sample handling and storage conditions or intervals, information on storage stability, or other critical supporting information. The Meeting was unable to confirm the CXL of 1 mg/kg for citrus fruits on the basis of the available information and recommended that it should be withdrawn.

The highest residues in strawberries were 1.4 mg/kg in the one German trial using a WP formulation according to Austrian GAP for EC formulations and <0.1 mg/kg in US trials after 17 days at similar rates with an EC formulation. Residues were <0.1 mg/kg in the single UK trial after 26 days. One trial on raspberries in the USA according to the GAP of European countries resulted in residues of <0.1 mg/kg. Because only summary reports were available, critical supporting information was lacking, and a good match could not be made between the limited data and GAP, the Meeting could not with confidence confirm the CXL of 1 mg/kg for strawberries and recommended that it should be withdrawn.

Vegetables

Artichokes. There were data from two 1968 French trials and one 1972-3 United States trial, without relevant information on GAP. There was therefore no basis for recommending a limit for artichokes.

Beans. There were data from two 1968 French trials and one 1965 United States trial and again no relevant information on GAP. The Meeting could not estimate a maximum residue level.

Two results (0.2 mg/kg) from two very old trials on beetroots in one country were not enough to support a limit. The Meeting recommended withdrawal of the CXL of 2 mg/kg.

Broccoli. There was no US GAP and only relatively old summary data. There is therefore no basis for retaining the current CXL.

Marginally sufficient data on Brussels sprouts were from trials at the GAP rate and PHI of The Netherlands. Maximum residues of 0.6 mg/kg from the use of WP formulations in accordance with Netherlands GAP for SC formulations suggest that the current 1 mg/kg CXL would not be exceeded. However, without any data for the SC formulation for comparison with the supervised trials data for WP formulations, the Meeting could not with confidence confirm the current CXL and recommended that it should be withdrawn.

Cabbages. There was no US GAP, only summary US data and only two results (France, 1968, green cabbage 0.3 and 1.2 mg/kg) which reflected GAP. The Meeting concluded that the data were insufficient to confirm the current 1 mg/kg CXL and recommended that it should be withdrawn.

Because there were only two results from trials on cauliflowers in one country with summary data from another and relevant information on GAP was lacking, the Meeting concluded that the available data were too limited to recommend an MRL.

Cucumbers. There were summary data from one country, two trials from another (with residues of 0.02 mg/kg from applications according to GAP) and information on GAP of questionable use from two others. The Meeting concluded that this was not a sufficient basis to confirm the CXL of 1 mg/kg and recommended that it should be withdrawn.

Although there were substantial data on lettuce, only two of 15 trials included more than summary information. Only two results (the higher at 0.7 mg/kg) could be related to French GAP. The Meeting recommended that the 1 mg/kg CXL for head lettuce should be withdrawn.

Limited data on melons and watermelons and the lack of relevant information on GAP precluded the estimation of a maximum residue level.

Because no residue data were provided in support of the 1 mg/kg CXL for peas the Meeting recommended that it should be withdrawn.

Only two old supervised trials from France on potatoes (residues <0.05 mg/kg) could be strictly related to GAP, although in 12 additional old trials in Australia and Canada residues were well below 0.1 mg/kg from application rates which were often much higher than the GAP rate of France. Although the more substantial US data also showed residues below 0.1 mg/kg and usually below 0.03 mg/kg, this information was of limited use because only summaries were provided and because there is no GAP in the USA. The Meeting considered the limited old data insufficient to support an MRL and recommended withdrawal of the current CXL (0.1* mg/kg).

There were data from 3 supervised trials on spinach in one country without any relevant information on GAP: an insufficient basis to propose an MRL for spinach.

Data on tomatoes from 26 supervised trials in 1972-73 in the United States were of limited use because only summaries were available and the trials were not according to GAP. Maximum residues did not exceed 0.9 mg/kg in four Indian trials approximating GAP or 0.3 mg/kg in two French trials according to Spanish GAP. Because data from trials according to GAP are limited (4-5 trials) for such a major crop, the Meeting recommended withdrawal of the CXL of 1 mg/kg. The Meeting also noted the need for processing studies if a limit should be proposed in the future.

Other crops

Although summary data from 7 US trials on cotton seed in 1964-6 with the residues determined colorimetrically indicated that there were no residues (<0.1 mg/kg) in delinted or non-delinted cotton seed, meal or crude oil, the lack of information on GAP and of critical supporting information precluded the estimation of a maximum residue level.

Summary data on hops from two 1966 trials with colorimetric determination of the residues in one country suggested that residues would not exceed 0.1 mg/kg in dry cones or 2 mg/kg in green cones, but again the lack of information on GAP and on supporting details precluded confirmation of the 2 mg/kg CXL for dry hops. The Meeting recommended that it should be withdrawn.

Summary data on nuts from 1967-70 supervised trials in the USA suggest that residues of phosalone in the meats of almonds, hazelnuts, walnuts and pecans may not exceed 0.1 mg/kg from applications roughly approximating European GAP, if the linking of US trials to European GAP is justified. No data were available for chestnuts to confirm the current 0.1 mg/kg CXL and no GAP was provided for pecans. Because only summary data were available without critical supporting information and because European GAP could not be closely matched with the

conditions of the field trials, no limits could be recommended for almonds, hazelnuts, or walnuts. Because no GAP was provided for pecans the CXL of 0.1 mg/kg could not be confirmed even if supporting critical information had been provided. The Meeting therefore recommended that the CXLs of 0.1 mg/kg for chestnuts and pecans should be withdrawn.

Summary data from one 1964 trial on sorghum in the USA with colorimetrically determined residues and from three 1967 trials on wheat in France with physico-bioassay analyses did not provide a suitable basis for the Meeting to estimate a maximum residue level for either commodity.

Oilseed rape. The results of two 1974 German trials, one 1975 Polish trial, five 1966 French trials and two 1968-9 Danish trials according to GAP suggest that residues in oilseed rape from authorised treatments would not exceed the 0.1 mg/kg CXL. One German trial according to GAP in 1974 with residues up to 0.4 mg/kg was an exception. The French data suggest residues in the oil of <0.5 mg/kg.

While the quantity of data is adequate, the Meeting noted with concern that only summaries were available for the French trials, and in 5 of the 7 trials residues were determined by outdated colorimetric and bioassay methods. Residues were also determined partly by bioassay in one of the three Danish trials (1968) which was again only reported in summary form. The other two included more trial details, but not other critical information such as sampling-to-analysis intervals and storage stability. The Polish trial report was also a limited summary. Only the reports of the German trials gave substantial trial details, but even these did not include important supporting information such as the interval from sampling to analysis, sample chromatograms, storage stability information or more than a citation of the analytical method used.

Because only the results of the three German trials could be used with some confidence, because one of these trials suggested that residues could exceed 0.1 mg/kg from applications according to GAP and because even in these trials important supporting information was lacking, the Meeting could not support the current 0.1* mg/kg CXL and recommended its withdrawal.

Four Indian and one Pakistani trials on tea according to GAP indicate that residues of phosalone and phosalone oxon in green tea would not exceed 0.5 and 0.1 mg/kg respectively after 7 days or 0.06 and 0.1 mg/kg after 10 days under higher rainfall conditions. Although data reflective of GAP for green leaves under dry weather conditions were not available, a comparison of residues in processed tea from trials according to GAP in wet and dry weather conditions clearly shows significantly higher residues from applications in dry weather. Residues of phosalone/phosalone oxon on processed (dry) tea would not be expected to exceed 7.2/1.1 mg/kg after 8 days in dry weather or 0.09/0.05 mg/kg after 10 days in wet weather. The concentration factor for green tea to dry tea is approximately 6. Residues of phosalone/phosalone oxon in beverage tea infused from dry tea could be expected to be of the order of 12/10 µg/l.

Although the data were old and somewhat limited, the Meeting considered that most of the studies were among the better documented phosalone residue trials and that they might provide a basis for recommending a limit for tea (dry). From the available data the Meeting would not expect residues in dry manufactured tea to exceed 10 mg/kg from GAP applications. However, the main concern is the lack of information on the interval from sampling to analysis and on the stability of the analytical samples during storage. The Meeting was also concerned by

the lack of information on the Indian PHI, since most of the data were from Indian trials. On the weight of the evidence the Meeting agreed not to estimate a maximum residue level for tea at present.

Animals

MRLs have not previously been recommended for phosalone in animal products except 0.5 mg/kg in sheep fat and 0.05 mg/kg (limit of determination) in sheep meat resulting from veterinary use, which have now become CXLs. Because no current information was provided for the periodic review of this use, the Meeting recommended that these limits should be withdrawn.

Feeding trials have been conducted with dairy cattle and chickens. In cows, a trial at a dietary feeding level of 100 ppm indicated that the total residues of phosalone and its oxon and sulphone metabolites are unlikely to exceed 0.3 mg/kg in the liver or 0.05 mg/kg in other tissues at this feeding level.

A study on chickens showed sulphone residues in all tissues and eggs. At the lowest feeding level of 10 ppm, total sulphone metabolite residues were of the order of 0.5 to 1 mg/kg in all tissues except kidney where the maximum was 0.1 mg/kg. However, the results at the highest feeding level of 100 ppm suggest that residues might not have reached their maximum in eggs and skin by the end of the 4-week feeding period. Because parts of the study were missing in the submission the Meeting could not draw any final conclusions. It recommended that the complete study be again submitted with any future submissions to the JMPR on phosalone.

The crops with current CXLs most likely to contribute to phosalone residues in animal tissues or milk include apples (CXL 5 mg/kg), citrus fruits (1 mg/kg), tomatoes (1 mg/kg) and perhaps grapes (5 mg/kg). Limited information on citrus processing indicates a concentration factor of 5-10 from fruit to dry pomace. No data were provided on residue levels in the dry pomace of apples, grapes or tomatoes.

Because the data were insufficient to confirm the CXLs for raw agricultural products used as animal feed (or for feed items that could be derived therefrom) the Meeting was unable to estimate maximum residue levels for animal products.

No information was available on the fate of residues in storage, in stored analytical samples, or in foods in commerce or at consumption. Only limited data on processing were available and on residues in the edible portion of food commodities (citrus, tea).

The Meeting recommended the withdrawal of the existing MRLs, shown in Annex I.

4.37 PHOSMET (103)

TOXICOLOGY

A temporary ADI of 0-0.005 mg/kg bw was allocated by the JMPR for phosmet in 1978. The compound was further reviewed in 1979, when additional teratogenicity data were made

available, and an ADI of 0-0.02 mg/kg bw was established. Further data have since become available, and these were reviewed at the present Meeting as a result of the CCPR periodic review programme.

Phosmet is rapidly absorbed, distributed and excreted, predominantly in the urine. Less than 1% of the label in the urine was in the form of phosmet or its oxon. In rats, there were two major urinary metabolites: *N*-(methylsulphinylmethyl)phthalamic acid and *N*-(methylsulphonylmethyl)phthalamic acid.

LD_{50}s have been estimated for a variety of species for most routes. The oral LD_{50} in mice ranges from 20 to 50 mg/kg bw and in rats from 100 to 300 mg/kg bw. WHO has classified phosmet as moderately hazardous.

In a four-week toxicity study, mice were fed diets containing 0, 5, 15, 50, 150 or 500 ppm. The NOAEL was 50 ppm, equivalent to 7.5 mg/kg bw per day, on the basis of reduced food intake, reduced body-weight gain and reduced liver and kidney weights. In a 14-week toxicity study, rats were fed diets containing 0, 20, 100 or 500 ppm. The NOAEL was 20 ppm, equivalent to 1 mg/kg bw per day, on the basis of brain cholinesterase inhibition. In a 14-week study in beagle dogs fed diets containing 0, 10, 75 or 563 ppm the NOAEL was 75 ppm, equivalent to 1.9 mg/kg bw per day, on the basis of brain cholinesterase inhibition. In a two-year toxicity study in dogs fed diets containing 0, 20, 40 or 400 ppm the NOAEL was 40 ppm, equivalent to 1 mg/kg bw per day, on the basis of brain cholinesterase inhibition. The Meeting concluded, however, that this study was inappropriate for the estimation of an ADI in view of the small group size and large dose interval between the NOAEL and the effect level.

In a two-year carcinogenicity study in mice fed levels of 0, 5, 25 or 100 ppm, there was evidence of hepatotoxicity at the high dose, together with a slightly but not statistically significantly increased incidence of hepatic adenomas in comparison with concurrent controls. There was, however, no increase in incidence in comparison with historical control data, and the Meeting concluded that there was no evidence of carcinogenicity in the mouse. Although brain cholinesterase activities were determined in this study, the results proved difficult to interpret: at the interim kill, brain cholinesterase activity was apparently reduced in all dose groups in each sex; at the terminal kill, brain cholinesterase activity was reduced at the high dietary level in females and not at all in males. The Meeting concluded that the apparent change seen at the interim kill did not represent a true reaction to treatment with phosmet in view of the absence of a similar effect at the terminal kill, after a longer treatment period. The NOAEL was 25 ppm, equal to 4 mg/kg bw per day, on the basis of hepatotoxicity and brain cholinesterase inhibition at the high dose.

In an early, inadequate, two-year toxicity/carcinogenicity study in rats treated via the diet the NOAEL was 40 ppm, equivalent to 2 mg/kg bw per day, on the basis of depressed body-weight gain and brain cholinesterase inhibition. In a two-year toxicity/carcinogenicity study rats were fed diets containing 0, 20, 40 or 200 ppm phosmet, and a smaller group received 400 ppm. The NOAEL was 40 ppm, equal to 1.8 mg/kg bw per day, on the basis of fatty changes in the liver and reduced brain cholinesterase activity in females. There was no evidence of carcinogenicity in rats.

Two multigeneration reproductive toxicity studies in rats have been conducted with phosmet. In an earlier three-generation study, animals were exposed to dietary levels of 0 or 40

ppm (first generation) and 0, 40 or 80 ppm (second generation). The NOAEL was 40 ppm, equivalent to 2 mg/kg bw per day. In a two-generation (two litters/generation) study of reproductive toxicity, rats were fed dietary concentrations of 0, 20, 80 or 300 ppm. The NOAEL was 20 ppm, equal to 1.3 mg/kg bw per day, on the basis of reduced mating and fertility at higher doses.

In a teratogenicity study, rats were dosed orally at 0, 5, 10 or 15 mg/kg bw per day on days 7-16 of gestation. The NOAEL for maternal toxicity was 5 mg/kg bw per day on the basis of reduced body-weight gain; there was no evidence of fetotoxicity or teratogenicity at the highest dose tested. In a teratogenicity study in rabbits dosed at 0, 2, 5 or 15 mg/kg bw per day, the NOAEL for maternal toxicity was 5 mg/kg bw per day on the basis of reduced body-weight gain, while the NOAEL for fetotoxicity was 2 mg/kg bw per day on the basis of the presence of minor skeletal anomalies.

The Meeting concluded that phosmet was not clastogenic, but its mutagenic potential was unclear. In an attempt to address this issue, studies of DNA binding *in vivo* are being requested.

In two studies, phosmet did not cause delayed neuropathy in chickens; however, the Meeting considered a summary of a study in which some inhibition of brain neuropathy target esterase was observed at a dose below the LD_{50}. It was therefore concluded that phosmet may have the potential to cause delayed neuropathy, although at doses higher than the unprotected LD_{50}. A further study is requested to clarify this issue.

An ADI was allocated on the basis of the NOAEL in the multigeneration study in rats (20 ppm, equal to 1.3 mg/kg bw per day) and a 100-fold safety factor.

A toxicological monograph was prepared summarizing the data received since the previous evaluation and containing summaries from the previous monograph and monograph addendum.

TOXICOLOGICAL EVALUATION

Levels that cause no toxic effect

Mouse: 25 ppm, equal to 4 mg/kg bw per day (two-year carcinogenicity study)

Rat: 40 ppm, equal to 1.8 mg/kg bw per day (two-year toxicity/carcinogenicity study)
20 ppm, equal to 1.3 mg/kg bw per day (two-generation reproductive toxicity study)
5 mg/kg bw per day (teratogenicity study, maternal toxicity)
15 mg/kg bw per day (teratogenicity study, developmental toxicity)

Rabbit: 5 mg/kg bw per day (teratogenicity study, maternal toxicity)
2 mg/kg bw per day (teratogenicity study, fetotoxicity)

Estimate of acceptable daily intake for humans

0-0.01 mg/kg bw

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

1. Long-term toxicity study in dogs.

2. Study of DNA binding *in vivo*.

3. Delayed neurotoxicity study in chickens, with estimation of neuropathy target esterase, at an appropriately high dose.

4. Further observations in humans.

In order to maintain the ADI, these data should be submitted in 1997, in time for review in 1998.

4.38 PIRIMIPHOS-METHYL (086)

RESIDUE AND ANALYTICAL ASPECTS

Pirimiphos-methyl was first evaluated by the 1974 JMPR. An MRL for peanut oil was first recommended at 10 mg/kg by the 1976 Meeting and amended to 15 mg/kg in 1985. Because the 1988 CCPR regarded the 1976 JMPR estimate as applying to crude oil, it advanced that proposal to Step 8 and proposed a separate limit at the same level for edible peanut oil at Step 3. The 1990 CCPR amended the 15 mg/kg limit for edible peanut oil to 10 mg/kg and requested information on practices in African countries where post-harvest use is permitted on peanuts. The Meeting received information on GAP from African countries and Australia.

Peanut oil, edible. The mean concentration of pirimiphos-methyl in edible peanut oil which had been refined from crude oil containing residues in the range 12-14.6 mg/kg was 9.4 mg/kg. However individual values occasionally exceeded the currently proposed MRL of 10 mg/kg.

There was no information from African countries or Australia on processing procedures to yield the refined peanut oil from stored peanuts, but the Meeting concluded that even if their processing differed from the procedure used in the available trials the residues of pirimiphos-methyl in the refined peanut oil would not differ significantly from those found in the trials, since pirimiphos-methyl seems to be stable to heat or other processing (as indicated in the 1985 evaluation) and is fat-soluble.

The Meeting considered the information on GAP in African countries and Australia and concluded that the application rates (4-20 g ai/t) were compatible with the rate used in the trials (20 g ai/t).

On re-examination of a full re-submission of the original trials data, the Meeting

confirmed the 1985 estimate of 15 mg/kg for both crude and edible oils.

4.39 PROFENOFOS (171)

RESIDUE AND ANALYTICAL ASPECTS

Profenofos was reviewed by the 1990 JMPR, which recommended TMRLs for a number of commodities pending the receipt of relevant information on registered national uses. The 1992 Meeting reviewed substantial information on GAP, confirmed or revised several recommendations and withdrew others for which GAP or residue data were inadequate. Additional GAP and/or supervised trials data were considered desirable for bulb onions and soya beans, and clarification of GAP for tea was required.

The Meeting received clarification of GAP for tea, additional information on GAP for other commodities for which residue data had previously been submitted, supervised trials data on beans, cotton, maize and chilli peppers and details of artichoke trials on which data had previously been submitted.

Artichoke. The 1992 Meeting considered the summary data on one supervised trial in Spain and one in Italy insufficient to support an MRL. The present Meeting received details (in Spanish) of the Spanish trial. The Meeting confirmed the 1992 conclusion.

Beans, dry. The Meeting re-examined the trials data reviewed by the 1990 JMPR in the context of new information on GAP in Italy. It could not directly compare the trials with Italian GAP, because the GAP application rates were in terms of g ai/hl whereas the rates in the Brazilian and Swiss trials were expressed as kg ai/ha. With maximum residues of 0.02 mg/kg from four trials in Brazil and Switzerland after 20-29 days compared with an Italian 21-day PHI, the data suggest that residues in dry beans would not exceed 0.02 or 0.05 mg/kg, especially in view of the residues at comparable levels in green beans after 21 days.

However, because (1) a limit for dry beans would require the reference of Brazilian and Swiss results to Italian GAP, (2) a true comparison of the Italian GAP with the trials application rates could not be made and (3) the rates applied to green beans suggest that the trials on dry beans may not have been at maximum GAP rates, the Meeting agreed not to recommend a limit for dry beans. This could be reconsidered at a future Meeting if information is provided to allow comparison of the application rates in the trials with Italian GAP (or if information on Swiss and Brazilian GAP is provided).

Beans, green. The trials in Italy and Switzerland in 1990 could be related to new information on Italian GAP, and new trials data on common beans from Malaysia could be related to previous information on GAP in the Philippines and Thailand. In one Italian trial the highest residue from applications according to GAP at the 21-day Italian PHI was 0.02 mg/kg. In the other 1.4 mg/kg was recorded after 28 days, but the 28-day and 6/7-day samples appeared to have been mislabelled. If so, the 28-day value would be 0.02 mg/kg. Residues were only 0.02 mg/kg in the Swiss trials after 11 days (the longest PHI). Maximum residues in the Malaysian trials were 0.05 mg/kg (corrected for a 0.02 mg/kg control) at the Philippine 7-day PHI and at application rates

comparable to those of the Philippines.

Although additional trials on green beans are desirable, the Meeting concluded that 6 trials in three different countries in three different years would be marginally sufficient to support a limit for green beans. The Meeting assumed that samples were mislabelled in one Italian trial and noted that (1) Italian GAP apparently allows spray concentrations up to 70 g ai/hl and more than 1 application whereas the trials were with single treatments at 50 g ai/hl; (2) in the Malaysian trials the maximum residues at the Philippine 7-day PHI would be 0.07 mg/kg if uncorrected for the 0.02 mg/kg control, while the analytical recoveries were 75%. The Meeting therefore recommended a limit of 0.1 mg/kg for common beans, based on a 7-day PHI. A 0.05 mg/kg limit would suffice for a 21-day PHI.

Brussels sprouts. The 1992 JMPR withdrew the 1990 temporary estimate of 0.5 mg/kg for Brussels sprouts because required information on GAP had not been provided. The present Meeting compared new information on GAP in South Africa with the 1990 JMPR summary of supervised trials data. The highest residues reflecting GAP rates after 9 or more days compared to the South African 10-day PHI were: The Netherlands, 0.25 mg/kg (one trial); Switzerland, 0.2 mg/kg (four trials) and South Africa, 0.42 mg/kg (one trial). Maximum residues in one Swiss trial were 1.1 and 0.41 mg/kg after 7 and 14 days respectively, but the rate could not be related to South African GAP.

Although comparison of European trials with South African GAP was not ideal, because some of the data could now be compared with GAP and because of the diversity of the trials, the Meeting confirmed the 1990 estimate of 0.5 mg/kg. Although the Meeting concluded that there was no need for it to be temporary, additional trials according to South African GAP or information on European GAP relevant to the previous European trials are desirable.

Cabbage. The 1992 JMPR recommended replacing the 0.5 mg/kg TMRL by an MRL of 1 mg/kg to accommodate 7-day PHIs which were GAP in two countries. Neither the 1990 nor 1992 Meetings could closely match available information on GAP to the trials data. The present Meeting reviewed additional information on GAP for Italy and South Africa. Only the latter could be closely related to the trials results and with a maximum residue of 0.13 mg/kg from GAP in that country did not require either a 0.5 or 1 mg/kg limit. The Meeting confirmed the 1992 JMPR conclusion that a 1 mg/kg limit was required to accommodate PHIs of 7 days.

Cauliflower. The 1992 JMPR withdrew a 1990 temporary estimate of 0.2 mg/kg (based on a 14-day PHI), since required information on GAP had not been provided. The Meeting compared new information on GAP for Italy and South Africa with the 1990 data from Germany, South Africa and Switzerland and reviewed an additional South African trial not previously provided. Maximum residues approximately reflecting GAP were 0.18 mg/kg in Switzerland and 0.57 mg/kg in South Africa. The highest residue in the German trials under the conditions of South African GAP was 0.2 mg/kg. Although most of the results could not be closely matched to GAP the Meeting noted that the data were from a diversity of locations at different times and covered the range of known GAP, and concluded that a 0.5 mg/kg limit, based on a 10-day PHI, could be supported.

Citrus fruits. Because information required by the 1990 JMPR had not been provided, the 1992 Meeting recommended withdrawal of the 1 mg/kg TMRL for oranges. The Meeting reviewed the 1990 data and new data on mandarins in the light of new information on GAP in Italy and South

Africa, the countries in which all the citrus trials had been conducted.

The maximum residue in oranges treated strictly according to GAP was 0.58 mg/kg, and from exaggerated conditions (threefold spray concentration, PHI 17 days instead of 60 days) 1.8 mg/kg. None of the trials on mandarins were exactly according to GAP. The highest residue from a GAP application rate was 0.3 mg/kg, but from seven applications whereas one is permitted. The maximum residue from a single application at the GAP rate was 1.03 mg/kg but this was at 22 days and the GAP PHI is 60 days. In lemons the only residue reflecting GAP was 0.16 mg/kg, with 1.2 mg/kg at the GAP rate but a PHI of 21 instead of 60 days. In grapefruit residues were 0.31 mg/kg from GAP application rates, but seven applications and at a PHI of 164 days. The persistence of the residues in peel and the slight influence of the PHI on residue levels gave some support to consideration of results at intervals other than the GAP PHI. Residues were almost entirely in the peel. While most of the data did not closely match GAP, the Meeting concluded that they would support a 1 mg/kg limit for oranges but were insufficient to support limits for other citrus fruits.

Cotton seed. The 1992 Meeting recommended replacement of the 1 mg/kg TMRL by an MRL of 3 mg/kg. The present Meeting reviewed additional data which did not require a change in the 1992 recommendation.

Maize and sweet corn. The 1992 JMPR recommended withdrawal of the TMRL of 0.05* mg/kg for maize because relevant GAP was not available. Of the four countries from which maize trials were reviewed by the 1990 JMPR, relevant information on GAP and reports of supervised trials were received from Spain. Two of the trials had previously been provided. Italian GAP was also reported, but trials data only on residues in whole maize plants. Trials on sweet corn reported from Canada were possibly the same as those previously provided. There was no relevant information on GAP.

While the 1990 monograph states that residues in grain from trials in France, Mexico, Spain and Switzerland did not exceed 0.02 mg/kg, the only trials submitted for review by the present Meeting which could reasonably be compared with GAP were from Spain. Even these trials were with granular applications which are not current GAP. Residue levels resulting from granular and EC applications may be quite different. The maximum residue in maize grain in the Spanish trials (from application rates which are GAP for EC formulations) was 0.06 mg/kg 100 days after the last application when not corrected for a 0.03 mg/kg control value. Residues in the grain after 40 and 51 days were <0.02 mg/kg.

The Meeting had no reason to expect residues in grain to exceed the 0.05 mg/kg TMRL on the basis of available information, but concluded that there were insufficient data from trials according to GAP to recommend a limit for a commodity as important as maize. Since some of the samples were stored for 8 months before analysis, the Meeting was also concerned that no storage stability data were available and noted that there was no information on processing.

The Meeting recommended a complete resubmission of all studies on maize and relevant GAP for review at a future Meeting when additional information on GAP relevant to the available residue data and/or additional data from trials according to known GAP become available. Any future submission should include information on maize processing, storage stability studies and sufficient information on residues in forage and fodder to permit the estimation of maximum residue levels for these feed items so that the need for MRLs for animal

products can be assessed.

Onions, Bulb. The 1990 JMPR recommended a temporary limit of 0.2 mg/kg, pending the availability of relevant information on GAP. Because the information on GAP provided to the 1992 Meeting did not closely match the trials data, which were limited, the 1992 Meeting concluded that the proposal could not be lowered but recommended its conversion to a full MRL. Information on GAP in South Africa was provided to the Meeting. Maximum residues from applications approximating GAP were 0.05 mg/kg, after 16 days compared with the GAP PHI of 14 days (the 1990 recommendation was based on 7 days). Because only few results from two countries were available, and these from only 2 applications compared to the 3 to 4 permitted, the Meeting concluded that the available data reflecting GAP were inadequate and agreed to withdraw the previous recommendation.

Peaches. Because data were limited (5 trials in Italy) and the required information on GAP had not been provided, the 1992 JMPR recommended withdrawal of the TMRL of 0.5 mg/kg. Information on Italian GAP (40-70 g ai/hl, 60-day PHI) was provided to the Meeting, which was informed that the 60-day PHI was originally established for early-season application, although in practice later treatments may be needed. There was no evidence of approved uses at shorter PHIs.

Residues did not exceed 0.4 mg/kg from GAP rates after 28 days, but the data were limited, there were no results at the 60-day PHI, there was no information on approved PHIs shorter than 60 days, and only single applications were made although multiple treatments are allowed by GAP. The Meeting therefore concluded that the information was still inadequate to support a limit.

Peppers, Chilli. Nine supervised trials in three countries showed maximum residues from treatments approximating GAP of 4.7 and 6 mg/kg (duplicate analyses, 1.2 times the GAP rate) at the 14-day GAP PHI. The results support a 5 mg/kg limit.

Peppers, Sweet. The 1992 JMPR recommended withdrawal of the 1 mg/kg TMRL because the information on GAP had not been provided. Information on GAP in Italy was
provided to the Meeting (the trials were in Italy, Switzerland and France). Maximum residues were 0.29 mg/kg 29 days after single applications at 0.5 or 0.7 kg ai/ha in the Italian trials; 0.06 mg/kg after 21 days in the Swiss trial and 0.05 mg/kg after 14 days in the French trial at comparable application rates. However, the application rates in the trials were expressed as kg ai/ha and could not be related to the Italian GAP which was in terms of g ai/hl. Also only single applications were made in the Italian trials while multiple applications are permitted by GAP, although 3 to 5 applications were made in the Swiss and French trials at comparable application rates with residues not exceeding 0.5 mg/kg even at shorter PHIs.

Because the trials application rates could not be compared with the GAP provided, the Meeting concluded that the information was still inadequate to support a limit for sweet peppers. If it is shown that the trial application rates correspond to GAP, the data suggest that 0.5 mg/kg would not be exceeded after the Italian 28-day PHI.

Tea. The required clarification of the application rate used in the supervised trials reviewed by the 1990 JMPR enabled the Meeting to confirm the 1990 estimate. The Meeting concluded that the TMRL could be replaced by an MRL of 0.5 mg/kg for "Teas (tea and herb teas)".

Additional clarification of GAP in uses on beans and sweet peppers was provided to the Meeting too late for consideration.

The Meeting estimated the maximum residue levels listed in Annex I, which are recommended for use as MRLs.

FURTHER WORK OR INFORMATION

Desirable

1. An additional soya bean processing study conducted with beans with finite residues to permit determination of concentration factors in all processed fractions (1992 JMPR).

2. Additional soya bean data reflecting GAP in countries in which the trials were conducted and/or additional information on GAP for the countries for which data have already been provided (1992 JMPR).

3. Additional residue data on common beans with relevant information on GAP, with multiple applications where these are GAP.

4. Clarification of the Italian trial on green beans where two samples appear to have been mislabelled.

5. Additional supervised trials on Brussels sprouts according to South African GAP, or information on European GAP relevant to the previous European trials.

4.40 PROPICONAZOLE (160)

RESIDUE AND ANALYTICAL ASPECTS

Propiconazole was evaluated in 1987 and 1991. The 1991 JMPR required information on GAP and residue data from applications of the parent compound to barley and rice. In addition, residue data on melons, peppers and tomatoes from trials carried out according to GAP were considered desirable.

Current use patterns have been submitted for barley, cucurbits, grapes, peppers, rice, sugar beet and wheat. The manufacturer does not recommend use on melons or peppers.

New residue trials were carried out in countries where propiconazole is registered or which have similar climatic conditions to countries where the compound is in use. The application rates and the number of the sprays applied accorded well with the corresponding GAP.

The results of new supervised trials were considered together with those evaluated by previous Meetings.

The Meeting estimated the proportion of parent propiconazole in the total residue containing the dichlorophenyl moiety from the results of field trials and plant metabolism studies reported in the 1987 Evaluations. In supervised trials reported from Canada the parent compound amounted to 12-14.5% and 28-32% of the total residue expressed as the parent in wheat forage and grain respectively. In barley forage the parent compound amounted to about 8% of the total residue after 28 days. The proportion of the parent compound was 8-17% in peanut plants 14-49 days after application, and 21-23% in grapes after 30-63 days. The results indicate that the parent compound is present in the total residue in varying proportions depending on the number of applications and the time after application.

The residues of parent propiconazole in barley were at or about the limit of determination (0.02-0.03 mg/kg) after a PHI of 5 weeks in supervised trials from Canada (4 trials, 1990), France (9 trials, 1986-1991) and Germany (6 trials, 1986-87). No residues were detectable (<0.02 mg/kg) after pre-harvest intervals of 48 days and longer. Total residues based on the determination of dichlorobenzoic acid (DCBA) were between 0.07 and 0.12 mg/kg after 5 weeks, and decreased to 0.05 mg/kg after 7 and 9 weeks. In view of the rapid decline of residues in cereals and the average proportion of 30% of the parent compound in the total residue in wheat grain, the Meeting concluded that the one high value (0.11 mg/kg) from a GAP application rate reported in the 1987 Evaluations from a UK trial on barley could be disregarded. The residues expressed as the parent compound should not exceed 0.05 mg/kg in barley 35-40 days after application at the recommended rate of 0.125 kg ai/ha. The Meeting estimated a maximum residue level of 0.05 mg/kg.

In rice the compound is usually used about 36-40 days before harvest. No propiconazole (<0.02 mg/kg) or total (<0.05 mg/kg) residues were detectable in the ears after a pre-harvest interval of 7 weeks or longer. After shorter PHIs only total residues were measurable 0.35-0.40, 0.07-0.10 and <0.05-0.15 mg/kg after 4, 5 and 6 weeks respectively.

The Meeting also considered the parent residues (0.08, 0.14, 0.15 and 0.19 mg/kg) detected 5 weeks after the last application of 0.1 or 0.2 kg ai/ha in Indonesian rice trials (1987 Evaluations, p. 132). The results suggested a maximum residue level of 0.2 mg parent compound/kg in rice from applications in conformity with Malaysian use patterns. The results were supplemented by the total residues ranging from <0.05 to 0.4 mg/kg found in trials according to US GAP, when the parent residue was calculated from the total residues by applying a factor of 0.3. However, the Meeting concluded that the data were not sufficient to estimate a maximum residue level for a major commodity such as rice.

The residues of propiconazole in peppers were <0.02-0.27 mg/kg after a pre-harvest interval of 13-23 days. Since the compound is registered for peppers in only one country and no residues were available at the registered PHI, no maximum residue level could be estimated.

The residues in sugar beet leaves were recorded in the 1987 Evaluations were reconsidered. Residues in three leaf samples were 0.08, 0.33 and 0.34 mg/kg 14 days after application. As the trial conditions were in agreement with the current use patterns, the Meeting concluded that they supported a limit of 0.5 mg/kg for sugar beet leaves or tops.

Animal transfer studies, reported in the 1987 Evaluations, at feeding levels of 15-100 ppm for cows and 4.5 ppm for goats resulted in undetectable parent residues in milk and tissues (<0.05 mg/kg). After feeding cows for 14 days at 15 ppm the total residues were undetectable in milk and 0.63 mg/kg in kidney. Taking into account the average daily feed consumption of cows (15 kg dry weight) and goats (3 kg dry weight), a maximum of approximately 20% of beet tops in their feed and a conversion factor of 6.25 for wet/dry beet leaves or tops, the maximum daily beet top consumption is about 19 kg for cows and 3.8 kg for goats. Consequently the maximum residues (since the proposed MRL is 0.5 mg/kg) which might be consumed daily by cows and goats would be 9.5 mg and 1.9 mg respectively. Since the feeding studies were with higher residue levels, the proposed 0.5 mg/kg MRL for beat leaves and tops would not result in detectable residues in milk or meat.

Since there was no information on relevant GAP for artichokes and the data are insufficient for both cucumbers and artichokes, maximum residue levels cannot be estimated for these crops.

Analytical methods for determining the parent propiconazole and the total residues based on DCBA have been updated. They are suitable for regulatory purposes.

The revised recommendations are shown in Annex I.

4.41 PROPYLENETHIOUREA (PTU) (150)

RESIDUE AND ANALYTICAL ASPECTS

Propylenethiourea (PTU) is a metabolite and decomposition product of propineb. Propineb was evaluated several times between 1977 and 1985, and in 1993. PTU was included in these evaluations. A temporary ADI for propineb was established in 1977 and withdrawn in 1985, but the CCPR maintained the Guideline Levels for PTU recorded in 1984. A TADI was allocated to PTU by the 1993 JMPR, but no recommendation was made to convert the GLs to TMRLs at that Meeting. The compound is included in the CCPR periodic review programme.

Approved uses of propineb continue on grapes, tomatoes, potatoes, pome fruits, onions and melons. Extensive residue data for propineb and PTU on these crops were provided for evaluation by the 1993 JMPR.

In apples, grapes and pears the residues of PTU were in the range <0.02 to 0.08 mg/kg, except in one grape trial, where a residue of 0.15 mg/kg PTU was measured.

Residues of PTU in tomatoes were at or below the lower limit of determination (0.02 mg/kg).

In melons, onions and potatoes residues of PTU were also below the LOD of 0.01 mg/kg.

The effects of processing commodities containing residues of propineb and PTU were extensively studied on apples, cherries, grapes, hops and tomatoes. The level of PTU in

processed products is primarily influenced by the residue level of propineb and the nature of the processing. The ratio of PTU in the processed product to propineb in the raw commodity was 0.04 for apple puree, 0.003 for beer, 0.2 for cherry juice, 0.1 for cherry jam, 0.2 for must and wine, 0.1 for tomato juice and 0.2 for ketchup. The residue levels of PTU were higher in those processed products for which the processing involves extensive contact with the peel of the harvested crop, as in the case of red wine and tomato ketchup.

No information was available on PTU levels in food moving in commerce or at consumption.

Residue analytical methods are available to determine PTU by HPLC. They are suitable for regulatory purposes with limits of determination of 0.05 mg/kg.

The Meeting noted the similar nature of the residues of PTU and ETU, and concluded that limits for PTU did not assist in deciding whether GAP in the use of propineb had been followed.

The Meeting agreed to recommend the withdrawal of all GLs (listed in Annex I, Part 2) for PTU. (Although a TADI was allocated to PTU in 1993, no recommendation was made to convert the existing GLs to TMRLs).

4.42 TEBUCONAZOLE (189)

(*RS*)-1-*p*-chlorophenyl-4,4-dimethyl-3-(1*H*-1,2,4-triazol-1-ylmethyl)pentan-3-ol

Tebuconazole is a triazole fungicide reviewed for the first time by the present Meeting.

Tebuconazole is taken up by plants and transported within the tissues. It can be used as a seed dressing and as a foliar spray. As a seed dressing tebuconazole is effective against various smut and bunt diseases of cereals. As a foliar spray it controls numerous pathogens such as rust species, powdery mildew and scale in various crops. It is registered on 53 crops in 40 countries.

TOXICOLOGY

After the oral administration of tebuconazole to rats, 65-80% of the dose was eliminated by the biliary/faecal route, whereas elimination in urine amounted to about 16-35%. Males had a higher biliary/faecal elimination than females.

Biotransformation proceeded by oxidative reactions, resulting in hydroxy, carboxy, triol and keto acid metabolites and conjugates, as well as triazole.

Administration of acute oral doses in rats induced sedation, abnormal gait and emaciation. Tebuconazole has low acute toxicity and has been classified by WHO as being unlikely to present acute hazard in normal use.

In a 13-week study, rats were fed tebuconazole at concentrations of 0, 100, 400 or 1600 ppm. The NOAEL was 100 ppm, equal to 9 mg/kg bw per day, on the basis of retardation of body-weight gain and histopathological changes in the adrenal glands at higher levels.

In two one-year studies in dogs fed diets containing 0, 40, 200 or 1000 ppm or 0, 100 or 150 ppm an NOAEL of 100 ppm for the two studies combined, equal to 3 mg/kg bw per day, was determined on the basis of histopathological alterations in the adrenal glands at 150 ppm and above and cataract production at 200 ppm and above.

Two 21-month toxicity/carcinogenicity studies were conducted in mice at dietary concentrations of 0, 20, 60 or 180 ppm or 0, 500 or 1500 ppm. The NOAEL was 20 ppm, equal to 6 mg/kg bw per day, on the basis of fatty changes in the liver. At 1500 ppm, pronounced liver toxicity and an increased incidence of liver tumours were observed. This tumorigenic potential was not considered relevant to humans.

In a two-year toxicity/carcinogenicity study in rats treated at dietary concentrations of 0, 100, 300 or 1000 ppm the NOAEL was 100 ppm, equal to 5 mg/kg bw per day, on the basis of reduced body-weight gain at higher doses. There was no evidence of carcinogenicity.

In a two-generation study of reproductive toxicity in rats fed dietary concentrations of 0, 100, 300 or 1000 ppm the NOAEL was 300 ppm, equal to 22 mg/kg bw per day, on the basis of reduced body-weight gain in the parental generation and adverse effects on litters at the highest dose.

Teratogenicity was investigated in mice, rats and rabbits. In mice, doses of 0, 10, 20, 30 or 100 mg/kg bw per day were administered. Increased enzyme activities in liver which were not dose-related were observed at all doses, so that there was no clear NOAEL for maternal toxicity. In mice fed at 0, 10, 30 or 100 mg/kg bw per day, a higher incidence of runts was seen at 30 mg/kg bw per day and a higher incidence of malformations (mainly cleft palates) at 100 mg/kg bw per day. The NOAEL for embryotoxicity/teratogenicity was thus 10 mg/kg bw per day.

In rats treated at 0, 10, 30 or 100 mg/kg bw per day or 0, 30, 60 or 120 mg/kg bw per day the NOAEL was 10 mg/kg bw per day for maternal toxicity on the basis of reduced body-weight gain at higher dose levels. Embryotoxicity and an increased incidence of malformations (mainly microphthalmia) and visceral and skeletal variations were found at 100 mg/kg bw per day and above, giving an NOAEL for embryotoxicity/teratogenicity of 60 mg/kg bw per day.

In rabbits treated at doses of 0, 3, 10 or 30 mg/kg bw per day or 0, 10, 30 or 100 mg/kg bw per day, the NOAELs were 10 mg/kg bw per day for maternal toxicity and 30 mg/kg bw per day for embryotoxicity and teratogenicity. At 100 mg/kg bw per day embryotoxicity and an increased incidence of external malformations (mainly peromelia) were observed.

Tebuconazole has been studied in a range of tests for genotoxicity *in vitro* and *in vivo*. The Meeting concluded that there was no evidence of genotoxicity.

An ADI was established on the basis of the NOAEL of 100 ppm in the one-year dietary studies in dogs and a 100-fold safety factor.

A toxicological monograph summarizing the data that were reviewed at the present

Meeting was prepared.

TOXICOLOGICAL EVALUATION

Levels that cause no toxic effect

Mouse: 20 ppm, equal to 6 mg/kg bw per day (21-month toxicity/carcinogenicity study)
<10 mg/kg bw per day (maternal toxicity, teratogenicity study)
10 mg/kg bw per day (embryotoxicity, teratogenicity study)

Rat: 100 ppm, equal to 5 mg/kg bw per day (two-year toxicity/carcinogenicity study)
10 mg/kg bw per day (maternal toxicity, teratogenicity study)
60 mg/kg bw per day (embryotoxicity, teratogenicity study)

Rabbit: 10 mg/kg bw per day (maternal toxicity, teratogenicity study)
30 mg/kg bw per day (embryotoxicity, teratogenicity study)

Dog: 100 ppm, equal to 3 mg/kg bw per day (one-year study)

Estimate of acceptable daily intake for humans

0-0.03 mg/kg bw

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

Further observations in humans

RESIDUE AND ANALYTICAL ASPECTS

In animal metabolism studies made available to the Meeting, rats, goats and chickens were dosed with [^{14}C]phenyl-labelled tebuconazole, and rats also with the [^{14}C]triazole-labelled compound. The following abbreviations are used for metabolites.

T:	triazole
TA:	triazolylalanine
TAA:	triazolylacetic acid
TLA:	triazolyllactic acid
HWG 2061:	*tert*-butyl alcohol derivative of tebuconazole
HWG 2443:	butyrate derivative of tebuconazole
ECW 4393 2/2:	glucuronide conjugate of HWG 2061

In general, when rats, goats and chickens were dosed with tebuconazole, the major residues identified (>10% of the total ^{14}C) in excreta, tissues, milk and eggs were tebuconazole (goats and chickens), the *tert*-butyl alcohol derivative HWG 2061 (all 3 species), the *tert*-butyl acid HWG 2443 (rats and chickens), the alcohol glucuronide conjugate (goats), and the alcohol sulphate conjugate (chicken livers and kidneys only).

In rats HWG 2443 amounted to 35% and HWG 2061 to 20% of the radioactivity in the excreta (urine plus faeces).

In chickens tebuconazole accounted for 33-75% of the total ^{14}C residues (excluding gizzard), and HWG 2061 for 29-49% of the total ^{14}C residues in muscle and eggs.

The total ^{14}C residue levels, expressed as tebuconazole, in the tissues from laying hens dosed for 3 consecutive days at 10 mg/kg bw/day were liver 7.9 mg/kg, fat 1.14 mg/kg and muscle 0.54 mg/kg. Eggs contained 0.22 mg/kg.

In goats tebuconazole accounted for 13.6% of the total ^{14}C in milk and 0% in muscle, HWG 2061 for 22.2% in milk, and the HWG 2061 glucuronide conjugate for 49.4% in milk and 67.6% in muscle and liver.

In the goat study (15 mg/kg bw/day for 3 days), total ^{14}C residues expressed as tebuconazole reached 0.05 mg/kg in muscle and milk, 0.15 mg/kg in fat, 3.96 mg/kg in kidney and 5.19 mg/kg in liver. Average residues in milk over the dosing period were 0.04 mg/kg. 93.1-100% of the ^{14}C residues in these samples were organosoluble, and 0-6.9% were bound.

The metabolism of tebuconazole to its *tert*-butyl alcohol derivative (HWG 2061) followed by conjugation resulted in the major metabolite, the glucuronide ECW 4393 2/2.

Total ^{14}C-residues in liver, kidney, fat, muscle and milk were identified as 2-14% tebuconazole, 2-22% HWG 2061 and 49-93% ECW 4393 2/2.

The plant metabolism studies submitted were with triazole[3,5-^{14}C]- or phenyl[U^{14}C]-tebuconazole.

In grapes treated with the triazole- or phenyl-labelled compound, tebuconazole accounted for 95% of the total ^{14}C residue.

In peanuts (triazole or phenyl label), the foliage contained 55.9-70% of the total ^{14}C residue as tebuconazole and 7-15% as a glucoside of HWG 2061, the shells 17-58% tebuconazole, 3.4-3.9% HWG 2061 and 2.6% triazolylalanine, and the kernels 19% tebuconazole, 4% HWG 2061, 9% triazole, 46% triazolylalanine and 8.5% triazolylacetic acid.

The total ^{14}C residue as tebuconazole equivalents in peanut foliage treated with [U-^{14}C]phenyl-labelled tebuconazole under confined greenhouse conditions at 3.5 times the recommended rate were 0.55 mg/kg in the kernels and 110 mg/kg in the foliage.

In wheat (triazole label) the straw after foliar treatment contained 90% tebuconazole and <1% HWG 2061, and after seed treatment 25% tebuconazole, 14.5% HWG 2061 and 14.55% of its glucoside. After foliar treatment the chaff contained 56% tebuconazole and <1% HWG 2061,

while the seeds contained 6% tebuconazole, 80% TA, 13% TAA and <1% HWG 2061.

The total ^{14}C residues expressed as tebuconazole in wheat foliage treated with [^{14}C]triazole-labelled tebuconazole, under confined greenhouse conditions at twice the recommended rate, were 0.5 mg/kg in the seeds, 37 mg/kg in the straw and 3.8 mg/kg in the chaff. The corresponding residues in wheat seed similarly treated but at 3.7 times the recommended rate were 0.02 mg/kg in the seeds, 0.1 mg/kg in the straw, 0.04 mg/kg in the chaff and 0.16 mg/kg in the roots. The residue levels resulting from seed treatment, expressed as a percentage of the applied radioactivity translocated, represent 2% for seeds, 17% for straw, 1% for chaff and 4% for roots.

The major terminal residue in foliar-treated plants reported in the above studies was the parent compound tebuconazole, except in peanut kernels and wheat seed where triazolylalanine (TA), triazolylacetic acid (TAA), triazolyllactic acid (TLA) and triazole (T) (the last two only in peanut kernels) predominated. The percentages of the total ^{14}C residue identified were 64%, 77% and 63% in peanut kernels, foliage and shells respectively, 99% in wheat seed and 90% in wheat straw.

In crop rotational studies, residues of TAA and TLA in immature wheat and mature wheat grain and straw from wheat grown on soil containing aged residues of tebuconazole and tebuconazole metabolites, were respectively 20-54% (0.4-3.1 mg/kg) and 37% (0.8 mg/kg) of the total ^{14}C eluted from ion exchange columns. TA residues ranged from 24 to 70.6% (0.51-12.7 mg/kg) in wheat straw, immature wheat and mature grain, with the highest residues in the grain.

In summary, the plant metabolism studies indicated that when tebuconazole is applied as a foliar or seed treatment it is absorbed and metabolized, and residues are translocated to the fruits, seeds and roots.

The photodecomposition and hydrolysis of tebuconazole were studied on the surface of a sandy loam soil exposed to natural sunlight for 34 days in Kansas, USA and in an aqueous solution buffered at pH 7 exposed to sunlight for 30 days.

Photochemical degradation occurred slowly on the soil, with 86% of the parent compound recovered by methanol extraction after 34 days of irradiation; no significant reaction products were identified. No photoreaction was observed in aqueous solution after 30 days of irradiation. Tebuconazole is evidently stable in water and on soil under exposure to natural sunlight.

Tebuconazole was stable in pH 5, 7 and 9 sterile aqueous phosphate buffers when stored in the dark at 25°C.

Degradation and dissipation in soil were studied in sandy loam, 1.8% organic matter, 10 mg/kg treatment level. The degradation of both phenyl- and triazole-labelled [^{14}C]tebuconazole was slow under aerobic conditions. The parent compound remained the main residue throughout the 12-month study with a half-life of >1 year.

Up to 30% of the recovered ^{14}C was identified as $^{14}CO_2$, indicating the slow mineralization of tebuconazole; <6% of the applied ^{14}C was detected as the major degradation product 1,2,4-triazole. With both labels all of the extractable ^{14}C (70-85%) was present as

tebuconazole after 50-60 days and 67% as parent (67% of the total ^{14}C residue was extractable) after 12 months. Negligible volatilization (0.7%) occurred and the bound residues increased with time to a maximum of 29.1% of the total terminal residues. The rate of degradation was slightly greater under anaerobic conditions. Tebuconazole was shown to be fairly stable in soil.

From residue data in a Canadian study the half-life of tebuconazole residues in soil ranged from 51 to 128 days, which agrees with that reported in a similar study in the USA (40-170 days), and with that found in a study of photochemical degradation in soil of 191 days. In another soil degradation study the half-life was >1 year.

Tebuconazole residues at soil surfaces were all ≤0.17 mg/kg at 0-120 days after treatment. There was no significant residues of tebuconazole in the 15-30 cm soil layers, indicating that there was no potential for tebuconazole to be leached. Several adsorption and leaching studies conducted in Europe and North America have confirmed that tebuconazole has low mobility in soil and hence a low tendency to contaminate ground water. On the basis of these results tebuconazole was classified as immobile.

Rotational crops. [^{14}C]Tebuconazole was used to treat a wheat crop and, after harvest, the soil. Tebuconazole was found to be extensively metabolized in wheat, beet and kale rotational crops, with the [^{14}C]triazole-labelled compound giving 3 major products: triazolylalanine (31-80%), triazolylacetic acid (21-54%) and triazolyllactic acid (37-54%). It was not clear whether the degradation occurred in the soil or in the plants. The highest residues were found 120 days after planting (e.g. 12.7 mg/kg TA, 3.1 mg/kg TAA in wheat grain).

In a study with unlabelled tebuconazole only cereal straw and forage showed a slight increase in tebuconazole residues at the 120-day interval after treatment with 7 x 250 g ai/ha. Residues were typically ≤0.05 mg/kg in wheat grain, turnip roots and spinach sampled 30 or 120 days after treatment, but cereal straw contained residues of 0.11 mg/kg at 120 days. The crops studied do not appear to absorb aged soil residues of tebuconazole, indicating that rotational crops with the exception of cereal straw will not contain residues above 0.1 mg/kg.

Methods of residue analysis were provided for the determination of tebuconazole and triazolylalanine in plant tissues and for tebuconazole and its metabolite HWG 2061 and its glucoside conjugate in animal tissues.

Extracts were cleaned up by conventional techniques and residues determined by gas chromatography with a nitrogen-specific thermionic detector; a method was also reported using a mass-selective detector and single ion monitoring. Analytical methods generally exhibited acceptable accuracy and precision over a wide range of concentrations (the LOD was 0.05 mg/kg for plant materials, 0.01 mg/kg for milk, 0.03 mg/kg for eggs and 0.05 mg/kg for animal tissues). The method (designated DFG S19) was shown to be suitable for enforcement purposes.

In interference studies, four of the 94 compounds tested showed interference with the GLC determination of tebuconazole: disulfoton, malathion, norflurazon and sethoxydim. After subjecting these four compounds to silica gel clean-up, only norflurazon and sethoxydim showed interference with the GLC determination.

FDA PAM multi-residue methods do not appear to be suitable for the determination of tebuconazole and its metabolite HWG 2061 in plant and animal tissues because of unacceptable

accuracy and precision in recovery studies.

Stability of stored analytical samples. Generally, plant and animal tissues spiked with tebuconazole or its metabolite HWG 2061 were stable at -10°C for 3-12 months. Tebuconazole in wheat straw was stable for >3 years.

Residues resulting from supervised trials

Reports of residue trials already submitted to national registration authorities to support registered uses or uses pending registration were evaluated.

The results of metabolism studies show that tebuconazole is the major terminal residue in plants to be determined in supervised residue trials or for monitoring or surveillance.

Pome fruit. Tebuconazole is registered for use on apples in Brazil (WP formulation, where 0.09 kg ai/ha up to 6 times is recommended at a PHI of 20 days). In France petitioned uses require an application rate of 0.1 kg ai/ha and a PHI of 14 days (WP formulation); in Italy a rate of 0.125 kg ai/ha and a PHI of 21 days is proposed. Uses are also registered in Peru, Uruguay and Zimbabwe.

Ten residue trials were conducted in France on apples with the WG/WP formulation. Four to 6 sprays between 0.075 and 0.1 kg ai/ha were applied. In the fruit residues of tebuconazole were up to 0.43 mg/kg at sampling day 0. This level decreased continuously until the harvest at 21-30 days when it ranged between <0.05 and 0.20 mg/kg. At 28-30 days residues were between <0.05 and 0.09 mg/kg. No GAP was available for France or Italy so the data could not be evaluated.

Four residue trials were conducted in Zimbabwe (6 to 8 sprays, 0.25 kg ai/ha). In the fruits, residues of 0.1 to 0.22 mg/kg were determined at days 26 to 30. Four trials according to GAP were considered insufficient to estimate an MRL for apples.

The only registered use for tebuconazole on pears is in Uruguay: up to 3 x 0.125 kg ai/ha (WP formulation) at a PHI of 35 days.

One residue trial was conducted in France on pears with the WP formulation. After an application of 0.1 kg ai/ha, 5 times a season, residues in the fruit at day 0 were 0.15 mg/kg. These residues declined until days 14-21 when they were lower than 0.05 mg/kg (the LOD).

Three residue trials were conducted in Italy with a WG formulation at 4 x 0.213 kg ai/ha. Residues at day 7-14 ranged from 0.12 to 0.43 mg/kg.

No information on GAP was available to evaluate the French and Italian trials on pears.

The Meeting concluded that insufficient data were available from trials according to GAP and could not recommend an MRL for tebuconazole use on pome fruit (apples or pears).

Stone fruit. Uses of tebuconazole on peaches and apricots have been petitioned for registration in Italy and France. An application rate of 0.125 kg ai/ha (WG formulation) is recommended at a PHI of 7 days in Italy and 14 days in France. Uses on peaches are registered in Peru and Uruguay.

In France 1 residue trial on apricots and 4 on peaches with the WG formulation approximated the proposed use, with one on apricots at a double rate. In apricots, residues of tebuconazole from 0.125 kg/ha were 0.14 and 0.15 mg/kg at 14 days. Residues in peaches declined from 0.15-0.33 mg/kg at day 0 until 14 days, when they were <0.02-0.10 mg/kg.

Six residue trials, 3 on apricots and 3 on peaches, were conducted in Italy with a WG formulation at about twice the proposed rate. Residues of tebuconazole were up to 0.65 mg/kg at day 0 in apricots. These declined until days 7 and 14 to 0.3 mg/kg and 0.04-0.28 mg/kg respectively. Residues in peaches at day 7 were 0.21-0.37 mg/kg.

Because no information on registered uses relevant to the supervised trials was available, the Meeting concluded that it could not recommend an MRL for tebuconazole on stone fruits (peaches and apricots).

Tebuconazole is registered for the use on grapes in Argentina, Bolivia, France, Germany, Israel, Peru, Portugal, Saudi Arabia, South Africa, Spain, Turkey and Uruguay. Sixty-two residue trials were conducted with WP, EC and EW formulations.

Thirty-four trials were conducted in Germany: 14 trials according to GAP showed residues of 0.17-0.88 mg/kg with most in the range 0.37-0.55 mg/kg (12 results). Eight of 10 trials from Portugal were according to GAP with residues of 0.14-1.1 mg/kg and most between 0.31 and 0.61 mg/kg. Ten of 14 trials from France corresponded to GAP with residues between <0.02 and 0.78 mg/kg and most between 0.17 and 0.38 mg/kg. Four South African trials were not consistent with GAP since a 21-day PHI was used (35 days is recommended GAP).

The Meeting recommended an MRL of 2 mg/kg for tebuconazole in grapes.

Bananas. Tebuconazole is registered in Malaysia and El Salvador as an EC formulation. In Malaysia up to 4 x 0.1 kg ai/ha are recommended and in El Salvador 1-3 x 0.1 kg ai/ha at a PHI of 35 days.

Eight residue trials in Australia, 2 each at rates of 0.2, 0.4, 0.6 and 1.2 kg ai/ha/season and 2 trials on Costa Rica at 0.965 kg ai/ha/season were reported. The residues of tebuconazole ranged between <0.05 and 0.35 mg/kg and appeared to increase with time after treatment.

The Meeting concluded that since no data were provided from trials according to GAP it could not recommend an MRL for tebuconazole in bananas.

Onions. Tebuconazole is registered for use on bulb vegetables in Israel, New Zealand, Uruguay and South Africa. In Israel 0.19 kg tebuconazole/ha is recommended per season, with a PHI of 21 days. In New Zealand up to 3 x 0.38 kg ai/ha is registered with a PHI of 35 days: EC, WP and EW formulations are registered for use. Up to 4 x 0.19 kg tebuconazole/ha is recommended in South Africa with a PHI of 14 days.

Residue trials on onions were conducted in the following countries: 5 in Australia, where 1 or 2 x 0.5 kg ai/ha were applied; 2 in Egypt, where the first application of 6.25 kg ai/ha was followed by two applications at 0.45 kg ai/ha; 2 in South Africa where 4-6 x 0.38 kg ai/ha was applied, and one in Italy at 2 x 0.25 kg ai/ha (WG formulation).

No information on GAP was available for Egypt or Australia with which to evaluate data from the trials in these countries.

The Meeting could not recommend an MRL for tebuconazole on bulb onions owing to insufficient data from trials according to GAP.

Tebuconazole is registered for use on beans in Brazil, Peru, South Africa and Spain.

Supervised residue trials were submitted from Brazil (4), South Africa (2), Germany (4) and the UK (2), but none of them approximated GAP (they were at exaggerated rates and/or reduced PHIs).

The Meeting concluded that insufficient data were available to recommend an MRL for tebuconazole in beans.

Peas. Tebuconazole is registered only in New Zealand. One or two x 0.063 kg ai/ha of an EC formulation is recommended.

Residue trials were not provided from New Zealand, but several trials were conducted in Germany (4), France (4), The Netherlands (3), the UK (1) and France (5). No information on GAP was available for European countries.

The Meeting concluded that insufficient data were available to recommend an MRL for tebuconazole in peas.

Cucumbers. Tebuconazole is currently registered in Israel and Spain for WP and EC formulations.

Three residue trials were conducted in Spain with a WP formulation. After applying 3 x 0.20 kg ai/ha, residues of tebuconazole were <0.02 mg/kg (the LOD) at a PHI of 7 days. The application rate in the trials was much lower than permitted by Spanish GAP (0.5 kg ai/ha).

Two residue trials with a WP formulation were conducted in Italy, where 5 x 0.1 kg ai/ha were applied. No residues above 0.02 mg/kg (the LOD) were found at the proposed PHI of 7 days.

The Meeting concluded that insufficient data were available to recommend an MRL for tebuconazole in cucumbers.

Squash, Summer. Tebuconazole is currently registered only in Spain. The EC formulation at an application rate of 0.25 kg ai/ha is recommended up to twice a season and at a PHI of 3 days. Two or three applications with rates of 0.50 to 0.75 kg ai/ha are allowed with the 50 WP formulation (PHI 7 days).

Six residue trials were conducted at or near GAP in Spain (3) and Italy (3) with WP and WG formulations, where 4 x 0.25 kg ai/ha or 5 x 0.12 kg ai/ha were applied. Residues were <0.02 mg/kg (LOD) in 4 trials and 0.02 mg/kg in 2 trials.

The Meeting recommended an MRL of 0.02 mg/kg for tebuconazole in summer squash.

Egg plants. Tebuconazole is registered in Israel and in Spain. Three residue trials were conducted in Spain. At 0.40 kg ai/ha and a PHI of 7 days residues were <0.02 mg/kg (LOD) (0.5 kg ai/ha and 7 days are recommended).

The Meeting concluded that insufficient data were available to recommend an MRL for tebuconazole in egg plants.

Sweet peppers. Tebuconazole EC and WP formulations are registered in Spain, where 1-2 x 0.25 kg ai/ha are recommended with a PHI of 3 (EC) and 7 (WP) days.

Five residue trials were conducted with a WP formulation in Spain and Italy. In two trials in Spain according to GAP, residues were 0.14 and 0.36 mg/kg at a PHI of 7 days.

The Meeting concluded that insufficient data were available to recommend an MRL for tebuconazole in sweet peppers.

Sweet corn. See Maize

Tomatoes. Several tebuconazole formulations are registered in South Africa, Israel and Spain for use on tomatoes. Residue trials were available from Brazil (4), South Africa (6), Spain (3) and Italy (3).

Six residue trials were conducted in South Africa with EC or EW formulations. Residues in two trials approximating GAP at PHIs of 0-2 days were 0.05 and 0.06 mg/kg.

Four residue trials were conducted in Brazil, with the WP (2) and EC (2) formulations; all were at 2-6 times the recommended maximum seasonal rates.

Five residue trials were conducted in Italy (2) and Spain (3) with WG and WP formulations respectively. The 3 trials in Spain were according to GAP and showed tebuconazole residues in the fruit of 0.03, 0.11 and 0.12 mg/kg.

The Meeting recommended an MRL of 0.2 mg/kg for tebuconazole in tomatoes.

Potatoes. Tebuconazole is registered in Brazil, Israel and Uruguay for the EC or WP formulation at 1-3 x 0.25 kg ai/ha in Israel, 2-3 x 0.19 kg ai/ha in Uruguay and 3-4 x 0.25 kg ai/ha in Brazil, all at a PHI of 35 days.

Two residue trials were conducted in South Africa corresponding to registered uses in Israel. No residues could be determined in the tubers above 0.02 mg/kg (the LOD).

Four residue trials were conducted in Brazil, where 2.5-8 times the registered rates were applied. However, residues in the tubers at a PHI of 30 days were ≤0.05 mg/kg (LOD).

The Meeting concluded that it could not recommend an MRL for tebuconazole in potatoes because no residue data were from supervised trials according to GAP and because of the very limited number of trials for a major crop.

Cereal grains. Tebuconazole is currently registered for use on cereals in several countries, the most important being France, the UK, Ireland, Germany, Brazil, Chile and Argentina.

Tebuconazole is registered for the foliar and seed treatment of barley in several countries. Residue trials data were submitted for foliar treatments from France (10 trials), New Zealand (4, plus 2 trials from Australia), Sweden (2, according to GAP in Norway), Germany (40), Czechoslovakia (5), Brazil (6) and the UK (13), and for seed treatments from Germany (6), Brazil (2), Australia (6) and Morocco (2).

Residues from the foliar treatments in all countries (62 trials were according to GAP) ranged between <0.05 (LOD) and 0.10 mg/kg, and from the seed treatments residue levels in progeny seed were all <0.05 mg/kg.

The Meeting recommended an MRL of 0.2 mg/kg for residues of tebuconazole in barley.

The recommended MRL was higher than that proposed for other cereal grains because of the propensity of barley to accumulate residues of tebuconazole.

Maize. Use on sweet and field corn is registered in Israel up to 0.19 kg ai/ha (EC formulation) per crop season at a PHI of 21 days, and in France use on field corn as a seed treatment is at 0.0076 kg ai/dt (WS). In Mexico the FS formulation is registered for the seed treatment of field corn at 0.63 kg ai/dt and in Saudi Arabia the WS for field corn at 0.010 kg ai/dt.

Four residue trials were conducted in France with the EC formulation. After applying 0.25 kg ai/ha (1.3 times the registered rate in Israel) once or twice, residues were <0.05 mg/kg (LOD) in mature grain at 34 days PHI.

The Meeting concluded that insufficient data from trials according to GAP were submitted to recommend an MRL for tebuconazole in maize or sweet corn.

Oats. Tebuconazole is registered for the foliar and seed treatment of oats in several countries. Data from supervised residues trials were submitted for foliar treatment from New Zealand (3 trials from Australia) and Sweden (1, according to GAP in Norway) and for seed treatment from Germany (4). For foliar application, 3 trials according to GAP (2 in Australia, 1 in Sweden) gave residues of 0.06, 0.09 and 0.12 mg/kg; in the 4 seed treatment trials in Germany no residues of tebuconazole were detected in progeny seed (LOD 0.05 mg/kg).

The available data indicate that residues in oats are not in the same range as in wheat and rye, so that data on residues in wheat and rye cannot be used to support an estimate for oats.

The Meeting considered the data submitted insufficient to recommend an MRL for tebuconazole in oats.

Rice. Tebuconazole is registered in Bolivia, Brazil, El Salvador, Peru and Uruguay for uses on rice at 3 x 0.19 to 3 x 0.25 kg ai/ha (EC or EW formulations); a PHI of 35 days is recommended in all countries.

Only four residue trials were conducted in Brazil with an EC formulation at recommended application rates, with 2 trials at 1.5 and 2 at 3 times those rates. Rice grain

contained no residues above 0.05 mg/kg (the LOD).

The Meeting concluded that for a major crop such as rice the data were insufficient to recommend an MRL.

Rye. Tebuconazole is registered for the foliar treatment of rye in several countries. Data from 7 supervised residues trials according to GAP were submitted from Germany (6) and Sweden (1, according to GAP in Norway). Residues in all trials were <0.05 mg/kg.

The Meeting recommended an MRL of 0.05* mg/kg for residues of tebuconazole in rye.

Wheat. Tebuconazole is registered for the foliar and seed treatment of wheat in several countries. Data from supervised residues trials were submitted for foliar treatment from France (9 trials), New Zealand (7, plus 7 from Australia), Sweden (5, according to GAP in Norway), Germany (47) Czechoslovakia (3), Brazil (4) and the UK (10), and for seed treatment from Germany (2), Brazil (2), Australia (8) and Morocco (2).

Residues from foliar treatments (75 according to GAP) in all countries were ≤0.05 mg/kg (LOD) and residue levels in progeny seed from seed treatments were all <0.05 mg/kg.

The Meeting recommended an MRL of 0.05 mg/kg for residues of tebuconazole in wheat.

Peanuts. Tebuconazole is currently registered for use on peanuts in Argentina, El Salvador, Israel, South Africa, Saudi Arabia, the USA and Zimbabwe (SC, EC and EW formulations).

Four residue trials in Australia with an EC formulation could not be evaluated because no information on GAP was available.

In South Africa 8 residue trials were conducted with the EW formulation, two each at 5 x 0.15, 5 x 0.3, 4 x 0.084 and 4 x 0.17 kg ai/ha.

Six trials according to GAP and 2 trials at a double rate all resulted in residues of <0.05 mg/kg.

The US recommended use pattern is 4 x 0.23 kg ai/ha of SC at 14-day intervals, with mature crops harvested at a PHI of 14 days.

In US trials, peanut plants were treated with 7 foliar applications of EC or WG formulations at the rate of 0.25 g ai/ha/application at 6 locations. PHIs for peanuts in shells and peanut vines were 10-17 days and varied from site to site.

Residues from treatments with either formulation at approximately twice the recommended rate and at PHIs of 12 or 15 days (14 days recommended) ranged between <0.02 and 0.04 mg/kg in peanut kernels. LODs for peanut kernels and vines were 0.02 and 0.05 mg/kg respectively.

When these results are used in support of those from South Africa, 12 trials indicate that residues in peanut kernels would be ≤0.04 mg/kg.

The Meeting recommended an MRL of 0.05 mg/kg for tebuconazole residues in peanuts.

Rape seed. Tebuconazole is registered as a spray formulation (EW) in Germany, the UK, France, Ireland and Austria. Rates between 0.25 and 0.375 kg ai/ha are recommended 1 to 3 times per crop season. PHIs are 56 and 63 days in Germany and Austria.

Thirty-three residue trials were conducted world-wide with the EC or EW formulations in rape seed; 12 in Germany at 1-2 x 0.5 kg ai/ha, 8 in the UK at 1-2 x 0.25, 0.375 or 0.75 kg ai/ha, 7 in France at 1 x 0.25 or 0.38 kg ai/ha, 3 in Sweden at 1-2 x 0.25 or 0.5 kg ai/ha, and 3 in Australia at 1 x 0.2, 0.4 or 0.6 kg ai/ha.

Seven trials according to GAP and 4 at exaggerated rates in Germany all resulted in tebuconazole residues of <0.05 mg/kg (LOD). Eight trials in the UK and 6 in France according to GAP all showed residues of <0.05 mg/kg, as did one trial in France at an exaggerated rate; 3 trials in Sweden showed residues of ≤0.05 mg/kg.

Residue trials in France, Sweden and Australia (not yet registered) were evaluated to elucidate the residual behaviour of tebuconazole used as a seed dressing. Irrespective of the formulation, the application rate and the trial location, no residues above 0.05 mg/kg (the LOD) were found in the mature rape seeds.

The Meeting concluded, on the basis of the residue data provided for foliar treatments of rape seed plants, that an MRL of 0.05 mg/kg could be recommended.

Animal feed commodities

Cereals straws and fodders. Residues in straw from wheat, barley and rye plants treated with tebuconazole according to GAP were 0.5-6.8, 0.6-7.0 and 1.3-2.4 mg/kg respectively.

The Meeting recommended MRLs of 10 mg/kg for wheat and barley straw and 5 mg/kg for rye straw.

The Meeting concluded that residues in straw at these levels would be unlikely to result in residues above the proposed MRLs in animal commodities.

Peanut fodder. In US trials mature peanut vines contained 4.9-23 mg/kg at harvest, 12-19 days after application. In South African trials the residues ranged from 0.2 to 22 mg/kg at harvest, 41 days after the last application.

The Meeting concluded that residues would be unlikely to exceed 30 mg/kg in peanut fodder when tebuconazole is used according to GAP and recommended an MRL of 30 mg/kg for tebuconazole residues in peanut fodder.

This residue level is not expected to result in meat or milk residues exceeding the MRLs proposed for these commodities.

Animal transfer studies

In the dairy goat metabolism study with phenyl-labelled tebuconazole, total ^{14}C residues reached 0.05 mg/kg in muscle and milk, 0.15 mg/kg in fat, 3.96 mg/kg in kidney and 5.19 mg/kg in liver. The average residues in milk over the dosing period were 0.013 mg/kg. 93.1-100% of the ^{14}C residues in these samples were organosoluble.

When dairy cattle were fed feed containing up to 75 ppm tebuconazole for 28 days, the residues of tebuconazole and HWG 2061 in all tissues were <0.1 mg/kg with occasional excursions to 0.1 mg/kg; residues in milk were typically <0.01 mg/kg. Cereal forages (green immature plants) would not be expected to contain residues of tebuconazole above 25 mg/kg, on the basis of the residues found in supervised trials.

When the tebuconazole content of a dairy cow diet was 25 ppm, tebuconazole was not detected (<0.05 mg/kg) in milk, muscle, fat or kidney, and was present in liver at <0.05-0.10 mg/kg. Residues in the total diet of cows are unlikely to exceed 10 ppm tebuconazole.

The Meeting estimated maximum residue levels of 0.05* mg/kg as being practical limits of determination for tebuconazole in cattle meat and offal, and 0.01* mg/kg in cattle milk.

The only residues at or above the 0.05 mg/kg LOD in poultry tissues were found in the liver from the highest (20 ppm) feeding level. When laying hens were fed 6 ppm tebuconazole in the diet no detectable residues appeared in tissues or eggs (0.05 mg/kg LOD). Residues in poultry diets are unlikely to exceed 6 ppm.

The Meeting estimated maximum residue levels for tebuconazole in chicken meat, offal and eggs of 0.05* mg/kg as being a practical limit of determination.

Processing studies

Pome fruit. Apples were processed to juice and puree according to household procedures. One supervised residue trial on apples was conducted in Italy, at 1.5 times the recommended application rate. It was found that tebuconazole residues in the fruit of 0.37 mg/kg (21 days after treatment) were reduced during processing to apple juice and purée.

In the purée the residue was 0.17 mg/kg while in the juice it was at the LOD (0.05 mg/kg). The residues were also reduced during washing and drying. Increased concentrations of tebuconazole were found only in the pomace, at 6.8 mg/kg.

Stone fruit. Peaches were processed to juice, jam and preserve.

Peach jam was prepared after sorting, washing, peeling, stoning, and chopping, by adding jellying sugar to the peaches and cooking for 10 minutes at 100°C.

For peach preserve, after sorting, washing, and peeling, the peaches were cut into halves, stoned and filled into preserving cans. Syrup was added to the prepared fruits and the mixture pasteurised for 4 minutes at 90°C.

To produce peach juice, peaches were sorted, washed, cut, stoned, and crushed, then separated into juice and marc in a high-pressure press. The juice was pasteurised in a plate heat-exchanger for 15 to 150 seconds at 82 to 90°C.

Supervised trials were conducted on peaches in southern Europe (France and Italy) according to the proposed uses. Tebuconazole residues at sampling day 10/14 in the fruit (up to 0.15 mg/kg) were reduced during washing and processing. Residues in the washed fruits ranged from <0.02 (LOD) to 0.13 mg/kg, and in the jam, juice and preserve the residues were below 0.02 mg/kg, except one residue of 0.03 mg/kg in juice. The results showed that tebuconazole residues were significantly reduced during processing.

Grapes. In processing to juice, pomace and raisins, a concentration of residues occurred in all the fractions except juice. Juice contained an average of 0.4 times the whole fruit residue, wet pomace 1.8 times, dry pomace 5.8 times, sun-dried raisins 1.4 times, oven-dried raisins 1.2 times and sun-dried raisin waste 2.7 times.

Tebuconazole residues in wine grapes (up to 2.3 mg/kg) were significantly reduced by a minimum of 50% by processing the grapes to juice, must, and wine. Residues in juice ranged between 0.54 and 1.1 mg/kg, in must between <0.02 and 1.6 mg/kg, and in wine between <0.02 and 0.97 mg/kg.

Wheat. A tebuconazole EC formulation was applied twice in spring, with a 14-day interval to winter wheat at the proposed rate of 250 g ai/ha/application.

Samples of grain were collected at a 17-day PHI for processing and analysis. Whole wheat with a residue of 0.08 mg/kg was processed into bran, middlings, shorts, patent flour and low grade flour ("rough" and "red dog").

In the processed fractions shorts contained 0.20 mg/kg, bran 0.08 mg/kg, middlings 0.05 mg/kg, patent flour 0.01 mg/kg and low grade flour 0.02 mg/kg. Only wheat "shorts" (fine particles of bran, germ, flour and tailings) showed any concentration of residues, at 2.5 times the residues in unprocessed grain.

Peanuts. Peanuts (shelled and dehulled), from plants which had been treated with 7 foliar applications of an EC formulation at rates of 250 g ai/ha/application were processed into meal, press cake (solvent-extracted meal), crude oil (solvent-extracted), refined oil and soapstock. The residues were <0.02 mg/kg in the kernels, ≤0.02 mg/kg in the meal and refined oil, <0.05 mg/kg in the crude oil and 0.01 mg/kg in the soapstock. Since there were no measurable residues in the treated kernels concentration factors could not be calculated. However no residues were detected in any of the processed fractions greater than the LOD of 0.02 mg/kg in the unprocessed peanuts, indicating that there was little potential for concentration in these fractions.

Rape seed. Rape seeds were processed to oil according to simulated industrial procedures. Three residue trials were conducted with an EC formulation on rape seed, in which 0.5 kg ai/ha was applied in one or two sprays. No residues above 0.05 mg/kg were found in the mature seeds or oil, so no concentration of tebuconazole residues is to be expected during oil production (LOD 0.05 mg/kg). The data were insufficient to determine whether quantifiable residues of tebuconazole in rape seed would result in measurable residues in rape seed oil.

The residue levels shown in Annex I are recommended for use as MRLs.

4.43 TECNAZENE (115)

TOXICOLOGY

Tecnazene was evaluated by the Joint Meeting in 1974, 1978, 1981 and 1983. A temporary ADI (0-0.01 mg/kg bw) was allocated in 1978, and an ADI of 0-0.001 mg/kg bw was established in 1983. Since the review of the toxicology of tecnazene in 1983, several new studies have been reported, which were reviewed at the present Meeting..

After oral administration of radiolabelled tecnazene to rats, about 90% of the dose was recovered within 48 h. Excretion was divided almost equally between the urine and faeces in males but occurred predominantly (80%) via the urine in females. The remainder of the dose was excreted more slowly, and radioactivity was still detectable in the urine and faeces seven days after dosing. Negligible levels of radioactivity were detected in expired carbon dioxide. Whole-body autoradiography showed that 24 h after dosing, the highest concentrations of radioactivity were located in the intestinal contents of animals of both sexes; the highest tissue concentrations were found in kidney, liver and the nasal passages.

Tecnazene is extensively metabolized in rats. A total of 42 metabolites have been separated in urine and bile, of which 15, as well as the parent compound, have been identified. The principal route of metabolism is via the tetrachlorobenzene glutathione conjugate pathway. Metabolites present in the urine and faeces include the tetrachlorophenyl-mercapturate conjugate, tetrachloroaniline and tetrachlorothioanisole. The pattern of metabolites in urine and faeces is the same in male and female rats, but the quantities differ.

In female rabbits, about 70% of an oral dose of tecnazene was recovered in the faeces within three days. The remainder was excreted in the urine, primarily as glucuronide, sulphate and mercapturic acid conjugates of 2,3,5,6-tetrachloroaniline. Some unconjugated 4-amino-2,3,5,6-tetrachlorophenol was also excreted.

Tecnazene has low oral toxicity in rats. WHO has classified tecnazene as unlikely to present an acute hazard in normal use.

In a 90-day study in rats fed dietary concentrations of 0, 50, 500 or 5000 ppm the NOAEL was 500 ppm, equal to 45 mg/kg bw per day, on the basis of effects on body-weight gain and on the liver and kidneys.

In a 90-day study in dogs given 0, 2, 15 or 200 mg/kg bw per day orally, the NOAEL was 15 mg/kg bw per day on the basis of effects on body and liver weights.

In a two-year study in which dogs were given 0, 3.8, 15, 60 or 240 mg/kg bw per day orally, the NOAEL was 15 mg/kg bw per day, on the basis of elevation of serum alkaline phosphatase activity. Owing to the small number of animals and lack of access to the original report, data from this study could not be considered in establishing an ADI.

In an 80-week carcinogenicity study in mice fed dietary concentrations of 0, 750 or 1500 ppm the NOAEL was 1500 ppm, equal to 155 mg/kg bw per day. There was no evidence of carcinogenicity, and no effects on body weight, mortality or clinical signs were seen.

In a 104-week carcinogenicity study in rats fed 0, 750 or 1500 ppm the NOAEL was also 1500 ppm, equal to 56 mg/kg bw per day. There was no evidence of carcinogenicity. As no clinical chemical or haematological parameters were evaluated in this study, the Meeting considered it inadequate for an evaluation of long-term toxicity.

In a two-generation reproductive toxicity study in rats fed dietary concentrations of 0, 300, 1000 or 5000/2000 ppm the NOAEL for parental toxicity was 1000 ppm, equal to 106 mg/kg bw per day. The NOAEL for filial toxicity was 2000 ppm, equal to 220 mg/kg bw per day. There were no adverse effects on reproduction.

In a study of teratogenicity in rats administered 0, 15, 50 or 150 mg/kg bw per day by gavage, the NOAEL was 50 mg/kg bw per day for both maternal toxicity and embryo-/fetotoxicity on the basis of reduced body-weight gain and minor skeletal defects, respectively. No teratogenic effects were observed.

In a study of teratogenicity in rabbits administered 0, 15, 45 or 135 mg/kg bw per day by gavage, the NOAEL was 45 mg/kg bw per day for maternal toxicity on the basis of body-weight loss and reduced food consumption. The NOAEL was 15 mg/kg bw per day for embryo-/fetotoxicity on the basis of minor skeletal defects. No teratogenic effects were observed.

Tecnazene can produce clastogenic effects *in vitro* but not *in vivo*. No mutagenicity was observed in bacteria. The Meeting concluded that tecnazene is not genotoxic.

An ADI was established on the basis of the NOAEL of 15 mg/kg bw per day in the 90-day study in dogs and on the embryo-/fetotoxicity seen in the teratogenicity study in rabbits. Owing to the lack of adequate data on the long-term toxicity of the compound, the Meeting applied a 1000-fold safety factor.

A toxicological monograph was prepared, summarizing the data received since the previous evaluation and containing relevant summaries from the previous monograph and monograph addenda on tecnazene.

TOXICOLOGICAL EVALUATION

Levels that cause no toxic effect

Mouse: 1500 ppm, equal to 155 mg/kg bw per day (80-week carcinogenicity study)

Rat: 500 ppm, equal to 45 mg/kg bw per day (90-day toxicity study)
1500 ppm, equal to 56 mg/kg bw per day (104-week carcinogenicity study)

Rabbit: 15 mg/kg bw per day (embryo-/fetotoxicity in a teratogenicity study)

Dog: 15 mg/kg bw per day (90-day toxicity study)

Estimate of acceptable daily intake for humans

0-0.02 mg/kg bw

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

1. One-year toxicity study in dogs.

2 Long-term toxicity study in rats.

RESIDUE AND ANALYTICAL ASPECTS

Tecnazene was reviewed by the JMPR in 1974, 1978, 1981, 1983, 1987 and 1989. Although CXLs exist for head lettuce and witloof chicory, the only use of tecnazene now supported by the manufacturer is for the post-harvest application of granular or dust formulations to potatoes as a sprout suppressant and fungicide.

A TMRL of 1 mg/kg was recommended for potatoes (washed before analysis) by the 1978 JMPR. Additional residue data were reviewed by the 1989 JMPR which recommended an MRL of 10 mg/kg for potatoes washed before analysis.

The 1989 Meeting noted that residues of tecnazene in the flesh of treated, uncooked potatoes would generally be less than 1 mg/kg and that further losses occurred during normal cooking, but drew attention to the high levels, up to nearly 100 mg/kg, that could be attained in the peel of treated potatoes.

Tecnazene has been extensively debated at the CCPR in 1990, 1991 and 1992, with several countries expressing reservations concerning the definition of the residue, the quality of the residue data, the interpretation of GAP and toxicological aspects.

Additional updated information on use patterns for tecnazene on potatoes, data on residues resulting from supervised trials, on the fate of residues in metabolism and processing, and on residues in food in commerce were provided for evaluation.

New, more detailed, studies of metabolism in the rat confirmed earlier studies and showed results comparable to those found in other species (rabbit, guinea pig and pigeon). Tecnazene was shown to be extensively metabolized and excreted in laboratory animals, mainly via glutathione conjugation.

The major routes of metabolism of tecnazene in stored potatoes involve both reduction to 2,3,5,6-tetrachloroaniline (TCA) and initial glutathione conjugation with subsequent catabolism.

The major component of the residue was tecnazene (64%); TCA and 2,3,5,6-tetrachlorothioanisole (TCTA) were minor components (<1%). A more significant (10%) multicomponent water-soluble fraction could be hydrolysed to 2,3,5,6-tetrachlorothiophenol and was apparently derived from initial glutathione conjugates. The water-soluble metabolites were similar to those in rats.

Peeling removed more than 90% of the residue from treated potatoes, and all methods of cooking reduced residue levels further. The extent of the loss of tecnazene on cooking depended on whether peeled or unpeeled potatoes were used, but was ≥20%.

Post-harvest residue trials were carried out in the UK in 1991 with potatoes treated according to GAP (116-135 g ai/tonne, nominal treatment rate 125 g ai/tonne). Samples were analyzed for tecnazene and the metabolites TCA and TCTA at 92-205 days after treatment (at normal store opening). Residues of TCA and TCTA were 0.02-0.55 mg/kg (average 0.13 mg/kg) and <0.01-0.18 mg/kg (average 0.059`mg/kg), respectively; residues of tecnazene ranged from 2.4 to 18 mg/kg (average 6.8 mg/kg). In treated tubers analyzed 42 days after treatment (42 days is the minimum post-treatment period for removal for use according to GAP) residues of TCA, TCTA and tecnazene, ranges and (means), were 0.017-0.07 (0.045), 0.01-0.12 (0.036) and 2.2-9.0 (6.5) mg/kg respectively.

In summary, ten supervised residue trials showed tecnazene residues from 2.4 to 18 mg/kg in potatoes treated and stored according to GAP, with an average of 6.8 mg/kg. Considerable variations are possible during application, during storage under varying conditions, and in the washing of tubers before analysis. From these considerations, the Meeting concluded that an MRL of 20 mg/kg would be required to cover residues of tecnazene in potato tubers resulting from the post-harvest treatment of potatoes for storage according to GAP, and recommended accordingly.

The Meeting concluded that the residue should be defined as "tecnazene", because the parent compound alone is a good indicator of the total residue and of use according to GAP.

Extensive retail monitoring data in the UK are available for tecnazene. In the most recent survey of 256 potato samples in 1991, tecnazene was not found (<0.01 mg/kg) in 55% of the samples and was ≤1 mg/kg in 95% of the samples. The highest tecnazene residue found was 5.5 mg/kg. TCA and TCTA were found in only about 10% of the samples, the highest levels being 0.5 mg/kg of TCA and 0.08 mg/kg of TCTA.

Potato metabolism and processing studies have shown that 90% of the terminal residues are in the tuber peel. Peels contained up to 47 mg/kg of total residues (66% as tecnazene). The Meeting noted that potato culls, waste, protein concentrates and bakery products were also used as livestock feeds.

No ruminant metabolism or lactating ruminant feeding studies were available. The Meeting was unable to estimate the possible transfer of residues to the meat or milk of cattle.

On the basis of the new residue data for the post-harvest use of tecnazene on potatoes the Meeting recommended an MRL of 20 mg/kg.

4.44 TEFLUBENZURON (190)

1-(3,5-dichloro-2,4-difluorophenyl)-3-(2,6-difluorobenzoyl)urea

Teflubenzuron is an insect growth regulator belonging to the benzoylurea group of compounds. It acts on the developmental stages of insect pests, primarily via ingestion and by interfering with chitin synthesis and the moulting process. It also has an ovicidal effect in some insects. Teflubenzuron was reviewed for the first time by the present Meeting.

TOXICOLOGY

In rats, teflubenzuron was absorbed only partially from the gastrointestinal tract, absorption being dose-dependent and saturable. Absorbed teflubenzuron was excreted mainly via the bile, urinary excretion representing only a minor route. Faecal excretion of absorbed and unabsorbed teflubenzuron represented the main route. There was no evidence of bioaccumulation in organs or tissues.

Teflubenzuron was eliminated largely unchanged in the faeces, although a number of unidentified minor metabolites were found. Hydroxylated metabolites of teflubenzuron were found in urine at low levels. 3,5-Dichloro-2,4-difluorophenylurea and its corresponding substituted aniline were observed in urine, indicating that cleavage of the benzoylurea moiety had occurred. Conjugates of these metabolites and the unconjugated 3,5-dichloro-2,4-difluorophenylurea were detected in bile.

Teflubenzuron has low acute oral, dermal and inhalational toxicity; it was more acutely toxic when administered by the intraperitoneal route. WHO has classified teflubenzuron as being unlikely to present an acute hazard in normal use.

In mice, rats and dogs given repeated doses in the diet, the major target organ was the liver. Pathological and clinical chemical findings of hepatotoxicity varied with species, dose and duration of dosing. The indicators of hepatotoxicity included effects such as increased activities of serum alanine and aspartate aminotransferases, alkaline phosphatase, lactate dehydrogenase and ornithine carbamoyl transferase, increased liver weights and hepatocellular necrosis, fatty changes, hypertrophy and hyperplasia. Haematological parameters generally remained unaltered by treatment.

In a 13-week toxicity study in mice fed levels of 0, 100, 1000 or 10,000 ppm, effects indicative of hepatotoxicity were observed at 1000 and 10,000. The NOAEL was 100 ppm, equal to 11.9 mg/kg bw per day. In a 28-day range-finding toxicity study and a 13-week toxicity study, rats were fed diets containing 0, 100, 1000 or 10,000 ppm. The NOAEL in both studies was 100 ppm, equal to 11.7 and 8.0 mg/kg bw per day respectively, on the basis of indications of hepatotoxicity. Two 13-week studies in dogs fed diets containing 0, 100, 1000 or 10,000 ppm or 0, 30 or 100 ppm teflubenzuron indicated an NOAEL of 100 ppm, equal to 4.1 mg/kg bw per

day, on the basis of focal gastritis in dogs treated at 1000 ppm in the first study. The NOAEL in the 13-week studies concurred with the NOAEL of 100 ppm, equal to 3.2 mg/kg bw per day, observed in a 52-week study in dogs in which liver weights were increased in males fed the highest level of 500 ppm.

Mice fed diets containing 0, 15, 75 or 375 ppm teflubenzuron for 18 months in a carcinogenicity study showed non-neoplastic hepatotoxicity at all doses. Changes observed in the livers of mice at the lowest dose were increased in incidence over that in controls but were not increased in severity. The lowest dose of 15 ppm, equal to 2.1 mg/kg bw per day, represented a lowest-observed-adverse-effect level (LOAEL). Histopathological investigations indicated an increased incidence of hepatocellular adenomas in males at 75 and 375 ppm in comparison with concurrent and historical control data. This tumorigenic potential in mice was considered not relevant to humans.

In a 120-week toxicity/carcinogenicity study, rats were fed diets containing 0, 20, 100 or 500 ppm teflubenzuron. The NOAEL was 100 ppm, equal to 4.8 mg/kg bw per day, on the basis of increased serum enzyme activities and liver weights in males. In a supplementary study, rats were fed diets containing 0, 2500 or 10,000 ppm for 111 weeks. No NOAEL could be assigned because non-neoplastic liver changes and increased serum enzyme activities were seen at both doses. There was no evidence of carcinogenicity.

In a two-generation (one litter/generation) study of reproductive toxicity in rats fed dietary concentrations of 0, 20, 100 or 500 ppm the NOAEL was 500 ppm, equal to 40 mg/kg bw per day, on the basis of lack of toxicity or effects on reproductive performance.

Two teratogenicity studies in rats treated by gavage showed no evidence of maternal toxicity, fetotoxicity or teratogenicity at doses up to either 250 or 1000 mg/kg bw per day. In a teratogenicity study in rabbits, there was no evidence of maternal toxicity, fetotoxicity or teratogenicity at doses of 0, 10, 50 or 250 mg/kg bw per day. A second teratogenicity study, in rabbits treated by gavage at 0 or 1000 mg/kg bw per day, showed no evidence of fetotoxicity or teratogenicity. Possible treatment-related findings were noted at necropsy in the livers of some dams treated at 1000 mg/kg bw per day. In another study, there was no evidence of liver enzyme induction in pregnant rabbits treated by gavage with doses of up to 500 mg/kg bw per day.

Teflubenzuron has been adequately tested for genotoxicity in a range of *in-vitro* and *in-vivo* assays. The Meeting concluded that it was not genotoxic.

It was concluded that an ADI could be allocated on the basis of the LOAEL of 15 ppm, equal to 2.1 mg/kg bw per day, in the 18-month carcinogenicity study in mice. A 200-fold safety factor was applied since no NOAEL was identified in this study.

A toxicological monograph was prepared summarizing the data that were reviewed at the present Meeting.

TOXICOLOGICAL EVALUATION

Levels that cause no toxic effect

Mouse: 100 ppm, equal to 11.9 mg/kg bw per day (13-week toxicity study)

Rat: 100 ppm, equal to 4.8 mg/kg bw per day (120-week toxicity/carcinogenicity study)
500 ppm, equal to 40 mg/kg bw per day (two-generation reproductive toxicity study)
1000 mg/kg bw per day (teratogenicity study, maternal and fetal toxicity)

Dog: 100 ppm, equal to 3.2 mg/kg bw per day (one-year toxicity study)

Rabbit: 1000 mg/kg bw per day (fetal toxicity in teratogenicity study)
250 mg/kg bw per day (maternal toxicity in teratogenicity study)

Lowest-observed-adverse-effect level

Mouse: 15 ppm, equal to 2.1 mg/kg bw per day (18-month carcinogenicity study)

Estimate of acceptable daily intake for humans

0-0.01 mg/kg bw

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

Further observations in humans

4.45 THIOPHANATE-METHYL (077)

[See also BENOMYL (069) and CARBENDAZIM (072)]

RESIDUE AND ANALYTICAL ASPECTS

Thiophanate-methyl was first evaluated in 1973 and has been reviewed on 4 other occasions. The 1988 JMPR initiated a re-evaluation of residues arising from the use of benomyl, carbendazim and thiophanate-methyl, all to be expressed as carbendazim, in response to concerns expressed at the 1988 CCPR (ALINORM 89/24, paras. 82-84). The 1989 CCPR requested that the recommendation for a group MRL for carbendazim in cereals should be replaced by recommendations for separate MRLs for individual crops, while at the 1992 CCPR (ALINORM 93/24, para. 105) several other MRLs were held at step 7B pending further review by the JMPR. Although some information was provided for the 1990 JMPR, that Meeting concluded that it would be premature to review the compounds until all of the required data became available and consideration was deferred to the 1992 JMPR. However, because of the work-load at that Meeting, the re-evaluation was again postponed until 1993. The data submitted for the 1990 and 1992 Meetings, together with additional data provided in 1993, have now been reviewed with particular attention to the information on GAP and some new residue data.

Information on GAP for thiophanate-methyl was provided from several sources, clearly showing the extensive applications of this fungicide. Post-harvest uses on pome and stone fruits and potatoes are registered in some countries. MRLs for pome and stone fruits were held at step 7B by the 1988 CCPR. The other 7B commodities, bean fodder, berries and other small fruits, cereal grains, citrus fruits, head lettuce, mushrooms, peppers, pineapples, sugar beet leaves or tops, and tomatoes, appear not to be subject to post-harvest treatments with thiophanate-methyl.

Data on residues in fruits were available for apples, pears, cherries, plums, grapes and strawberries, although most were obtained in the early 1970s. Of the Step 7B vegetables, limited data were given for head lettuce, mushrooms, peppers, sugar beet leaves, and tomatoes. An appreciable amount of data covered uses of thiophanate-methyl on cereals, the latest being obtained in 1983.

Some information was provided from Hungary on residues occurring in a few fruits and vegetables in commerce.

Any assessment of the residues from the use of thiophanate-methyl must also take into account those arising from benomyl and/or carbendazim, since all three pesticides yield carbendazim as the residue of prime importance. Recommendations are therefore dealt with under "carbendazim".

FURTHER WORK OR INFORMATION

Desirable

1. Residue data from supervised trials of thiophanate-methyl using currently registered post-harvest treatments of appropriate fruits and vegetables.

2. Residue data from supervised trials of thiophanate-methyl at the currently registered rates of use on lettuce, peppers, tomatoes and sugar beet.

3. Supporting residue data from supervised trials of thiophanate-methyl at currently registered rates of use on all appropriate crops for which CXLs are listed.

4.46 TOLCLOFOS-METHYL (191)

O-2,6-dichloro-*p*-tolyl *O,O*-dimethyl phosphorothioate

Tolclofos-methyl is an organophosphorus fungicide that is effective in the control of soil-borne fungus diseases caused by infection with Basidiomycete fungi such as *Rhizoctonia solani* and *Corticium rolfsii.* It is registered in a number of countries around the world mainly for the control of soil-borne diseases of potatoes but may also be used for the treatment of lettuce and certain other crops.

The compound was considered for the first time by the present Meeting.

TOXICOLOGY

Tolclofos-methyl is excreted rapidly in rats and mice, predominantly in the urine; less than 1% of the dose was retained in the tissues after seven days. In both species, metabolism occurred mainly by oxidation of P=S to P=O, oxidation of the *p*-methyl group, and cleavage of the P-O-aryl and P-O-methyl linkages. There are four main metabolites in mice, one of which is a glycine conjugate, and four in rats excreted as glucuronides.

Tolclofos-methyl was of low acute toxicity when administered by the oral, dermal, subcutaneous or intraperitoneal route. The overt signs of acute toxicity are not typical of an anticholinesterase, as no chromodaccryorrhoea, lachrymation or fasciculation was seen, although some inhibition of plasma, erythrocyte and brain cholinesterase was observed. WHO has classified tolclofos-methyl as unlikely to present an acute hazard in normal use.

In a nine-month toxicity study in which mice were fed tolclofos-methyl in the diet at 0, 10, 30, 100 or 3000 ppm the NOAEL was 100 ppm, equal to 12 mg/kg bw per day, on the basis of inhibition of brain cholinesterase and effects on body weight at 3000 ppm.

In a 32-34-day toxicity study in which rats were fed diets containing 0, 200, 1000, 5000 or 20,000 ppm the NOAEL was 1000 ppm, equal to 79 mg/kg bw per day, on the basis of inhibition of brain cholinesterase and increased relative kidney weight at 5000 ppm. In a 13-week toxicity study in which rats were fed diets containing 0, 100, 1000 or 10,000 ppm the NOAEL was again 1000 ppm, equal to 66 mg/kg bw per day, on the basis of effects on body, liver and kidney weights at 10,000 ppm. In a 28-week toxicity study in which rats were fed dietary levels of 0, 300, 1000, 3000 or 10,000 ppm the NOAEL was also 1000 ppm, equal to 65 mg/kg bw per day, on the basis of histopathological liver changes in females at 3000 ppm.

In a 26-week dietary study in dogs fed at 0, 200, 600 or 2000 ppm the NOAEL was 600 ppm, equal to 21 mg/kg bw per day, on the basis of reduced body-weight gain, an increased serum level of alkaline phosphatase and increased liver weight at 2000 ppm.

In a 52-week toxicity study in dogs given dietary concentrations of 0, 80, 400 or 2000 ppm the NOAEL was 400 ppm, equal 11 mg/kg bw per day, on the basis of increased liver weight (with hepatocytic hypertrophy), reduced body-weight gain and slight anaemia at 2000 ppm.

In a 104-week toxicity/carcinogenicity study in which mice were given dietary concentrations of 0, 10, 50, 250 or 1000 ppm the NOAEL was 50 ppm, equal to 6.5 mg/kg bw per day, on the basis of reduced brain cholinesterase and increased absolute and relative kidney weights at higher levels. There was no evidence of carcinogenicity.

A 122-129-week toxicity/carcinogenicity study was performed in which rats were given dietary concentration of 0, 100, 300 or 1000 ppm tolclofos-methyl. The NOAEL was 1000 ppm, equal to 41 mg/kg bw per day, on the basis of the absence of any significant findings. There was no evidence of carcinogenicity.

In a three-generation study (two litters/generation) in rats, tolclofos-methyl was given at dietary levels of 0, 100, 300 or 1000 ppm. The NOAEL was 1000 ppm, equivalent to 100 mg/kg bw per day, on the basis of the absence of any significant findings.

In a teratogenicity study in which rats were given 0, 5, 15 or 50 mg/kg bw per day of tolclofos-methyl by gavage, the NOAEL was 50 mg/kg bw per day on the basis of the absence of any significant findings. The study was not considered to be fully adequate because the highest dose tested was not maternally toxic. A similar study was conducted at levels of 0, 100, 300 or 1000 mg/kg bw per day. The NOAEL was 300 mg/kg bw per day on the basis of reduced body-weight gain in dams at 1000 mg/kg bw per day. There was no evidence of teratogenicity.

A teratogenicity study was conducted in rabbits given 0, 300, 1000 or 3000 mg/kg bw per day orally. The NOAEL for maternal toxicity was 300 mg/kg bw per day on the basis of lower body-weight gain in dams at 1000 mg/kg bw per day. There was no evidence of teratogenicity.

Tolclofos-methyl was studied in a wide range of tests for genotoxicity *in vivo* and *in vitro*. There was no evidence of genotoxicity.

Tolclofos-methyl did not cause delayed neuropathy in chickens.

The available observations in humans were considered by the Meeting but did not directly contribute to the estimation of an ADI.

An ADI of 0.07 mg/kg bw was established on the basis of an NOAEL of 50 ppm, equal to 6.5 mg/kg bw per day, in the 104-week toxicity/carcinogenicity study in mice, and a safety factor of 100.

A toxicological monograph was prepared summarizing the data that were reviewed at the present Meeting.

TOXICOLOGICAL EVALUATION

Levels that cause no toxic effect

Mouse: 50 ppm, equal to 6.5 mg/kg bw per day (104-week toxicity/carcinogenicity study)

Rat: 1000 ppm, equal to 41 mg/kg bw per day (122/129-week toxicity/carcinogenicity study)

Rabbit: 300 mg/kg bw per day (maternal toxicity in teratogenicity study)

Dog: 400 ppm, equal to 11 mg/kg bw per day (52-week toxicity study)

Estimate of acceptable daily intake for humans

0-0.07 mg/kg bw

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

Further observations in humans

RESIDUE AND ANALYTICAL ASPECTS

Tolclofos-methyl is an organophosphorus fungicide that is effective in the control of soil-borne fungus diseases caused by infection with Basidiomycete fungi such as *Rhizoctonia solani* and *Corticium rolfsii*. It is registered in a number of countries around the world mainly for the control of soil-borne diseases of potatoes but may also be used for the treatment of lettuce and certain other crops. It is usually applied as a seed-dressing and soil treatment shortly before sowing or planting. In the case of lettuce 2 or 3 post-planting applications may also be made.

The metabolism of tolclofos-methyl has been studied in rats, mice, goats and hens, as well as in cotton, peanut and sugar beet plants.

The identified residues are indicated as follows.

Parent compound: TM.
Oxidation products of 4-methyl group of parent:
alcohol TM-CH_2OH; aldehyde TM-CHO; acid TM-COOH.

Oxon: TMO.
Oxidation products of 4-methyl group:
alcohol TMO-CH_2OH; aldehyde TMO-CHO; acid TMO-COOH.

Demethyl-tolclofos-methyl (*O*-(2,6-dichloro-4-methylphenyl) *O*-methyl *O*-hydrogen phosphorothioate): DM-TM.
Oxidation products of 4-methyl group:
alcohol DM-TM-CH_2OH; aldehyde DM-TM-CHO; acid DM-TM-COOH.

Demethyl-oxon: DM-TMO.
Oxidation products of 4-methyl group:
alcohol DM-TMO-CH_2OH; aldehyde DM-TMO-CHO; acid DM-TMO-COOH.

Phosphorothiolate isomer of TM: SM-TM.
Phosphorothiolate isomer of DM-TM: DM-SM-TM.

Products from cleavage of P-O-aryl bond:
2,6-dichloro-4-methylphenol: PH-CH_3
2-chloro-4-methylphenol: DC-PH-CH_3
3,5-dichloro-4-hydroxybenzyl alcohol: PH-CH_2OH
3,5-dichloro-4-hydroxybenzaldehyde: PH-CHO
3,5-dichloro-4-hydroxybenzoic acid: PH-COOH

Rats of both sexes were given a single dose by oral intubation of a corn oil solution of 5

mg/kg bw of tolclofos-methyl labelled with ^{14}C uniformly in the phenyl ring. A second group of animals was dosed in the same way with 200 mg/kg bw. A third group was pre-treated with unlabelled tolclofos-methyl, administered daily for 14 consecutive days at the dose level of 5 mg/kg bw/day before administration of a single dose of the labelled compound 5 mg/kg/bw. In one experiment mice were given by oral intubation a single dose of a corn oil solution of 5 mg/kg bw of tolclofos-methyl labelled with ^{14}C in the 4-methyl group. Radiocarbon in the urine and faeces as well as $^{14}CO_2$ were monitored from 30 minutes after administration of labelled parent compound for a period of 7 days. Animals were slaughtered periodically for assay of the radioactivity in various tissues.

These studies gave similar results which indicated that the main routes of elimination of the residues were via the urine and faeces. More than 95% of the dosed radioactivity was excreted within 48 hours of administration. Within 7 days, 80-91% of the dose was excreted in the urine, 9-20% in the faeces and less than 1% in the expired air.

In a study of bile-cannulated rats, 6-12% of the dose was excreted in the bile, 47-60% in the urine and 24-42% in the faeces within 24 hours.

Total ^{14}C levels in most of the tissues reached maxima 2 hours after administration. They rapidly decreased, in proportion to the decline of residues in the blood, to less than 5% of the maximum level in each tissue 72 hours after administration.

Whole-body autoradiography showed that the radioactivity was primarily in the gastrointestinal tract, including the stomach, intestine, kidney and liver, in that order, 1 and 6 hours after administration. Only a low level of radioactivity was detected in the whole body 24 hours after administration. The tissue residues were less than 1% of the administered dose 7 days after administration. The small amounts of radioactivity remaining in the animals were primarily in the hair, fat, skin, red blood cells, liver and kidney.

No qualitative differences were observed between the sexes or the doses. The following major metabolites were found in the excreta of rats: DM-TMO (10-26% of the dosed ^{14}C), DM-TM-CH_2OH (12-25%), DM-TM-COOH (11-35%) and DM-TM (12-44%). In addition 10 minor metabolites were detected. Of these at least seven, including TM-COOH, PH-COOH, DM-TM and DM-TM-CH_2OH, were already present 2 hours after oral administration in the blood, liver and kidney.

In the study of bile-cannulated rats, most of the radioactivity excreted into the bile within 24 hours after administration was in the form of polar metabolites, the major ones being DM-TM-CH_2OH and PH-CH_3 glucuronide. Except for the formation of conjugates (glucuronic acids in rats and conjugation of the resulting acid with glycine in mice), the metabolites in rats and mice were essentially the same.

[^{14}C]Phenyl-labelled tolclofos-methyl was administered daily by capsule to a lactating goat of approximately 40 kg weight for four consecutive days. The dosage was equivalent to approximately 250 ppm in the diet. Urine and faeces were collected separately at 7, 24, 48, 72 and 79 hours after the start of the study. Milk was collected twice daily and the animal was slaughtered 7 hours after the last of the four doses.

The urine was the principal pathway of elimination and accounted for 26% of the total

applied dose by the end of the study at 79 hours, when the total radioactivity amounted to 485 mg/kg TM equivalent. Faecal elimination accounted for only 0.6% of the dose. The concentration of radioactivity in the faeces continuously increased during the study up to 143 mg/kg at 79 hours. The results indicated that passage of the administered material through the gut was slow and that the low recovery of administered radioactivity was probably due to retention in the gut contents.

In the urine (average of 24 and 79 hour samples) no parent material was found and the various fractions identified in the extracts, including some minor unknowns, accounted for 95.5% of the total radioactivity. The most important metabolite was the demethylated oxon DM-TMO (44.8%), which, together with its alcohol and acid derivatives, accounted for 55% of the total. The next most important group comprised the phenolic alcohol, aldehyde and acid (14.2, 2.8 and 8.9% respectively), which together accounted for nearly 26%. The remaining radioactivity was distributed among 14 other products of which 5 were not identified.

In the faeces (average of 24 and 79 hour samples) 60% of the extracted radioactivity was identified. More than 28% was accounted for by unchanged parent. Otherwise, the metabolite pattern was similar to that in the urine.

There was very little elimination of radioactivity in the milk, which accounted for 0.001% or less of the applied dose. Concentrations in whole milk reached 0.87 mg/kg tolclofos-methyl equivalent by the end of the study. In the milk sample taken at 48 hours, 65% of the total radioactivity was in the acetonitrile fraction. The rest of it was either extractable in hexane (9.3%), remained in the aqueous phase (3.1%) or remained unextracted in the solids (18.3%). The radioactivity in the acetonitrile was fractionated. The most important metabolites found were the oxon, TMO (42.4%) the carboxylic acid derivative, DM-TM-COOH (6.8%), and the *p*-hydroxybenzoic acid (PH-COOH) (9%).

Just under 0.6% of the applied dose was retained in the tissues with the highest levels in liver and kidney (3.0 and 4.3 mg/kg respectively). The muscle contained 0.2 mg/kg total residue. The major metabolites and their percentage of the total radioactivity in the kidney were TMO-CH_2OH (11%), TMO-COOH (21.2%), PH-COOH (21.1%). Two unknowns and two demethylated metabolites made up the rest of the organo-extractable radioactivity which amounted to 67.4% of the total. The rest of the radioactivity in the kidney consisted of methanol- and water-extracted material (37.5 and 6.3% respectively) and unextracted matter (3.8%), giving a total recovery of 114.9%. In the liver, just over 50% of the total radioactivity was in the extracted fractions. The four phenyl derivatives, (PH-CH_3, PH-Ch_2OH, PH-CHO, and PH-COOH) together accounted for 39.5% of the total radioactivity with a further 11% attributed to an unknown. The rest of the liver radioactivity consisted of methanol- and water-extractable residues (20.6%) and unextractable material (29.8%) in the solids. Radioactivity in the other tissues (fat and muscle) was too low for separation and identification.

[U-^{14}C]Phenyl-labelled tolclofos-methyl was administered orally for four consecutive days to 3 laying hens which were killed 7 hours after the last dose. This dosage was equivalent to approximately 167 ppm in the diet but was administered each day as a single dose.

The administered radioactivity was eliminated rapidly in the excreta. Over 71% of the first dose was eliminated in the first 7 hours and 87% within 24 hours. Equilibrium between excretion and intake was reached within 3 days. Unchanged tolclofos-methyl accounted for 36%

of the residues in the excreta. The major metabolites identified were PH-COOH (23%), TM-CHO (9%), TMO-COOH (7%) and TM-COOH (3%). DM-TMO-CH_2OH, PH-CH_2OH, PH-CH_3, PH-CHO, TMO, DM-TM and DM-TMO were identified as only minor metabolites.

Residues in egg yolks were 0.37 mg/kg tolclofos-methyl equivalents at 72 hours and 0.27 mg/kg at 79 hours. Corresponding levels in the white rose to a maximum of 0.07 mg/kg. The retention of residues in body tissues was low. The highest residues occurred in the fat, kidney and liver (0.23%, 0.11% and 0.2% of the total administered dose or 1.0, 6.0 and 3.4 mg/kg respectively). The levels expressed as mg/kg total residue in other tissues were heart 0.18, muscle 0.11, lung 0.44, spleen 0.12 and ovary 0.47.

In the liver, about 20% of the radioactivity was in the form of free metabolites with a further 8% liberated by acid and base hydrolysis. The unchanged parent was not detected, and the only identified metabolite was TM-CHO (3.4% of the total radioactivity in the liver). In the kidney the only metabolite identified was PH-COOH, which accounted for 9% of the total radioactivity. There were 8 other metabolites but further identification was not possible owing to the small amounts present.

In eggs and muscle the levels of radioactivity were too low to permit the identification of individual components.

The pattern of metabolism in rats, mice, goats and hens was essentially similar, the identified metabolites were the same and the parent compound was metabolized and excreted rapidly with less than 1% of the administered dose retained in various tissues after 3-7 days. The identified and quantified metabolites show that the major biotransformation reactions in animals are oxidation to the oxon and related derivatives, oxidation of the 4-methyl group to the alcohol and acid, cleavage of the P-O-aryl and P-O-methyl linkages, and conjugation of the resulting acids and phenols.

Phenyl-labelled tolclofos-methyl was applied to the leaves of six-month old sugar beet plants in pots in a greenhouse. Three days after the treatment only 40% of the applied radioactivity was recovered in the treated leaves, and of this 15% was in the surface wash and 23% in the extract from the macerated leaves. The radiocarbon on and in the treated leaves gradually decreased thereafter, accounting for 0.3% and 4.5% of the applied ^{14}C, respectively, 50 days after treatment. TM accounted for 98%, 66% and 33% of the surface residue at 3, 35 and 50 days. TMO was not present above 0.1% during the study period. The methanol/chloroform extract contained several metabolites in varying proportions at various intervals after treatment. After 2 weeks and later DM-TMO was the major metabolite, reaching a maximum of 7.8% of the applied dose after 14 days. DM-TMO represented 4.5% and 62% of the total extractable residue at 14 and 50 days respectively. In addition TM, TMO-COOH and DM-TM were present at 11%, 8.8% and 4.4% of the total extractable residue at 50 days. Other metabolites (TMO, TM-CH_2OH, TMO-CH_2OH, PH-CH_3, PH-CH_2OH were present in amounts of $\leq$0.1%. The radiocarbon in the untreated shoots amounted to 0.3%, 1.3%, 1.6% 1.5% and 1.0% of the applied dose 3, 7, 21, 35 and 50 days after application, indicating that there was little translocation within the plant.

The uptake of residues by sugar beet plants following soil treatment was very small, reaching a maximum of 2.5% of the radioactivity applied to the soil after 14 days. Of this, 1.5% was in the roots and 1.0% in the tops and most of the residue (1.7%) was the parent compound. By the end of the study, the total radioactivity recovered from the plants had fallen to 1.2% of

that applied. Residues in the soil fell from 62.7% of the applied radioactivity at 3 days to 46.5% by the end of the study at 75 days.

Cotton plants were grown in field conditions in soils which had been treated at 5.2 or 15.7 kg/ha with labelled tolclofos-methyl. In plants grown on the soils treated with 5.2 kg/ha no radioactivity was detected in the bolls, squares, seed or leaves above the limits of determination which were 0.004, 0.004, 0.003 and 0.008 mg/kg respectively. Small amounts were found in the stems (0.008-0.01 mg/kg). In plants from soils treated at the higher rate, the levels of total radioactivity in the bolls, squares and seed were still below the limits of determination but trace amounts were found in the leaves (0.015 mg/kg) and stems (0.015-0.026 mg/kg at different heights). The residue levels were too low to allow the identification of any metabolites.

A study on peanuts was carried out in parallel with the study on cotton. The treatments included a foliar application (4.2 and 22 mg ai/plant) 75 days after soil treatment. The extraction of the leaves was preceded by a solvent wash to determine surface deposits. The radioactive residues on the surface of the leaves at maturity from the high treatment rate consisted of TM 2.3%, TM-CH_2OH 6.9%, PH-CH_2OH 14.6%, and polar conjugates 69.6%. In the leaves the main residues were PH-CHO 15.7%, TM-CH_2OH 5.2%, PH-CH_3 3.7%, TMO 3.7% and three unidentified components 23.1%. The parent compound was not detected. Between 10 and 18% of the extracted residue remained at the origin on TLC separation and this was hydrolysed with cellulase to liberate PH-CH_2OH (65%) and TM-CH_2OH (29%) with smaller amounts of TMO, PH-CHO and TMO-CH_2OH. The level of radioactivity in the nuts was too small to identify the residues. The residues in the hulls included TM (5.8%), DM-TMO (9.8%) and two unknowns (12.1 and 5.5%). About 67% of the radioactivity remained at the origin on the TLC plate.

The TMO and TM-CH_2OH residues were determined in wheat and soya grown at two locations in Japan. In wheat the product was applied as a 50% wettable powder at 1.5 kg ai/ha, while the soya beans were treated with either a 50% wettable powder at 15 kg ai/ha or a 20% dust at 60 kg ai/ha. The PHIs were 275-287 days for wheat and 14-30 days for soya beans. No residues of TMO (<0.005 mg/kg) or TM-CH_2OH (<0.01 mg/kg) could be detected in any of the samples. The parent compound was not detectable in wheat (<0.005 mg/kg), but in soya beans its concentration ranged from <0.005 to 0.06 mg/kg at 14 days and from 0.006 to 0.036 mg/kg at 30 days.

In summary, the plant metabolism studies indicated that the uptake of residues from soil and their translocation within the plants were limited, the same metabolites were formed in plants as in animals, the parent tolclofos-methyl was a major residue component, the residues declined rapidly, and volatilization was an important factor in the loss of surface residues.

The environmental fate of tolclofos-methyl was extensively studied in various soils under aerobic and partially or completely anaerobic conditions in the laboratory, and under natural field conditions with the labelled and unlabelled compound.

Tolclofos-methyl labelled in the aryl ring was incubated with several soils of widely varying composition. The soils were fresh and the test material was added at rates ranging from 0.38 mg/kg to 26 mg/kg. The soil moisture was kept at the same level during incubation which was in the dark at temperatures from 15°C to 25°C for 30 to 365 days. Samples were taken periodically and analyzed for extractable metabolites, bound residues and liberated volatiles. The unextracted radioactivity was determined by combustion analysis. The total radiocarbon

recovered was generally above 90%.

The estimated half-lives were between 9.3 and 60 days under aerobic and up to 80 days under anaerobic laboratory conditions. In field studies the total residue level in the top 7.5 cm layer of the soils declined to about 17% and 7% of the initial concentration within 75 and 150 days after application. Under field conditions the calculated half-lives in the soil ranged from about 7 to 39 days.

The pattern of degradation did not differ greatly between the soils in spite of their widely differing compositions. Altogether 27 degradation products were detected and 12 identified in the extracts of soils incubated under aerobic conditions. Of these TMO (0.1-1.2%), DM-TMO (0.1-1.8%), PH-CH_3 (0.1-6.3%) and DM-TM (0.3-18%) were the major products. In addition, TM-CH_2OH, TMO-CH_2OH, TM-COOH, TMO-COOH, DM-TM-COOH, PH-CH_2OH, SM-TM and PH-COOH were detected at less than 1% of the added dose. They were present in such small amounts as to be regarded as only intermediates in the mineralization of the residues. It is significant that the degradation products and the total residues reached a maximum at some point during the study and were all decreasing in the later stages.

In summary, the main reactions in the degradation of residues under aerobic conditions were oxidation of the phosphorothioate to phosphate, de-esterification with the loss of either a methyl or the aryl group and oxidation of the *p*-methyl on the aryl ring to CH_2OH and eventually to COOH.

The bound ^{14}C amounted to over 33% of the applied dose 60 days or more after the soil treatment. The bound residues were mainly in the fulvic and humic acid fractions, in proportions which changed with time.

Volatilization played an important role in the dissipation of residues. In most of the studies the volatile products accounted for over 35% of the initial activity. The parent compound, CO_2 and other volatile products continued to be liberated up to the end of the studies. The main volatile products, apart from CO_2 and the parent compound, were 2,6-dichloro-4-methylanisole and the corresponding free phenol which accounted for 5.6 and 1.7% of the applied radioactivity respectively. When the compound was incorporated into the soil the loss by volatilization decreased below 10%.

The results indicated that mineralization and volatilization were the main routes of loss, with some of the unextractable radioactivity probably incorporated into the carbon pool of the soil organic matter.

Sterile conditions reduced the rates of degradation of the parent compound in the soil and the mineralization of the metabolites, which suggests that biochemical processes play an important part in the degradation process. Since oxidation reactions are responsible for some of the steps in the pathway, degradation is also slowed by anaerobic conditions although less so than by sterilization.

Under anaerobic conditions 4-methylphenol, 2-chloro-4-methylphenol and four minor unknowns were found in the soil; they were not detected under aerobic conditions. DM-TM, DM-TMO and PH-CH_3 were the major compounds of the 26 products detected, reaching maximum ranges of 4.8-31%, 1-2.6% and 2.6-3.7% of the added doses respectively. The other

compounds identified were the same as under aerobic conditions.

In a soil/water system under anaerobic conditions the main products identified in the aqueous phase, apart from tolclofos-methyl itself, were DM-TM and smaller amounts of 2-chloro-4-methylphenol (DC-PH-CH_3), 4-methylphenol and PH-CH_3. DM-TM and DC-PH-CH_3 reached a maximum at about 60 days but their subsequent rapid decline showed them to be only transient. The total radioactivity in the aqueous phase increased until day 62 and the fact that this increase was approximately parallel to the increase of DM-TM suggested that the migration of DM-TM from the soil to water accounted for much of the increased radioactivity in the aqueous phase.

The appearance of 4-methylphenol is of special interest as it indicates a dechlorination pathway in the degradation of the aromatic moiety. It rose to a maximum after 50-60 days and declined thereafter to undetectable levels over a year. 4-Methylphenol was degraded under these conditions to carbon dioxide and methane.

In field trials the degradation was qualitatively similar to that observed under laboratory conditions. Practically all of the extractable radioactivity in the soil (82-94%) was still in the form of the parent at both 75 and 150 days. The rest was mainly TMO with some TM-CH_2OH and small amounts of unknowns. Extractable radioactivity constituted between 60 and 70% of the total during the sampling period of 75 to 150 days.

Photodegradation was studied with thin layers of various soils. Exposure to sunlight increased the dissipation of residues on dry soil surfaces, but had no effect when the soil was wet. Volatilization played an important role in the loss. The products detected in soils exposed to sunlight and in those kept in the dark were the same. The main differences between the light and dark series were the greater production of TMO and DM-TMO and greater volatilization in the light series.

Studies on adsorption to the soil indicated that tolclofos-methyl is strongly adsorbed by typical agricultural soils.

The leaching behaviour of the parent compound and aged residues was studied in several soils. The residues generally remained in the top layer of the soil columns. In a detailed study on a sandy loam soil with low organic matter content, about 75% of the aged radioactivity in the soil could be extracted before leaching. Of this, some 48% was unchanged parent and 17% was DM-TM with eight other components accounting for a further 9.6%. An additional 8.7% was accounted for by bound residues. About 20.3% of the applied radioactivity was found in the eluate, in which no parent compound was detectable and DM-TM amounted to about 99.5% of the residue. Only 0.3% of the DM-TM originally in the treated soil remained in the column. Only about 6% of the parent and other residues moved below the top 5 cm of the untreated soil, even under the intensive leaching conditions of the study.

In field trials only trace levels of residues reached a depth of 15-20 cm, and it was calculated that after 75 days, 90% of the radioactivity remained in the treated top 7.5 cm. Radioactivity was not detected outside the treated disc, indicating that lateral migration was also negligible.

In summary, it may be concluded from these studies that tolclofos-methyl is strongly

adsorbed to the soil and the majority of the residues remain in the top soil. It is degraded readily in typical agricultural soils, and although a number of degradation products have been identified the ultimate fate is complete mineralization without accumulation of either the parent or any of its identified degradation products. It is unlikely that either parent or degradation products would be present in soil in subsequent years or would reach ground water when tolclofos-methyl has been applied according to GAP.

The environmental fate in water/sediment systems was studied in sterile and natural waters and sediments. The Ph ranged between 5 and 9 at temperatures from 20°C to 60°C. Half-lives (days) in buffer solutions at the three pH values of 5, 7 and 9 were 139 and 12.7, 417 and 21.4 and 238 and 19.3 at 22°C and 40°C respectively. At 25°C in the pH range 5-9, the parent compound amounted to about 63-73% of the total residue, while the main degradation products and their proportions were DM-TM (11.2-23.1%), TMO (7.7-12.0%), and PH-CH_3 (0.4-0.6%). The effect of pH on both the rate of hydrolysis and the products formed was very limited. In natural water and sediments the degradation pattern was the same but the rate of degradation was faster. About 42-52% of the applied dose was present as the parent compound and the proportion of degradation products was higher following 4 weeks incubation at 20°C. A study on the further degradation of DM-TM under similar conditions indicated that although degradation was slower than in the case of the parent compound, mineralization occurred as shown by the production of CO_2.

The degradation of the parent compound as well as DM-TM was much slower in sterile water.

Photodegradation studies in sterile natural waters and buffer solutions revealed that tolclofos-methyl is not particularly light-sensitive. Although it has a weak absorption band around 290 nm, its main absorption occurs at about 215 nm, beyond the range of natural sunlight. Under exposure to sunlight the half-lives decreased to about half the values obtained in the dark. However in aqueous acetone solution (the acetone acting as a photosensitizer) the half-life of tolclofos-methyl was decreased about fifty-fold by irradiation.

The analytical methods for the parent compound are based on extraction with solvent mixtures and clean-up by passage through either a silica gel or Florisil column, or less frequently by repeated partitioning. The residues are determined by GLC using either a flame-thermionic or an electron-capture detector. Recoveries were generally above 90%, and the limits of determination ≤0.01 mg/kg. The methods for TMO, TM-CH_2OH and PH-CH_3 are basically similar to those for the parent compound except that GLC conditions are modified and some differences in solvent treatment are needed for PH-CH_3.

The residues of the parent compound did not show any degradation in potatoes stored in a deep-freeze for 3 months.

Numerous field trials have been conducted in Australia, Germany, Greece, Denmark, Poland and the UK. Tolclofos-methyl was applied as a dust, SC and WP formulations for the seed treatment of potatoes within recommended and at higher rates. In 73 seed treatments at maximum recommended rates 95% of the residues were at or below 0.1 mg/kg and 98% at or below 0.2 mg/kg, with only one value of 0.21 mg/kg above 0.2 mg/kg. This residue was found in a study in the UK where seed was treated with 25% SC at the maximum rate of 250 g/t. The residues from soil treatments before planting were lower.

The Meeting estimated a maximum residue level of 0.2 mg/kg for potato.

Supervised trials with lettuce were performed in Italy, The Netherlands and the UK, applying EC, WP and dust formulations within recommended and at higher rates. The treatments, in 52 trials, were carried out before and after planting. 90% of the residues were below 0.2 mg/kg and 98% below 1 mg/kg. A single higher value (1.56 mg/kg) was obtained from pre-emergence soil treatments with recommended rates in the UK.

In view of the continuous distribution of residues from 0.28 to 1.56 mg/kg in the UK trials, the Meeting estimated a maximum residue level of 2 mg/kg for lettuce.

Radishes were grown in soil treated at recommended and higher rates in France and The Netherlands. The residues from the trials according to GAP ranged from <0.01 to 0.06 mg/kg.

The Meeting estimated a maximum residue level of 0.1 mg/kg for radish.

In supervised trials reported from Norway on cauliflower, Chinese cabbage, kohlrabi, onions and turnips the residues were below the limit of determination (0.05 mg/kg) in the harvested crops. In carrots residues ranged from <0.02 to 1.6 mg/kg. As no GAP has been established in Norway and the reports did not specify the mode of application, the results could not be evaluated.

Several potato samples were analyzed whole and after peeling. The residues were concentrated essentially in the peel. Starch prepared from potato peel contained less than 1% of the residues.

Analysis of food commodities moving in commerce in The Netherlands and Sweden indicated that measurable residues occurred in beans, carrots, celeriac, cabbages, cucumbers, potatoes, radishes and spinach. Detectable residues in lettuce occurred in 102 of 140 samples analyzed in The Netherlands and 20 of 76 samples in Sweden. With one exception in The Netherlands where >10 mg/kg was measured in one sample, the residues in lettuce were below 1 mg/kg.

In view of the recommended uses of the compound and the low residues in treated crops, the Meeting concluded that no residues would occur in food of animal origin when tolclofos-methyl is used according to GAP.

Recommendations for MRLs are shown in Annex I.

FURTHER WORK OR INFORMATION

Desirable

A metabolism study in potatoes.

6. FUTURE WORK

The following items should be considered at the 1995 or 1996 Meeting.
The compounds listed include those recommended for priority attention by the 26th or earlier Sessions of the CCPR, as well as compounds scheduled for re-evaluation in the CCPR periodic review programme.

6.1 1995 Meeting (tentative)

Toxicological evaluation

New compounds

Chlloropropham
Fenarimol
Fenpyroximate
Haloxyfop

Periodic review compounds

Benomyl (069)
Carbendazim 072)
Cartap (097)
Fenthion (039)
Parathion (058)
Parathion-methyl (059)
Piperonyl-butoxide (062)
Quintozene (064)
Thiophanate-methyl (077)

Other evaluations

Captan (007)
Ethephon (106)
Flusilazole (165)
Folpet (041)
Iprodione (111)
Vinclozolin (159)

Residue evaluation

New compounds

Chlorpropham
Fenarimol
Fenpropimorph
Fenpyroximate
Haloxyfop
Metiram

Periodic review compounds

Cartap (097)
Fenthion (039)
Quintozene (064)

Other evaluations

Azinphos-methyl (002)
Bifenthrin (178)
Buprofezin (173)
Dithianon (180)
Metalaxyl (138)
Parathion (058)
Penconazole (182)
Triadimefon (133)

6.2 1996 Meeting (tentative)

Toxicological evaluation

New compounds

Flumethrin
Tebufenozide

Periodic review compounds

Carbaryl (008)
Carbofuran (096)
2,4-D (020)
Dimethoate (027)
Formothion (042)
Dodine (084)
Ferbam
Guazatine (114)
Maleic hydrazide (102)
Mevinphos (053)
Omethoate (055)*
Triforine (116)
Ziram

Residue evaluation

New compounds

Flumethrin
Tebufenozide
Teflubenzuron

Periodic review compounds

Chlorfenvinphos (014)
Dimethoate (027)
Formothion (042)
Ferbam
Omethoate (055)*
Guazatine (114)
Phosmet (103)
Thiram
Triforine (116)
Ziram

Other Evaluations

Propoxur (075)

* The 26th (1994) Session of the CCPR was informed (ALINORM 95/24, para 139) that the manufacturer had indicated that omethoate was no longer supported.

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CORRECTIONS TO REPORT OF 1993 JMPR

Additions and changes are underlined. Minor typographical errors are not included. Page numbers refer to the English edition of the report.

Page 24, para 6, line 5.

Change "...0.05 mg/kg carbosulfan and 0.2 mg/kg for the sum of..."

to "...0.05 mg/kg carbosulfan and 0.4 mg/kg for the sum of..."

Page 44, para 8, line 3.

Change "Half-lives at 30°C determined at pH 1, 5, 7, 9 and 13 are of the order 74, 50, 18, 16 and 0.65 hours..."

to "Half-lives at 30°C determined at pH 1, 5, 7, and 9 were 74, 50, 18, and 16 hours..."

Page 137 (Annex I), Ethephon, Note, line 3.

Change "...scheduled for residue evaluation in 1984..."

to "...scheduled for residue evaluation in 1994..."

E	Extraneous Residue Limit (ERL).
F following recommendations for milk and milk products	The residue is fat-soluble and MRLs for milk and milk products are derived as explained in the introduction to Part 2 of the Guide to Codex Maximum Limits for Pesticide Residues and to Volume II of the Codex Alimentarius.
(fat) following recommendations for meat	The recommendation applies to the fat of the meat.
Po	The recommendation accommodates post-harvest treatment of the commodity.
PoP following recommendations for processed foods (classes D and E in the Codex Classification)	The recommendation accommodates post-harvest treatment of the primary food commodity.
T following ADIs	The ADI is temporary, and due for re-evaluation in the year indicated.
T following MRLs	The MRL is temporary, irrespective of the status of the ADI, until required information has been provided and evaluated.
V following recommendations for commodities of animal origin	The recommendation accommodates veterinary uses.
W in place of an MRL	The previous recommendation is withdrawn.

If a recommended MRL is an amendment, the previous value is also recorded. The absence of a figure in the "Previous" column indicates that the recommendation is the first for the commodity or group concerned.

The table includes the Codex Classification Numbers (CCNs) of both the compounds and the commodities listed, to facilitate reference to the Guide to Codex Maximum Limits for Pesticide Residues and other Codex documents.

Commodities are listed in alphabetical order. This is a change from previous practice where commodities were listed in the order of the "Types" in the Codex Classification of Foods and Animal Feeds, and in alphabetical order within each Type.

The change has been made to facilitate checking and comparison with the CCPR Tables of MRLs, which are in alphabetical order.

PART 1. ACCEPTABLE DAILY INTAKES (ADIs) AND MAXIMUM RESIDUE LIMITS (MRLs)

Pesticide (Codex ref. No.)	ADI (mg/kg bw)	Commodity		Recommended MRL or ERL (mg/kg)	
		CCN	Name	New	Previous
Abamectin	0.0002	FB 0275	Strawberry	0.02	-
(177)		Residue: sum of avermectin B_{1a}, avermectin B_{1b} and Ä-8,9 isomer of avermectin B_{1a} Notes Previous ADI 0.0001 mg/kg bw			
Acephate	0.03	VB 0400	Broccoli	W	5
(095)		VB 0402	Brussels sprouts	W	5
		VB 0041	Cabbages, Head	W	5
		VB 0404	Cauliflower	W	5 T
		FC 0001	Citrus fruits	W	5 T
		VO 0448	Tomato	W	5 T
		Residue: acephate			
Aldicarb **	0.003	FI 0327	Banana	W	0.5
(117)		GC 0640	Barley	0.02	-
		AS 0640	Barley straw and fodder, dry	0.05	-
		VD 0071	Beans (dry)	0.1	0.1
		VB 0402	Brussels sprouts	0.1	0.1
		FC 0001	Citrus fruits	0.2	0.2
		SB 0716	Coffee beans	0.1	0.1
		SO 0691	Cotton seed	0.1	0.1
		OR 0691	Cotton seed oil, edible	0.01*	-
		FB 0269	Grapes	0.2	-
		GC 0645	Maize	0.05	0.05
		AF 0645	Maize forage	0.5	5
		AS 0645	Maize fodder	0.5	-
		MM 0095	Meat	0.01*	0.01*
		ML 0106	Milks	0.01*	0.01*
		VA 0385	Onion, Bulb	0.1	0.05*
		SO 0697	Peanut	0.02	0.05*
		OR 0697	Peanut oil, edible	0.01*	-
		TN 0672	Pecan	1	0.5
		VR 0589	Potato	0.5 T	0.5
		GC 0651	Sorghum	0.1	0.2

Pesticide (Codex ref. No.)	ADI (mg/kg bw)	Commodity		Recommended MRL or ERL (mg/kg)	
		CCN	Name	New	Previous
		AS 0651	Sorghum straw and fodder, dry	0.5	0.5
		VD 0541	Soya bean (dry)	0.02*	0.02*
		VR 0596	Sugar beet	0.05*	0.05*
		AV 0596	Sugar beet leaves or tops	1	1
		GS 0659	Sugar cane	0.1	-
		SO 0702	Sunflower	0.05*	-
		VR 0508	Sweet potato	0.1	0.1
		GC 0654	Wheat	0.02	-
		AS 0654	Wheat straw and fodder, dry	0.05	-
		Residue: sum of aldicarb, its sulphoxide and its sulphone, expressed as aldicarb.			
Azocyclotin (129)	0.007	Note previous ADI 0.001 mg/kg bw			
Benomyl (069)	0.02	Residue: carbendazim Note Residues of benomyl are covered by the recommendations for carbendazim (see below)			
Bentazone	0.1	GC 0640	Barley	0.1	0.05*
(172)		VD 0561	Field pea (dry)	1	0.05*
		GC 0645	Maize	0.2	0.05*
		AS 0645	Maize fodder	0.2	3
		GC 0647	Oats	0.1	0.05*
		GC 0650	Rye	0.1	0.05*
		GC 0651	Sorghum	0.1	0.05*
		GC 0654	Wheat	0.1	0.05*
		Residue: Pant materials: sum of bentazone, 6-hydroxybentazone and 8-hydroxybentazone, expressed as bentazone. Animal materials: sum of bentazone and 2- amino-*N*-isopropylbenzamide, expressed as bentazone.			
Captan	0.1	FP 0226	Apple	10	25 T
(007)		FB 0020	Blueberries	20	20 T
		FS 0013	Cherries	20	-
		FB 0269	Grapes	20	-
		FS 0245	Nectarine	5	-
		FS 0247	Peach	15	15 T
		FP 0230	Pear	10	25 T
		FS 0014	Plums (including Prunes)	5	-
		FB 0275	Strawberry	15	20 T
		VO 0448	Tomato	2	15 T

Pesticide (Codex ref. No.)	ADI (mg/kg bw)	Commodity		Recommended MRL or ERL (mg/kg)	
		CCN	Name	New	Previous
		Residue: captan			
Carbendazim	0.01	FS 0240	Apricot	0.1 B[1]	10 Po
(072)		GC 0640	Barley	0.1 C,Th	0.5[2]
		AL 0061	Bean fodder	W	50 C
		FB 0018	Berries and other small fruits	1 B,Th	5
		VR 0577	Carrot	W C	5 Po
		GC 0080	Cereal grains	W B,C,Th	0.5
		FS 0013	Cherries	2 Th	10 Po
		FC 0001	Citrus fruits	W	10 Po B,C,Th
		VL 0482	Lettuce, Head	5 Th	5
		VO 0450	Mushrooms	1 Th	1
		FS 0245	Nectarine	2 B	2
		GC 0647	Oats	0.1 C	0.5[2]
		FS 0247	Peach	2 B	10 Po
		VO 0051	Peppers	0.1 Th	5
		FI 0353	Pineapple	W	20 Po B
		FS 0014	Plums (including Prunes)	0.5 Th	2 Po
		FP 0009	Pome fruits	2 B,C,Th	5 Po
		GC 0649	Rice	W B,C,Th	0.5[2]
		GC 0650	Rye	0.1 C,Th	0.5[2]
		AV 0596	Sugar beet leaves or tops	5 B,Th	10
		VO 0448	Tomato	0.1 Th	5
		GC 0654	Wheat	0.1 B,C,Th	0.5[2]
		Residue: carbendazim Notes [1]Source of data: benomyl; C carbendazim; Th thiophanate-methyl [2]Group MRL for Cereal grains			
Chlorfenvinphos ** (014)	0.0005	Note previous ADI 0.002 mg/kg bw			
Chlorpyrifos-methyl (090)	0.01	GC 0649	Rice	10 Po	0.1
		Residue: chlorpyrifos-methyl			
Chlormequat ** (015)	No ADI	Notes ADI withdrawn (previously 0.05 mg/kg bw). Estimated maximum residue levels recorded as Guideline Levels: see part 2			
Clethodim *	0.01	VD 0071	Beans (dry)	0.1	-
(187)		MO 1280	Cattle, kidney	0.1	-
		MO 1281	Cattle, liver	0.1	-

Pesticide (Codex ref. No.)	ADI (mg/kg bw)	Commodity		Recommended MRL or ERL (mg/kg)	
		CCN	Name	New	Previous
		MM 0812	Cattle meat	0.05*	-
		ML 0812	Cattle milk	0.05*	-
		PE 0840	Chicken eggs	0.05*	-
		PE 0840	Chicken meat	0.05*	-
		SO 0691	Cotton seed	0.5	-
		OC 0691	Cotton seed oil, crude	0.1	-
		OR 0691	Cotton seed oil, edible	0.05	-
		VD 0561	Field pea (dry)	0.1	-
		VR 0589	Potato	0.2	-
		SO 0495	Rape seed	0.5	-
		OC 0495	Rape seed oil, crude	0.05	-
		OR 0495	Rape seed oil, edible	0.05	-
		VD 0541	Soya bean (dry)	10	-
		OC 0541	Soya bean oil, crude	1	-
		OR 0541	Soya bean oil, edible	0.1	-
		VR 0596	Sugar beet	0.2	-
		SO 0702	Sunflower seed	0.2	-
		OC 0702	Sunflower seed oil, crude	0.05	-
		OR 5702	Sunflower seed oil, edible	0.05	-
		Residue: sum of clethodim and its metabolites containing the 5-(2-ethylthiopropyl)cyclohexene-3-one and 5-(2-ethylthiopropyl)-5-hydroxycyclohexene-3-one moieties and their sulphoxides and sulphones, expressed as clethodim.			
Cyhexatin (067)	0.007	Notes Previous ADI 0.001 mg/kg bw			
DDT (021)	0.02	GC 0080	Cereal grains	0.1 E	0.1 E T
		Residue: sum of p,p_-DDT, o,p_-DDT, p,p_-DDE and p,p_-TDE (DDD) (fat-soluble)			
Diazinon (022)	0.002	DH 1100	Hops, dry	0.5	-
		Residue: diazinon (fat-soluble)			
Dicofol (026)	0.002	MO 0812	Cattle, Edible offal of	1	0.05*
		MM 0812	Cattle meat	3 (fat)	0.5 (fat)
		VP 0528	Garden pea (young pods)	W	2
		ML 0106	Milks	0.1 F	0.05 F
		PM 0110	Poultry meat	0.1 (fat)	0.5 (fat)
		Residue: dicofol (sum of *o,p'* and *p,p'* isomers) (fat-soluble) for commodities of plant origin. sum of dicofol (sum of *o,p'* and *p,p'* isomers) and 2,2-dichloro-1,1-bis(4-chlorophenyl)ethanol (*p,p'*-FW 152), expressed as dicofol (fat-soluble)			

Pesticide (Codex ref. No.)	ADI (mg/kg bw)	Commodity		Recommended MRL or ERL (mg/kg)	
		CCN	Name	New	Previous
		for animal products			
Dimethoate (027)	0.01	VP 0061	Beans, except Broad bean and Soya bean	W	2
		VB 0400	Broccoli	W	2
		VB 0404	Cauliflower	W	2
		VC 0424	Cucumber	W	2
		VL 0483	Lettuce, Leaf	W	2
		FS 0014	Plums (including Prunes)	0.5	2
		GC 0654	Wheat	W	0.2
		Residue: dimethoate			
Diquat **	0.002	AL 1020	Alfalfa fodder	100	-
(031)		GC 0640	Barley	5	5
		VP 0062	Beans, shelled	W	0.5
		VD 0071	Beans (dry)	0.2	-
		AL 1023	Clover	50	-
		SO 0691	Cotton seed	W	1
		OR 0691	Cotton seed oil, edible	W[1]	0.1
		MO 0105	Edible offal (Mammalian)	0.05*	0.05*
		PE 0112	Eggs	0.05*	0.05*
		VD 0533	Lentil (dry)	0.2	-
		GC 0645	Maize	0.05*	0.1
		MM 0095	Meat	0.05*	0.05*
		ML 0106	Milks	0.01*	0.01*
		GC 0647	Oats	2	-
		VA 0385	Onion, Bulb	W	0.1
		VP 0064	Peas, shelled (succulent seeds)	W	0.1
		VD 0072	Peas (dry)	0.2	-
		SO 0698	Poppy seed	W	5
		VR 0589	Potato	0.05	0.2
		PO 0111	Poultry, Edible offal of	0.05*	-
		PM 0110	Poultry meat	0.05*	-
		SO 0495	Rape seed	2	2
		OR 0495	Rape seed oil, edible	W[1]	0.1
		GC 0649	Rice	10	5
		CM 0649	Rice, husked	1	0.2

Pesticide (Codex ref. No.)	ADI (mg/kg bw)	Commodity		Recommended MRL or ERL (mg/kg)	
		CCN	Name	New	Previous
		CM 1205	Rice, polished	0.2	0.2
		OR 0700	Sesame seed oil, edible	W[1]	0.1
		GC 0651	Sorghum	2	2
		VD 0541	Soya bean (dry)	0.2	-
		VR 0596	Sugar beet	W	0.1
		SO 0702	Sunflower seed	1	0.5
		OR 0702	Sunflower seed oil, edible	W[1]	0.1
			Vegetables (except as otherwise listed)	W	0.05*
		OC 0172	Vegetable oils, crude	0.05*	-
		GC 0654	Wheat	2	2
		CM 0654	Wheat bran, unprocessed	5	5
		CF 1211	Wheat flour	0.5	0.2
		CF 1212	Wheat wholemeal	2	2
		Residue: diquat cation Notes Diquat is generally available as the dibromide [1]Replaced by recommendation for Vegetable oils, crude			
Disulfoton	0.0003	VD 0071	Beans (dry)	0.05	0.01
(074)		VB 0400	Broccoli	0.1	0.2[1,2]
		VB 0404	Cauliflower	0.05	0.2[1,2]
		ML 0107	Milk of cattle, goats and sheep	0.01	0.02[1]
		TN 0672	Pecan	0.1[3]	0.01*[1]
		GC 0651	Sorghum	1	0.5[1]
		AF 0651	Sorghum forage (green)	5	20[1,4]
		VO 0448	Tomato	W	0.1[1,2]
		AF 0654	Wheat forage (green)	1	2[1,4]
		AS 0654	Wheat straw and fodder, dry	5	10[1]
		Residue: sum of disulfoton, demeton-S and their sulphoxides and sulphones, expressed as disulfoton Notes [1]1991 JMPR proposal [2]The 1991 JMPR recommended withdrawal of the 0.5 mg/kg CXL for vegetables [3]The current CXL [4]The 1991 JMPR recommended withdrawal of 5 mg/kg for forage crops (green)			
Ethephon **	0.05	FP 0226	Apple	5	5[1]
(106)		GC 0640	Barley	1	-

Pesticide (Codex ref. No.)	ADI (mg/kg bw)	Commodity		Recommended MRL or ERL (mg/kg)	
		CCN	Name	New	Previous
		AS 0640	Barley straw and fodder, dry	5	-
		FB 0264	Blackberries	W	30
		FB 0020	Blueberries	20	20
		VC 4199	Cantaloupe	1	2[2]
		FS 0013	Cherries	10	10
		SB 0716	Coffee beans	W	0.1
		SO 0691	Cotton seed	2	-
		FB 0265	Cranberry	W	5
		FB 0278	Currant, Black	W	5
		PE 0840	Chicken eggs	0.2*	-
		MO 0096	Edible offal of cattle, goats, horses, pigs and sheep	0.2*	-
		FT 0297	Fig	W	5
		DF 0297	Figs, dried	10	-
		FB 0269	Grapes	1	10
		TN 0666	Hazelnuts	0.2	0.5
		FC 0002	Lemons and Limes	W	2 Po
		FC 0003	Mandarins	W	0.5
		MM 0096	Meat of cattle, goats, horses, pigs and sheep	0.1*	-
		VC 0046	Melons, except Watermelon	W[3]	2
		ML 0107	Milk of cattle, goats and sheep	0.05*	-
		VA 0385	Onion, Bulb	W	0.5
		FS 0247	Peach	W	0.5
		HS 0790	Peppers	30	30
		FI 0353	Pineapple	1	2
		PO 0111	Poultry, Edible offal of	0.2*	-
		PM 0110	Poultry meat	0.1*	-
		GC 0650	Rye	1	-
		GC 0650	Rye straw and fodder, dry	5	-
		VO 0448	Tomato	2[4]	3 Po
		TN 0678	Walnuts	0.5	0.5
		GC 0654	Wheat	1	-
		AS 0654	Wheat straw and fodder, dry	5	-
		Residue: ethephon Notes			

Pesticide (Codex ref. No.)	ADI (mg/kg bw)	Commodity		Recommended MRL or ERL (mg/kg)	
		CCN	Name	New	Previous
		[1]Previous levels were recorded as GLs, not recommended as MRLs. The ADI was allocated in 1993. [2]Previous GL for Melons, except Watermelon [3]Replaced by recommendation for cantaloupe [4]The currently listed use patterns do not include Po uses			
Ethion **	0.002	TN 0660	Almonds	W	0.1*
(034)		FP 0226	Apple	W	2
		FS 0240	Apricot	W	0.1*
		MM 0812	Cattle meat	W	2.5 (fat) V
		MO 0812	Cattle, Edible offal of	W	1
		FS 0013	Cherries	W	0.1*
		TN 0664	Chestnuts	W	0.1*
		FC 0001	Citrus fruits	5	2
		VP 0526	Common bean (pods and/or immature seeds)	W	2
		SO 0691	Cotton seed	W	0.5
		VC 0424	Cucumber	W	0.5
		VO 0440	Egg plant	W	1
		PE 0112	Eggs	W	0.2*
		VA 0381	Garlic	W	1
		MM 0814	Goat meat	W	0.2* (fat)
		MO 0814	Goat, Edible offal of	W	0.2*
		FB 0269	Grapes	W	2
		TN 0666	Hazelnuts	W	0.1*
		MM 0816	Horse meat	W	0.2* (fat)
		MO 0816	Horse, Edible offal of	W	0.2*
		GC 0645	Maize	W	0.05*
		VC 0046	Melons, except Watermelon	W	2
		ML 0106	Milks	W	0.02 F V
		FS 0245	Nectarine	W	1
		VA 0385	Onion, Bulb	W	1
		FS 0247	Peach	W	1
		FP 0230	Pear	W	2
		TN 0672	Pecan	W	0.1*
		VO 0051	Peppers	W	1
		VO 0445	Peppers, sweet	W	1

Pesticide (Codex ref. No.)	ADI (mg/kg bw)	Commodity		Recommended MRL or ERL (mg/kg)	
		CCN	Name	New	Previous
		MM 0818	Pig meat	W	0.2* (fat)
		MO 0818	Pig, Edible offal of	W	0.2*
		FS 0014	Plums (including Prunes)	W	2
		PM 0110	Poultry meat	W	0.2* (fat)
		PO 0111	Poultry, Edible offal of	W	0.2*
		MM 0822	Sheep meat	W	0.2* (fat)
		MO 0822	Sheep, Edible offal of	W	0.2*
		VC 0431	Squash, Summer	W	0.5
		FB 0275	Strawberry	W	2
		DT 1114	Tea	W	5
		VO 0448	Tomato	W	2
		TN 0678	Walnuts	W	0.1*
		VC 0433	Winter squash	W	0.5
		Residue: ethion (fat-soluble)			
Fenpropimorph * (188)	0.003	Notes new compound, not evaluated for residues			
Fentin	0.0005[1]	TN 0672	Pecan	W	0.05*
(040)		Residue:fentin, excluding inorganic tin and di- and monophenyltin Notes [1]Applicable to the sum of fentin acetate, fentin chloride and fentin hydroxide			
Folpet	0.01 T	VC 0424	Cucumber	0.5	2 T
(041)		Residue: folpet			
Glufosinate-	0.02	VS 0621	Asparagus	0.05*	-
ammonium		FI 0327	Banana	0.2	0.05*
(175)		FB 0018	Berries and other small fruits	W	0.1
		FB 0018	Berries and other small fruits (except currants)	0.1	-
		VD 0523	Broad bean (dry)	2	-
		VD 0526	Common bean (dry)	2	-
		VR 0577	Carrot	0.05*	-
		VP 0526	Common bean (pods and/or immature seeds)	0.05*	-
		VL 0470	Corn salad	0.05*	-
		FB 0021	Currants, Black, Red, White	0.5	0.1[1]
		FB 0269	Grapes	W[2]	0.1
		GC 0645	Maize	0.1	0.05*
		AF 0645	Maize forage	0.2	-

Pesticide (Codex ref. No.)	ADI (mg/kg bw)	Commodity		Recommended MRL or ERL (mg/kg)	
		CCN	Name	New	Previous
		VA 0385	Onion, Bulb	0.05	-
		VD 0072	Peas (dry)	3	-
		SO 0495	Rape seed	5	1
		OC 0495	Rape seed oil, crude	0.05*	-
		VD 0541	Soya bean (dry)	0.1	2
		VR 0596	Sugar beet	0.05*	-
		AV 0596	Sugar beet leaves or tops	0.1	-
		SO 0702	Sunflower seed	5	2
		OC 0702	Sunflower seed oil, crude	0.05*	-
		Residue: sum of glufosinate-ammonium and 3-[hydroxy(methyl)phosphinoyl]propionic acid, calculated as glufosinate (free acid). Notes [1]Included in Berries and other small fruits [2]included in Berries and other small fruits (except currants)			
Glyphosate	0.3	VD 0541	Soya bean (dry)	20	5
(158)		AL 0541	Soya bean fodder	200	20
		CM 0654	Wheat bran, unprocessed	20	40
		Residue: glyphosate Note [1]40 mg/kg was recommended by the 1988 JMPR, but the draft MRL at this level was lowered to 20 mg/kg by the 1994 CCPR.			
Heptachlor (043)	0.0001	Residue: sum of heptachlor and heptachlor epoxide (fat-soluble) Note The Meeting agreed that for the general monitoring of heptachlor and its metabolite, a suitable limit of determination for the total residue would be 0.01 mg/kg			
Imazalil	0.03	VC 0046	Melons, except Watermelon	2 Po	-
(110)		Residue: imazalil			
Iprodione **	0.2	TN 0660	Almonds	0.2	-
(111)		FP 0226	Apple	W[1]	10 Po
		GC 0640	Barley	2	-
		VD 0071	Beans (dry)	0.1	0.2
		FB 0264	Blackberries	30	-
		VB 0400	Broccoli	25	-
		VR 0577	Carrot	10 Po	-
		VP 0562	Common bean (pods &/or immature seeds}	2	-
		FS 0013	Cherries	10	-
		VC 0424	Cucumber	2	5
		FB 0021	Currants, Black, Red, White	W	5
		VA 0381	Garlic	W	0.1

Pesticide (Codex ref. No.)	ADI (mg/kg bw)	Commodity		Recommended MRL or ERL (mg/kg)	
		CCN	Name	New	Previous
		FB 0269	Grapes	10	10
		FI 0341	Kiwifruit	5	5
		VL 0482	Lettuce, Head	10	10
		VL 0483	Lettuce, Leaf	25	-
		VA 0385	Onion, Bulb	0.2	0.1
		FS 0247	Peach	10	10 Po
		FP 0230	Pear	W[1]	10 Po
		VO 0445	Peppers, Sweet	W	5
		FS 0014	Plums (including Prunes)	W	10
		FP 0009	Pome fruits	5 Po	
		SO 0495	Rape seed	0.5	-
		FB 0272	Raspberries, Red, Black	30	5
		CM 0649	Rice, husked	10	3
		VR 0596	Sugar beet	0.1*	-
		SO 0702	Sunflower seed	0.5	-
		FB 0275	Strawberry	10	10
		VO 0448	Tomato	W	5
		VS 0469	Witloof chicory (sprouts)	1	1
		Residue: iprodione Note [1]now included in recommendation for Pome fruits			
Methamidophos	0.004	VB 0400	Broccoli	W	1
(100)		VB 0041	Cabbages, Head	W	1
		VB 0404	Cauliflower	W	1
		FC 0001	Citrus fruits	W	0.5
		VO 0440	Egg plant	W	1
		VC 0046	Melons, except Watermelon	W	0.5
		FS 0247	Peach	W	1
		FP 0009	Pome fruits	0.5	-
		VR 0589	Potato	0.05	0.1
		VO 0448	Tomato	W	1
		Residue: methamidophos			
Methidathion	0.001	FS 0245	Nectarines	0.2[1]	0.2
(051)		Residue: methidathion Note [1]Revokes 1992 recommendation to withdraw current CXL of 0.2 mg/kg			

Pesticide (Codex ref. No.)	ADI (mg/kg bw)	Commodity		Recommended MRL or ERL (mg/kg)	
		CCN	Name	New	Previous
Parathion-methyl **	0.02	VS 0620	Artichoke, Globe	2	-
(059)		AL 1030	Bean forage (green)	1	-
		VD 0071	Beans (dry)	0.05*	-
		VB 0400	Broccoli	0.2	0.2[1]
		VB 0041	Cabbages, Head	0.2	0.2[1]
		VR 0577	Carrot	1	-
		VS 0624	Celery	5	-
		AL 1023	Clover	10	-
		VP 0526	Common bean (pods and/or immature seeds)	0.05*	-
		VP 0528	Garden pea (young pods)	1	-
		AS 0162	Hay or fodder (dry) of grasses	5	-
		DH 1100	Hops, dry	1	0.05*[2]
		VL 0482	Lettuce, Head	0.05*	-
		VL 0483	Lettuce, Leaf	0.5	-
		VP 0534	Lima bean (young pods and/or immature beans)	0.05*	-
		VL 0485	Mustard greens	0.5	-
		VD 0072	Peas (dry)	0.2	-
		VR 0589	Potato	0.05*	-
		GC 0649	Rice	3	-
		CM 0649	Rice, husked	1	
		AS 0649	Rice straw and fodder, dry	10	-
		VL 0502	Spinach	0.5	-
		VR 0596	Sugar beet	0.05*	0.05*[2]
		AV 0596	Sugar beet leaves or tops	0.05*	-
		VR 0506	Turnip, Garden	0.05*	-
		VL 0506	Turnip greens	2	-
		GC 0654	Wheat	5	-
		CM 0654	Wheat bran, unprocessed	10	
		AS 0654	Wheat straw and fodder, dry	10	-
		Residue: parathion-methyl Notes [1]CXL for brassica recommended for withdrawal by 1992 JMPR [2]CXL recommended for withdrawal by 1992 JMPR			
Phorate (112)	0.0005	Note Previous ADI 0.0002 mg/kg bw			
Phosalone **	0.001	FP 0226	Apple	W	5

Pesticide (Codex ref. No.)	ADI (mg/kg bw)	Commodity		Recommended MRL or ERL (mg/kg)	
		CCN	Name	New	Previous
(060)		VR 0574	Beetroot	W	2
		VB 0400	Broccoli	W	1
		VB 0402	Brussels sprouts	W	1
		VB 0041	Cabbages, Head	W	1
		FS 0013	Cherries	W	10
		TN 0664	Chestnuts	W	0.1*
		FC 0001	Citrus fruits	W	1
		VC 0424	Cucumber	W	1
		FB 0269	Grapes	W	5
		DH 1100	Hops, dry	W	2
		VL 0482	Lettuce, Head	W	1
		FS 0247	Peach	W	5
		FP 0230	Pear	W	2
		VP 0063	Peas	W	1
		TN 0672	Pecan	W	0.1*
		FS 0014	Plums (including Prunes)	W	5
		VR 0589	Potato	W	0.1*
		SO 0495	Rape seed	W	0.1*
		MF 0822	Sheep fat	W	0.5 V
		MM 0822	Sheep meat	W	0.05* V
		FB 0275	Strawberry	W	1
		VO 0448	Tomato	W	1
		Residue: phosalone			
Phosmet ** (103)	0.01	Notes previous ADI 0.02 mg/kg bw			
Pirimiphos-methyl	0.03	OR 0697	Peanut oil, edible	15 Po P	10[1] Po P
(086)		Residue: pirimiphos-methyl (fat-soluble) Note [1]The 1985 JMPR recommendation was 15 mg/kg, lowered to 10 mg/kg by the 1990 CCPR			
Profenofos	0.01	VB 0402	Brussels sprouts	0.5	0.5 T[1]
(171)		VB 0404	Cauliflower	0.5	0.2 T[1]
		VP 0526	Common beans (pods and/or immature seeds)	0.1	-
		VA 0385	Onions, Bulb	W	0.2
		FC 0004	Oranges, Sweet, Sour	1	1 T[1]
		VO 0444	Peppers, Chilli	5	-
		DT 0171	Teas (tea and herb teas)	0.5	0.5 T

Pesticide (Codex ref. No.)	ADI (mg/kg bw)	Commodity		Recommended MRL or ERL (mg/kg)	
		CCN	Name	New	Previous
		Residue: profenofos Note [1]1990 JMPR proposal, withdrawn by 1992 JMPR			
Propiconazole	0.04	GC 0640	Barley	0.05[1]	0.2 T
(160)		AV 0596	Sugar beet leaves or tops	0.5	0.1
		Residue: propiconazole Note [1]The limit is no longer temporary.			
Propylenethiourea (PTU) (150)	0.0002 T (1999)	Note A TADI was allocated in 1993, but the previously recorded Guideline Levels were not recommended for conversion to TMRLs. The Meeting has now withdrawn these GLs: see Part 2			
Tebuconazole *	0.03	GC 0640	Barley	0.2	-
(189)		AS 0640	Barley straw and fodder, dry	10	-
		MO 0812	Cattle, Edible offal of	0.05*	-
		MM 0812	Cattle meat	0.05*	-
		ML 0812	Cattle milk	0.01*	-
		PO 0840	Chicken, Edible offal of	0.05*	-
		PE 0840	Chicken eggs	0.05*	-
		PM 0840	Chicken meat	0.05*	-
		FB 0269	Grapes	2	-
		SO 0697	Peanut	0.05	-
		AL 0697	Peanut fodder	30	-
		SO 0495	Rape seed	0.05	-
		GC 0650	Rye	0.05*	-
		AS 0650	Rye straw and fodder, dry	5	-
		VC 0431	Squash, Summer	0.02	-
		VO 0448	Tomato	0.2	-
		GC 0654	Wheat	0.05	-
		AS 0654	Wheat straw and fodder, dry	10	-
		Residue: tebuconazole			
Tecnazene (115)	0.02	VR 0589	Potato	20 Po	1[1,2] Po 10[1,3] Po
		Residue: tecnazene Notes Previous ADI 0.01 mg/kg bw [1]Washed before analysis [2]CXL [3]Proposed amendment at Step 7C			
Teflubenzuron * (190)	0.01	Notes New compound, not evaluated for residues			
Thiophanate-methyl (77)	0.08	Residue: carbendazim Note Residues of thiophanate-methyl are covered by the recommendations			

Pesticide (Codex ref. No.)	ADI (mg/kg bw)	Commodity		Recommended MRL or ERL (mg/kg)	
		CCN	Name	New	Previous
		for carbendazim (see above)			
Tolclofos-methyl *	0.07	VL 0482	Lettuce, Head	2	-
(191)		VL 0483	Lettuce, Leaf	2	-
		VR 0589	Potato	0.2	-
		VR 0494	Radish	0.1	-
		Residue: tolclofos-methyl			

PART 2. GUIDELINE LEVELS FOR COMPOUNDS WITHOUT ADIs[iii]

Pesticide (Codex ref. No.)	Commodity		Guideline Level (mg/kg)	
	CCN	Name	New GL	Previous MRL or GL
Chlormequat **	GC 0640	Barley	0.5	-
(015)	AS 0640	Barley straw and fodder, dry	20	50
	SO 0691	Cotton seed	0.5	-
	DF 0269	Dried grapes	W	1
	FB 0269	Grapes	W	1
	ML 0107	Milk of cattle, goats and sheep	W	0.1*
		Milk products	W	0.1*
	GC 0647	Oats	10	10
	AF 0647	Oat forage (green)	20	-
	AS 0647	Oat straw and fodder, dry	20	50
	FP 0230	Pear	10	3
	SO 0495	Rape seed	5	-
	OC 0495	Rape seed oil, crude	0.1*	-
	GC 0650	Rye	3	5
	CM 0650	Rye bran, unprocessed	10	-
	AF 0650	Rye forage (green)	20	-
	AS 0650	Rye straw and fodder, dry	20	50
	CF 1251	Rye wholemeal	3	-
	GC 0654	Wheat	2	5
	CM 0654	Wheat bran, unprocessed	5	-
	CF 1211	Wheat flour	0.5	-
	AS 0654	Wheat straw and fodder, dry	20	50
	CF 1212	Wheat wholemeal	2	-
	Residue: chlormequat cation Note Chlormequat is usually used as the chloride			
Propylenethiourea	FP 0226	Apple	W	0.1
(PTU) (150)	VR 0578	Celeriac	W	0.05*
	FS 0243	Cherry, Sour	W	0.1
	FB 0269	Grapes	W	0.1
	FS 0247	Peach	W	0.05*
	FP 0230	Pear	W	0.1
	FS 0014	Plums (including Prunes)	W	0.1
	VR 0589	Potato	W	0.02*
	VO 0448	Tomato	W	0.1
	Note Although a TADI was allocated in 1993, no recommendation was made to convert the existing GLs to TMRLs. The 1994 Meeting has now withdrawn these GLs.			

ANNEX II

INDEX OF REPORTS AND EVALUATIONS

Numbers in parentheses are Codex Classification Numbers.

BHC (technical)	1965 (T), 1968 (T,R), 1973 (T,R) (*see also* lindane)
BIFENTHRIN (178)	1992 (T,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)
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)
sec-BUTYLAMINE (089)	1975 (T,R), 1977 (R), 1978 (T,R), 1979 (R), 1980 (R), 1981 (T), 1984 (T,R: withdrawal of TADI, but no evaluation)
CADUSAFOS (174)	1991 (T,R), 1992 (R), 1992 (R)
CAMPHECHLOR (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 rpt), 1990 (R)
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 evaluation), 1990 (T,R), 1991 (corr. to 1990 R evaluation), 1994 (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)
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)
CARBOFURAN (096)	1976 (T,R), 1979 (T,R), 1980 (T), 1982 (T), 1991 (R), 1993 (R)

CARBON DISULPHIDE (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 rpt), 1993 (R)
CARTAP (097)	1976 (T,R), 1978 (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)
CHLORMEQUAT (015)	1970 (T,R), 1972 (T,R), 1976 (R), 1985 (R), 1994 (T,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 rpt and T evaluation), 1985 (T,R), 1987 (T), 1988 (R), 1990 (T,R), 1991 (corr. to 1990 evaluation), 1992 (T), 1993 (R)
CHLORPROPHAM	1965 (T)
CHLORPYRIFOS (017)	1972 (T,R), 1974 (R), 1975 (R), 1977 (T,R), 1981 (R), 1982(T,R), 1983 (R), 1989 (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, 1993 (R), 1994 (R)
CHLORTHION	1965 (T)

CLETHODIM (187)	1994 (T,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)
CYANOFENPHOS (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 rpt), 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 rpt, Annex I)
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)
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)
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)
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)

1,2-DIBROMOETHANE (023)	1965 (T,R), 1966 (T,R), 1967 (R), 1968 (R), 1971 (R), 1979 (R), 1985 (R)
DICHLOFLUANID (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)
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)
DIMETHIPIN (151)	1985 (T,R), 1987 (T,R), 1988 (T,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)
DIMETHRIN	1965 (T)
DINOCAP (087)	1969 (T,R), 1974 (T,R), 1989 (T,R), 1992 (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)
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 rpt, Annex I), 1994 (R)
DITHIANON (180)	1992 (T,R)
DITHIOCARBAMATES (105)	1965 (T), 1967 (T,R), 1970 (T,R), 1983 (R, propineb and 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)
DNOC	1965 (T)

DODINE (084)	1974 (T,R), 1976 (T,R), 1977 (R)
EDIFENPHOS (099)	1976 (T,R), 1979 (T,R), 1981 (T,R)
ENDOSULFAN (032)	1965 (T), 1967 (T,R), 1968 (T,R), 1971 (R), 1974 (R), 1975 (R), 1982 (T), 1985 (T,R), 1989 (T,R), 1993 (R)
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)
ETHIOFENCARB (107)	1977 (T,R), 1978 (R), 1981 (R), 1982 (T,R), 1983 (R)
ETHION (034)	1968 (T,R), 1969 (R), 1970 (R), 1972 (T,R), 1975 (R), 1982 (T), 1983 (R), 1985 (T), 1986 (T), 1989 (T), 1990 (T), 1994 (R)
ETHOPROPHOS (149)	1983 (T), 1984 (R), 1987 (T)
ETHOXYQUIN (035)	1969 (T,R)
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[2]), 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)
FENBUTATIN OXIDE (109)	1977 (T,R), 1979 (R), 1992 (T), 1993 (R)
FENCHLORPHOS (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)
FENPROPATHRIN (185)	1993 (T,R)
FENPROPIMORPH	1994 (T)

[2]R evaluation omitted. Published 1986.

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)
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 rpt), 1988 (R), 1990 (R), 1991 (corr. to 1990 evaluation)
FERBAM	*see* dithiocarbamates, 1965 (T), 1967 (T,R)
FLUCYTHRINATE (152)	1985 (T,R), 1987 (R), 1988 (R), 1989 (R), 1990 (R), 1993 (R)
FLUSILAZOLE (165)	1989 (T,R), 1990 (R), 1991 (R), 1993 (R)
FOLPET (041)	1969 (T,R), 1973 (T), 1974 (R), 1982 (T), 1984 (T,R), 1986 (T), 1987 (R), 1990 (T,R), 1991 (corr. to 1990 R evaluation), 1993 (T,R), 1994 (R)
FORMOTHION (042)	1969 (T,R), 1972 (R), 1973 (T,R), 1978 (R)
GLUFOSINATE-AMMONIUM (175)	1991 (T,R), 1992 (corr. to 1991 rpt, Annex I), 1994 (R)
GLYPHOSATE (158)	1986 (T,R), 1987 (R and corr. to 1986 rpt), 1988 (R), 1994 (R)
GUAZATINE (114)	1978 (T.R), 1980 (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 rpt, 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)
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)
IPRODIONE (111)	1977 (T,R), 1980 (R), 1992 (T), 1994 (R)

ISOFENPHOS (131)	1981 (T,R), 1982 (T,R), 1984 (R), 1985 (R), 1986 (T,R), 1988 (R), 1992 (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)
MALATHION (049)	1965 (T), 1966 (T,R), 1967 (corr. to 1966 R), 1968 (R), 1969 (R), 1970 (R), 1973 (R), 1975 (R), 1977 (R), 1984 (R)
MALEIC HYDRAZIDE (102)	1976 (T,R), 1977 (T,R), 1980 (T), 1984 (T,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)
METHACRIFOS (125)	1980 (T,R), 1982 (T), 1986 (T), 1988 (T), 1990 (T,R), 1992 (R)
METHAMIDOPHOS (100)	1976 (T,R), 1979 (R), 1981 (R), 1982 (T,R[3]), 1984 (R), 1985 (T), 1989 (R), 1990 (T,R), 1994 (R)
METHIDATHION (051)	1972 (T,R), 1975 (T,R), 1979 (R), 1992 (T,R), 1994 (R)
METHIOCARB (132)	1981 (T,R), 1983 (T,R), 1984 (T), 1985 (T), 1986 (R), 1987 (T,R), 1988 (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)
METHOPRENE (147)	1984 (T,R), 1986 (R), 1987 (T and corr. to 1986 rpt), 1988 (R), 1989 (R)
METHOXYCHLOR	1965 (T), 1977 (T)
METHYL BROMIDE (052)	*see* bromomethane
METIRAM (186)	1993 (T,R)

[3]R evaluation omitted. Published 1989.

MEVINPHOS (053)	1965 (T), 1972 (T,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)
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)
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 sulphoxide), 1967 (T), 1968 (R), 1973 (T,R), 1982 (T), 1984 (T,R), 1989 (T,R), 1992 (R)
OXYTHIOQUINOX	*see* chinomethionat
PACLOBUTRAZOL (161)	1988 (T,R), 1989 (R)
PARAQUAT (057)	1970 (T,R), 1972 (T,R), 1976 (T,R), 1978(R), 1981 (R), 1982 (T), 1985 (T), 1986 (T)
PARATHION (058)	1965 (T), 1967 (T,R), 1969 (R), 1970 (R), 1984 (R), 1991 (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)
PENCONAZOLE (182)	1992 (T,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 rpt)
2-PHENYLPHENOL (056)	1969 (T,R), 1975 (R), 1983 (T), 1985 (T,R), 1989 (T), 1990 (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)

PHOSALONE (060)	1972 (T,R), 1975 (R), 1976 (R), 1993 (T), 1994 (R)
PHOSMET (103)	1976 (R), 1977 (corr. to 1976 evaluation), 1978 (T,R), 1979 (T,R), 1981 (R), 1984 (R), 1985 (R), 1986 (R), 1987 (R and corr. to 1986 evaluation), 1988 (R), 1994 (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)
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 rpt, Annex I, and evaluation), 1992 (R)
PROCYMIDONE (136)	1981 (R), 1982 (T), 1989 (T,R), 1990 (R), 1991 (corr. to 1990 Annex I), 1993 (R)
PROFENOFOS (171)	1990 (T,R), 1992 (R), 1994 (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)
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)
PROPYLENETHIOUREA (PTU) (150)	1993 (T,R), 1994 (R)
PYRAZOPHOS (153)	1985 (T,R), 1987 (R), 1992 (T,R), 1993 (R)
PYRETHRINS (063)	1965 (T), 1966 (T,R), 1967 (R), 1968 (R), 1969 (R), 1970 (T), 1972 (T,R), 1974 (R)

QUINTOZENE (064)	1969 (T,R) 1973 (T,R), 1974 (R), 1975 (T,R), 1976 (Annex I, corr. to 1975 R), 1977 (T,R)
2,4,5-T (121)	1970 (T,R), 1979 (T,R), 1981 (T)
TEBUCONAZOLE (188)	1994 (T,R)
TECNAZENE (115)	1974 (T,R), 1978 (T,R), 1981 (R), 1983 (T), 1987 (R), 1989 (R), 1994 (T,R)
TEFLUBENZURON	1994 (T)
TERBUFOS (167)	1989 (T,R), 1990 (T,R)
THIABENDAZOLE (065)	1970 (T,R), 1971 (R), 1972 (R), 1975 (R), 1977 (T,R), 1979 (R), 1981 (R)
THIODICARB (154)	1985 (T,R), 1986 (T), 1987 (R), 1988 (R)
THIOMETON (076)	1969 (T,R), 1973 (T,R), 1976 (R), 1979 (T,R), 1988 (R)
THIOPHANATE-METHYL (077)	1973 (T,R), 1975 (T,R), 1977 (T), 1978 (R), 1988 (R), 1990 (R), 1994 (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)
TOLCLOFOS-METHYL (189)	1994 (T,R)
TOLYLFLUANID (162)	1988 (T,R), 1990 (R), 1991 (corr. to 1990 rpt)
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 evaluation), 1988 (R), 1989 (R), 1992 (R)
TRIADIMENOL (168)	1989 (T,R), 1992 (R)
TRIAZOLYLALANINE	1989 (T,R)
TRIAZOPHOS (143)	1982 (T), 1983 (R), 1984 (corr. to 1983 rpt, Annex I), 1986 (T,R), 1990 (R), 1991 (T and corr. to 1990 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)
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 rpt and R evaluation), 1988 (T,R), 1989 (R), 1990 (R), 1992 (R)
ZINEB (105)	*see* dithiocarbamates, 1965 (T), 1967 (T,R), 1993 (T)
ZIRAM (105)	*see* dithiocarbamates, 1965 (T), 1967 (T,R)

ANNEX III

INTAKE PREDICTIONS

At the request of the Meeting, WHO calculated the predicted intakes of residues on the agenda of the Joint Meeting, on the basis of the methods described in the *Guidelines for Predicting Dietary Intake of Pesticide Residues*. In calculating TMDIs for the Meeting, all MRL proposals of the Meeting as well as those of previous JMPR meetings are included. When two proposals exist for a commodity, the most recent JMPR recommendation is used. These procedures may result in TMDI estimates that differ from those calculated for CCPR.

Detailed EMDIs (Estimated Maximum Daily Intakes) were not calculated for those pesticides for which the TMDI (Theoretical Maximum Daily Intake), based on global diets, exceeded the ADI, because there was insufficient opportunity at the Joint Meeting to review the detailed processing data that had been supplied on the compounds of interest. The results of EMDI calculations will be made available to the Twenty-seventh Session of the Codex Committee on Pesticide Residues (CCPR) in April 1995.

The TMDI calculations were based on the ADIs and MRLs proposed by the Meeting and existing and pending MRLs in the Codex system. For the following compounds the TMDI did not exceed the ADI:

abamectin, acephate, aldicarb, azocyclotin, bentazone, captan, clethodim, cyhexatin, DDT, dimethoate, ethephon, fentin, folpet, glufosinate-ammonium, glyphose, imazalil, iprodione, methamidophos, parathion-methyl, profenofos, propiconazole, tebuconazole and tolclofos-methyl.

The TMDI exceeded the ADI for the following compounds:

benomyl, carbendazim, chlorfenvinphos, chlorpyrifos-methyl, diazinon, dicofol, diquat, disulfoton, ethion, heptachlor, methidathion, pirimiphos-methyl, phirate, phosmet, tecnazene and thiophanate-methyl.

Information on processing factors must be reviewed before EMDIs can be calculated for these pesticides.

The TMDI was not calculated for the following compounds which have either no ADI, no proposed MRLs or all existing MRLs proposed for withdrawal:

fenpropathrin, phosalone, propylenethiourea (PTU) and teflubenzuron.

The TMDIs grossly overestimate the true pesticide residue intake. It should, therefore, not be concluded that the MRLs proposed by the Meeting are unacceptable when the TMDI exceeds the ADI. Instead, TMDI calculations should be used as a screening tool that may eliminate the need for further calculations of the intake of a pesticide when its value is below the ADI. When the TMDI exceeds the ADI the EMDI and, if necessary, the EDI (Estimated Daily Intake) should be calculated.

ANNEX IV

JMPR MANUAL FOR FAO PANEL MEMBERS

INTRODUCTION

The format and language of JMPR evaluations and reports have evolved over the lifetime of the CCPR-JMPR system. One aim of this evolution has been to make it easier for readers to find the information they are seeking expressed in a clear and consistent way.

The purpose of this manual is to assist members of the FAO Panel to prepare documents for the Meeting in a consistent format. It may also be useful to people preparing submissions for review by the FAO Panel. The manual is not intended to deal with the evaluation process or to provide guidance on the estimation of maximum residue levels. Documents prepared in the correct format assist JMPR members to digest information quickly, and after the Meeting make it easier for the editor to produce final copy for publication.

CONTENTS

1. General

Please produce documents by word-processing with a standard program. Use WordPerfect 5.1 or WordPerfect 6.0 if possible; failing that, an earlier version of WordPerfect.

References to key combinations such as (Shift-F8, 1, 9) in the following text refer to those used in WordPerfect 5.1.

Please bring both disks and hard copy to the Meeting.

It is very helpful if one copy of the draft monograph can be produced single-sided with the text 1½- or double-spaced for editing. Tables can be single-spaced.

Try to insert all codes for pagination, font, page numbering, etc. at the start of the document and avoid repeating them unless a temporary change is needed. Such codes scattered about in the body of the text can make editing difficult.

2. Format

The text of the final report and evaluations will be printed in a 12 cpi (characters per inch) font, so please use this size if you have it.

Left/right margins should be 1 inch (2.5 cm) and top/bottom margins 0.5 inch. Lines should be fully justified, with widow/orphan protection (Shift-F8, 1, 9).

Tabs for general text should be set at half-inch (12.5 mm) intervals. If tabs are needed in tables they should be re-set so that a single tab, not a series of tabs, separates sections.

The first line of a paragraph immediately following a heading should begin at the left-hand margin. The first line of subsequent paragraphs should be indented one tab, as in this manual.

A page header should be introduced on the top left of each page of the document to show the title of the document, for example: PHORATE Evaluation, or PHORATE Report, or RESIDUES IN FEEDS Report.

3. Page numbering

Please set page numbering (Shift-F8, 2, 6) to "Top centre". (The document will automatically begin on page 1. Do <u>not</u> set either a specific "New page number" or "No page numbers". If you do, it will create havoc when the individual documents are assembled into the complete report or evaluations (pages will be numbered from 1 to say 203 and then either start at 1 again or be cancelled altogether. Both these hitches have occurred previously).

4. Tables

Please insert tables in their intended positions in the text or thereabouts, not at the end of the monograph. Although it is customary to collect tables at the end of articles for publication in journals, different considerations apply to the production

of camera-ready copy. It makes editing quicker and easier if tables are in their correct places from the beginning.

y Please always use the WordPerfect Tables program if possible. It is the easiest way to create tables and makes them much easier to edit. It is ideal for such tables as lists of recommendations and Annex I, which are likely to be changed several times, because lines can be added or deleted easily and quickly without affecting the structure of the table. See for example Annex I of the 1992 report, but note that commodities listed in Annex I (and in the RECOMMENDATIONS section) are now arranged alphabetically (see Section 8, *Draft report, compounds*).

Generally, separate items of information should be recorded in separate cells of tables. For example, in tables of recommendations, the Codex Commodity Number and the Codex commodity description should be in separate cells of the row. It is particularly desirable that separate lines of tables are in separate rows of cells. WordPerfect will not divide cells when moving to a new page, so a cell that is several lines deep can cause problems in tables occupying more than one page.

WordPerfect normally creates tables divided into individual cells with lines round them. If you don't want the lines you can delete them, but it makes editing easier if you leave them in and add a note asking the editor to delete them. In particular, do not join cells vertically (as distinct from deleting lines separating them): this causes the same problems as cells that are several lines deep.

Always use the portrait (vertical) rather than the landscape (horizontal) layout for tables if possible. Quite wide tables can be accommodated vertically by reducing the typeface to 15-17 cpi or by using the WordPerfect "Fine" or "Small" attribute (Ctrl-F8, 3 or 4). For examples see 1991 Evaluations, Azinphos-methyl Tables 1, 3; Parathion Tables 4, 7, 10 etc. Please at all costs keep to the standard margins. Tables which occupy the full width of a page can be very difficult to edit.

Please do not include the caption of a table within the table itself: it forces the same caption to appear on subsequent pages and thus makes it difficult for the reader to find the beginning of a long table.

It is generally better not to construct a table covering several pages as a series of separate single-page tables. This usually produces a number of partly-filled pages.

5. Diagrams

These will usually be hand-drawn or photocopies provided by manufacturers, but WordPerfect accepts diagrams drawn with Windows 3.0 or 3.1 if you have it. If hand-drawn, WordPerfect can draw accurately positioned horizontal and vertical lines of any chosen length, so diagrams will look neater if you connect the items in them by WP lines rather than drawing angled lines by hand. For examples see 1991 Evaluations, Cadusafos Figure 1 (p. 198); Glufosinate-ammonium Figure 1 (p. 420).

6. References

References to unpublished reports, journals and books should be listed alphabetically in the form shown in the examples below.

REFERENCES [bold, centred, caps]

Fischer, R. and Schulze, E.-F. 1983a. The effect of Hoe 02782 OF AT202 (fentin acetate, active ingredient 96.4%) on Salmo gairdneri (Rainbow trout) in a static test. Hoechst Pfl. Fo. Biol., Germany. Rep. OEK 83 001E. Unpublished.

Fischer, R. and Schulze, E.-F. 1983b. The effect of Hoe 29664 OF AT205 (fentin hydroxide, active ingredient 97.0%) on Salmo gairdneri (Rainbow trout) in a static test. Hoechst Pfl. Fo. Biol., Germany. Rep. OEK 83/028E. Unpublished.

Gildemeister, H., Bürkle, W.L. and Sochor, H. 1985. Hoe 029664-14-C. Anaerobic soil metabolism study with the fungicide triphenyltin hydroxide (TPTH). Hoechst Analyt. Labor., Germany. Rep. (B) 221/85. Unpublished.

MacDougall, D. 1964. Guthion. In: Zweig, G., Analytical Methods for Pesticides, Plant Growth Regulators and Food Additives, Vol. II, Academic Press, New York, London.

Meagher, W.R., Adams, J.M., Anderson, C.A. and MacDougall, D. 1960. Colorimetric determination of Guthion residues in crops. J. Agric. Fd Chem. 8, 282-286.

Note. (1). In earlier editions of the manual, authors were asked to number references. Experience has shown that there are operational difficulties for the reviewer in doing this.

(2). Inclusive pagination should be shown as, e.g., 282-6 rather than 282-286.

(3). Citations in the text should name both of two authors, but only the first of three or more. Thus if the first three references above were quoted together in the text the citation should be (Fischer and Schulze, 1983a,b; Gildemeister *et al.*, 1985). Note the form of *et al.* (italics, with stop after *al*).

(4). If there are two or more multi-author works with the same first author in the same year, the year should be followed by "a", "b" etc., even if the co-authors are different, e.g.:

Rogers, E., Tufts, K. and Westberg, G.L. 1989a. Determination of ethylene thiourea in crops. Method MTF-88AM-004. Morse Laboratories, Inc., USA. Unpublished.

Rogers, E., Tufts, K., Normington, S. and Westberg, G.L. 1989b. Determination of ethylene thiourea in meat. Method ETU-89AM-004. Morse Laboratories, Inc., USA. Unpublished.

7. A residue evaluation (draft monograph)

The format of an FAO Panel residue evaluation is shown in Annex 1. The use of capitals, centre and side headings, bold and underlining should follow this format.

When a compound is evaluated for the first time, replace the EXPLANATION section (Annex 1) by the IDENTITY section (Annex 2). When a periodic review compound is evaluated add the IDENTITY section after EXPLANATION.

7.1. Explanation

Provide a very brief history of the compound in the introductory sentence, for example: "Folpet was first evaluated in 1969 and has been reviewed several times since, most recently in 1984, 1986 and 1987....." If a question was raised at the CCPR refer to the Session number and year, e.g. .. `at the 23rd (1991) Session of the CCPR it was suggested (ALINORM 91/24A, para ...)'

If the compound is being reviewed in the CCPR periodic review programme, state this in the first paragraph, for example: "Parathion-methyl, originally evaluated by the JMPR in 1965 and re-evaluated for residues several times up to 1984, is included in the CCPR periodic review programme."

Mention briefly previous JMPR requests for further information if relevant to the topic. Summarize the information available to the Meeting. State that information was supplied by (*list of countries*) and the basic manufacturers. Do not include company names.

For new and periodic review compounds state explicitly whether information was or was not provided on critical supporting studies (metabolism, animal transfer, processing, analytical methods, freezer storage stability).

7.2. Draft evaluation

Prepare a draft evaluation for the Meeting containing all the sections listed in Annex 1 except APPRAISAL, RECOMMENDATIONS and FURTHER WORK OR INFORMATION, which are assembled as a separate draft document. (See Section 8, *Draft report, compounds*).

Note that the order of the sections has been changed from that followed in previous editions, and FATE OF RESIDUES has been split into METABOLISM AND ENVIRONMENTAL FATE and FATE OF RESIDUES IN STORAGE AND PROCESSING. METHODS OF RESIDUE ANALYSIS is now placed early in the monograph, just before USE PATTERN. The Appraisal will be generated at the end of the Meeting by the editor, using the report adopted by the Meeting.

4 At the top right side of the first page give the year, the author's name and the draft number. A reference number and a word-processing filename will be assigned to the compound at the Meeting. The reference number should then be added after the year (FAO/94/ref no.). Add the extension .EV1 to the filename to show that it is draft 1 of the evaluation. The filename will consist of the pesticide name or an abbreviation of it with not more than 8 letters (the maximum allowed in a filename). The layout is shown below.

FAO/94/
AUTHOR
FILENAME.EV1
DRAFT 1

Avoid trade names in the description and table of use patterns; give the composition and formulation type, e.g. 100 g/kg WP, 200 g/l EC. Use CIPAC abbreviations for formulation types (see Annex 5).

Animal metabolism studies (including farm animal metabolism) appear in the METABOLISM AND ENVIRONMENTAL FATE section. For a new compound animal metabolism studies should be available to both the FAO Panel and the WHO Group. Metabolism in laboratory animals, normally rats, should be reviewed from the FAO Panel perspective. It should provide information which helps in the interpretation of farm animal metabolism and transfer studies. This information includes rates and pathways of excretion, identity and relative abundance of metabolites, and possible target organs for residues. Animal metabolism studies are sometimes supplied to the WHO Group only; the FAO Panel reviewer should specifically request these studies for a new compound if they have not been provided.

Animal metabolism studies can usefully be introduced with a paragraph which acts as a checklist of the information to be recorded.

Tissue, egg and excreta residues were measured in laying hens (groups of 5, each bird weighing 1.0-1.4 kg) dosed orally for 7 days by capsule with radiolabelled mancozeb ([^{14}C]ethylenediamine) equivalent to 3, 14 or 36 ppm mancozeb in the feed (study reference). The feed intake was 88-96 g/bird/day. Eggs and excreta were collected throughout, and birds were slaughtered 24 hours after the final dose for tissue collection.

Examine the animal metabolism in terms of the requirements for animal transfer studies (see JMPR Report 1993, 2.7 *Guidelines on the need for animal transfer studies in estimating pesticide maximum residue levels*). Draw conclusions from the animal metabolism which will assist interpretation of the animal transfer studies. Make statements about bioaccumulation and possible target tissues for residues.

A paragraph which acts as a checklist for experimental details can also be used to introduce plant metabolism studies.

A tomato crop was treated with radiolabelled mancozeb ([^{14}C]ethylenediamine) at 2.7 kg ai/ha, on nine occasions at approximately weekly intervals, and ripe tomatoes were harvested 5 days after the final treatment (study reference).

Draw conclusions from the plant metabolism studies which assist interpretation of the residue trials. State whether the residues are on the surface or within the tissues. Describe the mobility of the residues within the crop and say whether transfer from foliage to fruit,
root or other edible portion is likely. Draw attention to any plant metabolite which is not also an animal metabolite.

Explain the basis for a proposed residue definition under the section 'Residue Definition' within METHODS OF RESIDUE ANALYSIS. The explanation would normally take into account metabolism of the compound, practical regulatory analytical methods and other matters. The opinion of the WHO Expert Group should be sought on the toxicological importance of some metabolites.

Tables of residue data should generally be in the same order as commodities in the Codex Commodity Classification. The general order is fruits, vegetables, grasses, nuts and seeds, herbs and spices, feed commodities. Each commodity type should be further divided if the amount of information is large. The Codex order should generally be preserved, for example citrus fruits, pome fruits, stone fruits, berries and other small fruits, etc.

Where there are many residue tables, it is useful to list them at the beginning of the RESIDUES RESULTING FROM SUPERVISED TRIALS section, in numerical order.

Interpretation of the residue data should generally be in the report and the APPRAISAL section of the evaluation rather than in RESIDUES RESULTING FROM SUPERVISED TRIALS. The RESIDUES RESULTING FROM SUPERVISED TRIALS section should contain details which are not readily included in the tables but are still needed to assess the validity and relative importance of the results, for example the intervals between spray applications, the number of replicate plots, whether samples are replicates from the same or different plots or merely replicate analyses of the same sample, the size of plots, growing season, method of application, irrigation and, in animal trials and transfer studies, animal weights and ages. The reviewer's judgement is required to decide which details could influence the residues or the validity of the trials.

Include animal transfer studies in the section RESIDUES RESULTING FROM SUPERVISED TRIALS. Animal transfer studies use unlabelled compounds to establish the relationship between the levels of the residues in the feed and likely residues in tissues, milk and eggs.

Animal transfer studies can again be introduced by a paragraph which acts as a checklist of the information.

Groups of 10 laying hens (each bird weighing 1.0-1.3 kg) were fed aged mancozeb residues at nominal levels of 5, 15 and 50 ppm (1×, 3× and 10×) in the diet for 28 days (study reference). Eggs were collected each day for analysis. On day 29 six hens from each group were slaughtered for tissue collection. The remaining hens from each group were placed on a residue-free diet and slaughtered on days 36 and 43. Birds consumed 130 g feed each per day.

7.3. Table of GAP (Good agricultural practices or Approved uses)

Comparison of GAP with conditions in the supervised trials is a necessary part of the evaluation process. The table of GAP should be prepared in such a way that it allows easy comparison with supervised trials conditions. If at all possible fit the table to the normal portrait page rather than changing to landscape. (See also Section 4, *Tables*).

The first column in the table should list the crops, and all uses on each crop should be brought together. This facilitates evaluation of the residue data. Other columns in the table should list countries (in alphabetical order), application (number, rate, spray concentration) and PHI. Note that this is the general case and there is often a need for further information such as formulation, details of the use pattern (e.g. furrow treatment, seed treatment) crop growth stage, grazing withdrawal, etc. Listing by country was the practice in earlier monographs, but listing by crop is better for residue data evaluation.

An example is provided below.

Table 2. Registered uses of folpet on vegetables and cereals.

Crop	Country	Form	Application [1]				PHI, days
			Method	Rate kg ai/ha	Spray conc, kg ai/hl	Number	
Barley	France			1.5			21
Beans	Greece	WP	foliar	0.6-1.5	0.1-0.25	3-4	7
Beans	Portugal	WP	foliar		0.13	1-2	7
Beans, green	Spain	WP	foliar	1.6	0.16		21
Brassica vegetables	Italy	WP	foliar	0.35-0.40			10
Lettuce	France	WP	foliar	0.64			21-41[2]
Lettuce	Israel[3]	WP	foliar	2.0		weekly	11

[1] g: glasshouse use.

[2] Summer PHI 21 days, winter PHI 41 days.

[3] proposed registration.

Remarks can be added as footnotes, as in the example.

Suggested abbreviations for footnotes to the GAP table are:

a: aerial application
fg: field and glasshouse use
g: glasshouse use only
gs: growth stage restriction
Po: post-harvest use
pr: proposed registration
st: seed treatment
t: table grapes only
w: wine grapes only

If there are many uses it may be wise to split them into separate tables for fruits, vegetables, etc. If there are very large numbers of uses it may be necessary to establish separate tables for different groups of fruits, vegetables, etc, arranged according to the Codex Classification. Individual crops within the chosen groupings

should be arranged in alphabetical order.

Submissions to the JMPR often include the PHI in the table of national MRLs. The PHI is a part of GAP and should be included with other GAP information.

Use the following units for application rates and spray concentrations; note that abbreviations are without stops:

field treatment	kg ai/ha
grain treatment, post-harvest	g ai/t
furrow treatment	g ai/m
space fumigation	g ai/m^3
spray concentration	kg ai/hl

7.4. Tables of residue data

Express residue concentrations as mg/kg.

Deal with commodities in the order of the "Types" in the Codex Classification of Foods and Feeds, namely Fruits, Vegetables,..., and within the types in the order of the groups Citrus fruits, Pome fruits, Stone fruits, etc. A systematic and consistent presentation of data in a standardized order will make it easier for the reader to find information in a large evaluation, and assists Panel members to find the relevant data for discussion during the Joint Meeting.

Tables of residues resulting from supervised trials should be carefully prepared in such a way as to assist evaluations. (See also Section 4, *Tables*).

The table caption should be clear and comprehensive. It should normally mention the compound and the crops or crop groups, and indicate that the residues were found in supervised trials. If all the trials took place in one country or one year or with one formulation type it is better to put the information in the caption rather than use a column in the table. See, e.g., 1991 Evaluations, Azinphos-methyl Tables 6, 9a (pp. 17, 19).

Please always use the portrait, not landscape, format for residue tables. It is never necessary to use landscape if the sampling intervals are arranged vertically, and rarely necessary even if they are arranged horizontally. (See also Section 4, *Tables*). Use the "Header" function in the "Table edit" mode (Alt-F7, 4) to ensure that the table header appears at the top of each page of a multi-page table.

Space can be saved by using the first column of the table for three categories of information which cannot be confused, as shown below. The year is the year of the trial rather than the year of the report. Include references or study numbers in residue tables. It is important to identify the source of any reported data.

CROP Country, year	Application	Residues	Reference
BROCCOLI			
Germany, 1976			PBH360/77

Netherlands, 1980			RL401-90NL
CABBAGES, HEAD			
Canada, 1986			8013.86a
Germany, 1978			PBJ287/78

"Application" should normally include the formulation, the number of applications, and both the rate of application (kg ai/ha) and spray concentration (kg ai/hl), as shown below.

Application			
Form	No	kg ai/ha	kg ai/hl

The intervals after the final application at which the residues were found should be arranged in rows or columns to suit the set of trials. If metabolite residues are also reported, the table should be arranged so that it is quite clear which metabolite concentration relates to which parent concentration. Examples are given below of possible arrangements of the residues section of the table.

Residues, mg/kg, after PHI, days.				
0	4	7	14	21

Day	Residues, mg/kg[1]	
	Compound	Metabolite
0	1.3, 2.2	0.56, 0.85
4	1.1, 0.43	0.63, 0.31
7	0.76, 0.68	0.44, 0.10
14	0.14, 0.24	<0.05, 0.07
21	0.06, <0.05	<0.05, <0.05

[1] Underlined residues are from treatments according to GAP

Report individual residues as far as possible. If results are grouped avoid wide ranges. If there are a number of values at the same level they can be recorded as <0.05 (7), where there are 7 values of <0.05 mg/kg.

Underline residues resulting from treatments within GAP, but wherever such underlining is used its meaning must be explained in a footnote, a note in the table caption, or a note in the introduction to the tables. This is very helpful for people assessing the results, particularly when they are extensive, and allows other Panel members to see where the reviewer has judged data to be within or outside GAP.

Round numbers in tables to a practical level, usually 2 significant figures. A formulation concentration should be reported as 250 g ai/kg, not 250.00 g ai/kg. Residues should be reported as 0.36 and 4.5 mg/kg, not 0.363 and 4.47 mg/kg.

Near the LOD (limit of determination) rounding to 1 significant figure is recommended. For example, if the LOD is 0.05 mg/kg, report residue data from 0.05 to 0.09 mg/kg to 1 significant figure.

Avoid abbreviations if they make the table difficult to understand. If an abbreviation is unlikely to be familiar to readers and is not in the list of abbreviations at the beginning of the reports and evaluations, explain its meaning in a footnote.

Common specialized abbreviations which do not need explanation are: MRL, GAP, ADI, TMDI, LOD, CXL, kg ai/ha, kg ai/hl, mg/kg, g ai/t, g ai/m, g ai/m^3.

MRL	maximum residue limit (especially Codex Draft Maximum Residue Limit; cf CXL below)
GAP	good agricultural practice(s)
ADI	acceptable daily intake
TMDI	theoretical maximum daily intake
LOD	limit of determination
CXL	Codex Maximum Residue Limit (a Codex Draft Maximum Residue Limit becomes a CXL after its adoption by the Codex Alimentarius Commission)
kg ai/ha	kilograms active ingredient per hectare
kg ai/hl	kilograms active ingredient per hectolitre
mg/kg	milligrams per kilogram
g ai/t	grams active ingredient per tonne
g ai/m	grams active ingredient per metre
g ai/m^3	grams active ingredient per cubic metre

Note that the above abbreviations, and those of names of countries and organizations, are printed without stops (thus also UK, USA, FAO, CCPR) but general abbreviations in common use have stops (c., e.g., etc., i.e., viz.). Consult the list at the beginning of recent JMPR Reports and Residue Evaluations for the correct form of abbreviations. Note the form of *et al*. (italics, with stop after *al*).

Convert non-metric units to metric. Convert lb ai/acre to kg ai/ha, formulation concentration % to g/kg or g/l, residue concentration ppm to mg/kg. But express feed concentrations of active ingredients in feeding trials as ppm. This convention is used to avoid confusion between mg/kg feed and mg/kg body weight.

Use Codex commodity descriptions if possible (FAO/WHO, 1984-1990. *Guide to Codex Recommendations Concerning Pesticide Residues. Part 4. Codex Classification of Foods and Animal Feeds.* Also *Codex Alimentarius Volume 2 - 1993. Section 2. Codex Classification of Foods and Animal Feeds*.)

7.5. Processing studies

Set out tables carefully so that it is absolutely clear which sample is derived from which in the processing. Indicate the scale of the process by the weight of commodity processed. Note any problems with sampling or analysis. Provide a brief description of the field treatments in the trial and state the application rate in the study with respect to the maximum label rate (e.g. 5 times label rate).

Some commercial processes are quite complex. It may be useful to provide a flow diagram to explain the process. See 1991 Evaluations, Parathion, Figures 1-5 (pp 556-564).

A copy of the section on processing studies and residues in the edible portion of food commodities should be sent to reach the WHO Joint Secretary by the end of August. See also Section 12, *Actions before the Meeting*.

7.6. National Maximum Residue Limits

It will usually be necessary to summarize the information in a table. Do not include PHIs in this table.

The normal column headings will be Country, Commodity, MRL. Footnotes or an extra column will be required if countries are using different residue definitions.

8. Draft report, compounds (Section 4)

Reports are published separately from evaluations and so should be written without reference to them. But the reports are also used as the texts of the APPRAISAL section within the evaluations, and need to contain the logic and a full explanation for each recommendation.

At the top right side of the first page give the year, the author's name, the word-processor filename and the draft number as shown below. Add the extension .RE1 to the filename to show that it is draft 1 of the report. Add the reference number as in the draft evaluation. Annex 3 shows the format for a draft report.

FAO/94/
AUTHOR
FILENAME.RE1
DRAFT 1

Line-numbering of the document assists discussion at the Meeting. Introduce line-numbering to the draft report using the Format function (Shift-F8, 1, 5). Early drafts should be in 1½ spacing.

Include the FURTHER WORK OR INFORMATION and RECOMMENDATIONS sections in the report. The RECOMMENDATIONS section will not appear as such in the final report (although the individual recommendations are listed in Annex I), but is required for the APPRAISAL section of the evaluation.

The report should be complete in itself. Briefly explain the reasons for the review and summarize the information available. The subject order in the report should generally follow the order in the evaluation.

Provide in full the interpretation used to estimate a maximum residue level. Explain extrapolations, comparability, and any conditions of use, crop characteristics etc. which influence the interpretation. In particular, indicate the GAP on which a judgement is based if this is not obvious. Interpretations of residue data should be in the report. They will then also appear in the Appraisal.

Do not include tables in the text of the report section. Side headings should also generally not be used. When a report is extensive and deals with many commodities, crops and animals, it is helpful to underline the commodity name the first time it appears in each paragraph. At the end of the final paragraph on each

commodity or commodity group, state the recommendations of the Meeting. Examples of such sentences are:

The Meeting agreed to withdraw the recommendations for cherries (1 mg/kg), peaches (3 mg/kg) and plums (1 mg/kg).

The Meeting estimated a maximum residue level of 5 mg/kg for apples.

The Meeting estimated a maximum residue level for sweet corn of 0.1 mg/kg as being a practical limit of determination*.

The Meeting estimated a maximum residue level of 1 mg/kg for carrots to replace the previous recommendation (0.5 mg/kg).

The Meeting agreed to withdraw the previous recommendation for citrus fruits (5 mg/kg), to be replaced by recommendations for oranges (1 mg/kg) and mandarins (2 mg/kg).

The Meeting agreed to maintain the current recommendation of 0.2 mg/kg for potatoes.

The report should conclude with a sentence such as one of the following:

The residue levels shown in Annex I are recommended for use as MRLs.

The residue levels shown in Annex I are recommended for use as ERLs.

The changes shown in Annex I are recommended.

The withdrawals shown in Annex I are recommended.

The format of a report, with RECOMMENDATIONS and FURTHER WORK OR INFORMATION, is shown in Annex 3.

8.1. Recommendations

Please list commodities alphabetically in the RECOMMENDATIONS Table.
(Note that commodities were listed in the order of the Codex Classification until 1992. The change has been made to facilitate checking and comparison with the CCPR tables of MRLs, which are in alphabetical order.)

The Recommendations table for periodic review compounds should include all current MRLs. The table will then show whether each MRL is maintained, amended or withdrawn.

Any recommendations to withdraw MRLs should be entered in the table of Recommendations, which will be reproduced in Annex I to the report, and not merely mentioned as a recommendation in the text. A statement such as "the Meeting recommended the withdrawal of the MRL for pome fruits" is easily missed when Annex I is being compiled.

8.2. Further work or information

The items listed as required or desirable should be numbered if there are than one.

Required

All items listed as required should have a year proposed as the due date. Choose 2 years from the current Meeting as the due date in the absence of other information, e.g. a definite commitment by a country or company to provide information by a nominated date.

Each item listed as required should be tied to a TMRL. If the required information is not supplied by the due date, the Meeting can then recommend withdrawal of the TMRL.

TMRLs are generally not introduced for new compounds or periodic review compounds. Their use should be kept to a minimum.

Desirable

Information requested as desirable is not vital to the continued existence of MRLs, but is requested because it may assist in an explanation, support an extrapolation, or provide a more complete data base.

9. Draft report, general items (Sections 2 and 3)

At the top right side of the first page give the year, space for the section number (the number [2.XX or 3.XX] will be assigned during the Meeting), the author's name, the word-processor filename and the draft number, as shown below. Create the filename from a key word or words in the title of the report (using up to 8 letters) with the extension RE1 after the decimal point for draft 1 of the report item.

GENERAL REPORT
FAO/94/
AUTHOR
FILENAME.RE1
DRAFT 1

Introduce line-numbering (Shift-F8, 1, 5) into the draft report. The line numbers assist people to find parts of the document to be discussed. Early drafts should be in 1½ spacing.

Use the style and language of reports in recent years.

If the report is prepared in response to a recommendation or referral from the

CCPR state this in the first paragraph. Use a phrase such as `... at the 23rd (1991) Session of the CCPR ...' or if there is need to refer to a specific paragraph `... at the 23rd (1991) Session of the CCPR (ALINORM 91/24A, para.....).....'

10. Duties of the FAO Panel Chairman

The Chairman maintains liaison with the WHO Group Chairman on the progress of the Meeting, and together they arrange the schedule for joint sessions. The FAO Panel Chairman serves as either Chairman or Vice-Chairman of the Joint Meeting.

The Chairman ensures that all items are given reasonable discussion and tries to bring the Meeting to an agreement. Reasonable progress must be made, and the intention is to distribute drafts of general report items to the WHO Group by the Friday afternoon of the Joint Meeting and final drafts of most report items by the second Monday afternoon of the Joint Meeting.

11. Duties of the FAO Panel Rapporteur

The system has evolved where individual Panel members act as rapporteurs for discussion on any documents they have prepared. With the volume of work to be dealt with it would not be practical to channel all the work through one person.

The FAO Panel Rapporteur keeps in touch with the WHO Group Rapporteur, ensures that documents are exchanged, and keeps records of the exchanges.

The FAO Panel Rapporteur acts as the channel for typing and copying, keeps records of this and ensures that documents are not delayed.

12. Actions before the Meeting

A copy of the table of Recommendations should be sent to reach the editor (Mr Tony Machin, Boundary Corner, 2 Ullathorne Road, London SW16 1SN, ENGLAND, telephone and FAX: +4481 769 0435) by the end of August. If the table is extensive, a disk copy should also be sent.

A copy of the section on processing studies and residues in the edible portion of food commodities should be sent to reach the WHO Joint Secretary by the end of August. See also Section 7.5, *Processing studies*.

Prepare a brief list of questions on each compound and points for discussion by Panel members. The list should be available on the first day of the Panel meeting and should aim to focus attention on any difficult questions which have arisen during the review.

ANNEX 1

Format of a residue evaluation

FAO/94/
AUTHOR
FILENAME.EV1
DRAFT 1

COMPOUND (Codex number) [Bold caps, centred]

EXPLANATION [Bold caps, at left margin]
[The EXPLANATION section is not included for new compounds.]

IDENTITY [Bold caps, at left margin]
[The IDENTITY section is included only for new compounds and periodic review compounds. See Annex 2]

METABOLISM AND ENVIRONMENTAL FATE [Bold caps, at left margin]

Animal metabolism [Bold, initial cap only, at left margin]
Plant metabolism [Bold, initial cap only, at left margin]
Environmental fate in soil [Bold, initial cap only, at left margin]
Environmental fate in water/sediment systems [Bold, initial cap only, at left margin]

METHODS OF RESIDUE ANALYSIS [Bold caps, at left margin]

Analytical methods [Bold, initial cap only, at left margin]
Stability of pesticide residues in stored analytical samples [Bold, initial cap only, at left margin]
Residue definition [Bold, initial cap only, at left margin]

USE PATTERN [Bold caps, at left margin]

RESIDUES RESULTING FROM SUPERVISED TRIALS [Bold caps, at left margin]

FATE OF RESIDUES IN STORAGE AND PROCESSING [Bold caps, at left margin]

In storage [Bold, initial cap only, at left margin]
In processing [Bold, initial cap only, at left margin]

Residues in the edible portion of food commodities [Bold, initial cap only, at left margin]

RESIDUES IN FOOD IN COMMERCE OR AT CONSUMPTION [Bold caps, at left margin]

NATIONAL MAXIMUM RESIDUE LIMITS [Bold caps, at left margin]

APPRAISAL [Bold caps, at left margin]

RECOMMENDATIONS [Bold caps, at left margin]

Definition of the residue:

FURTHER WORK OR INFORMATION [Bold caps, at left margin]

Required (by [year]) [Heading underlined, initial cap only, at left margin]

Desirable [Underlined, initial cap only, at left margin]

.....REFERENCES [Bold caps, centred]

ANNEX 2

Identity section for new and periodic review compounds

COMPOUND (Codex number) [Bold caps, centred]

IDENTITY [Bold caps, at left margin]

ISO common name:
Chemical name
IUPAC: [Indented one Tab]
CA:
CAS No:
CIPAC No:
Synonyms:
Structural formula:
Molecular formula:
Molecular weight:

Physical and chemical properties [Bold, initial cap only, at left margin]

Pure active ingredient [Underlined, initial cap only, at left margin]

Vapour pressure: [Indented one Tab]
Melting point:
Octanol/water partition coefficient:
Solubility:
Specific gravity:
Hydrolysis:
Photolysis:

Technical material [Underlined, initial cap only, at left margin]

Purity: [Indented one Tab]
Melting range:
Stability:

Formulations [Bold, initial cap only, at left margin]

ANNEX 3

Format of a draft report item, previously evaluated compound

FAO/94/
AUTHOR
FILENAME.RE1
DRAFT 1

4.XX COMPOUND (Codex number) [Bold caps, at left margin]

RESIDUE AND ANALYTICAL ASPECTS [Bold caps, centred]

FURTHER WORK OR INFORMATION [Bold caps, at left margin]

Required (by [year]) [Heading underlined, initial cap only, at left margin]

Desirable

RECOMMENDATIONS [Bold caps, at left margin]

[Note: the RECOMMENDATIONS do not appear in the text of the report; they are added to the draft report item as a final detachable section for inclusion in the APPRAISAL, the text of which is normally identical to that of the report item. They are also included in Annex I of the report].

An example is shown below.

Definition of the residue: myclobutanil

Commodity		Recommended MRL (mg/kg)		PHI on which based, days
CCN	Name	New	Previous	
FS 0240	Apricot	0.2	-	7
MO 0812	Cattle, Edible offal of	0.01*	-	
MM 0812	Cattle meat	0.01*	-	
ML 0812	Cattle milk	0.01*	-	
FS 0013	Cherries	1	-	7
PE 0112	Eggs	0.01*	-	
FB 0269	Grapes	1	-	14
FS 0247	Peach	0.5	-	7
FS 0014	Plums (including Prunes)	0.2	-	14
FP 0009	Pome fruits	0.5	-	14
PO 0111	Poultry, Edible offal of	0.01*	-	
PM 0110	Poultry meat	0.01*	-	

DF 0014	Prunes	0.5	-	

The withdrawal of an MRL recommendation is shown as a "W" in the Table with a footnote.

Commodity		Recommended MRL (mg/kg)		PHI on which based, days
CCN	Name	New[1]	Previous	
FS 0240	Apricot	W	0.2	
FS 0013	Cherries	0.1	-	7

[1] W: the previous recommendation is withdrawn.

ANNEX 4

Format of a draft report item, new compound

FAO/94/
AUTHOR
FILENAME.RE1
DRAFT 1

4. COMPOUND (number) [Bold, at left margin]

Systematic IUPAC name [Centred, but will probably occupy most of line]

Paragraph(s) describing the uses of the compound. [First paragraph starts at left margin; subsequent paragraphs after one Tab]

The compound was considered for the first time by the present Meeting.

RESIDUE AND ANALYTICAL ASPECTS [Bold caps, centred]

ANNEX 5

Codes for formulations

(CIPAC Handbook D, 1988, Appendix C)

AB	Grain bait
AE	Aerosol dispenser
AL	Other liquids to be applied undiluted
BB	Block bait
BR	Briquette
CB	Bait concentrate
CG	Encapsulated granule
CS	Capsule suspension
DC	Dispersible concentrate
DP	Dustable powder
DS	Powder for dry seed treatment
EC	Emulsifiable concentrate
ED	Electochargeable liquid
EO	Emulsion, water in oil
ES	Emulsion for seed treatment
EW	Emulsion, oil in water
FD	Smoke tin
FG	Fine granule
FK	Smoke candle
FP	Smoke cartridge
FR	Smoke rodlet
FS	Flowable concentrate for seed treatment
FT	Smoke tablet
FU	Smoke generator
FW	Smoke pellet
GA	Gas
GB	Granular bait
GE	Gas generating product
GG	Macrogranule
GP	Flo-dust
GR	Granule
GS	Grease
HN	Hot fogging concentrate
KK	Combi-pack solid/liquid*
KL	Combi-pack liquid/liquid*
KN	Cold fogging concentrate
KP	Combi-pack solid/solid*
LA	Lacquer
	Solution for seed treatment
MG	Microgranule
	Oil miscible flowable concentrate (oil
OL	Oil miscible liquid
OP	Oil dispersible powder
PA	Paste
PB	Plate bait
	Gel concentrate or paste concentrate
PO	Pour-on
PR	Plant rodlet
	Seed coated with a pesticide
RB	Bait (ready to use)
SA	Spot-on
SB	Scrap bait
	Suspension concentrate(= flowable
SE	Suspo-emulsion
	Water soluble granule
SL	Soluble concentrate
SO	Spreading oil
SP	Water soluble powder
	Water soluble powder for seed
	Ultra-low volume (ULV) suspension
TB	Tablet
TC	Technical material
TK	Technical concentrate
TP	Tracking powder
	Ultra-low volume (ULV) liquid
VP	Vapour releasing product
WG	Water dispersible granule
WP	Wettable powder
	Water dispersible powder for slurry
XX	Others

* Special two-letter codes for twin-packs.

INDEX

[i.] A value based on toxicological data. It represents tolerable human intake of a former agricultural pesticide that may occur as a contaminant in food, drinking water and the environment.

[ii.] The monographs on those compounds reviewed in 1994 whose evaluations were postponed from 1993 (see section 2.1 - Amendments to the agenda) have not been converted to the new format

[iii.] A TADI was established for propylenethiourea in 1993, but no recommendation was made to convert the existing GLs to TMRLs. The 1994 Meeting withdrew the GLs, which are listed for information

[iv.] T = Toxicology
R = Residue and analytical aspects