# Pesticide residues in food - 1988

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# REPORT 1988

FAO
PLANT
PRODUCTION
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PAPER

92


FOOD
AND
AGRICULTURE
ORGANIZATION
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UNITED NATIONS

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Report of the Joint Meeting of the
FAO Panel of Experts on Pesticide Residues
in Food and the Environment
and a WHO Expert Group on Pesticide Residues
Rome, 19-28 September 1988

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Monographs containing summaries of residue data and toxicological data consideredc at the 1988 JMPR, together with recommendations, are available upon request from FAO under the title:

Pesticide residues in food — 1988
Evaluations 1988
Part I: Residues
Part II: Toxicology
FAO Plant Production and Protection Paper



This report contains the collective views of two international groups of experts and does not necessarily represent the decisions or the stated policy of the Food and Agriculture Organization of the United Nations or of the World Health Organization.

INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

The preparatory work for the toxicological evaluations of pesticide residues carried out by the WHO Expert Group on Pesticide Residues for consideration by the FAO/WHO Joint Meeting on Pesticide Residues in Food and the Environment is actively supported by the International Programme on Chemical Safety (IPCS).
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1988 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 1988

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## ABBREVIATIONS WHICH MAY BE USED IN THIS REPORT

(n.b.: chemical elements and pesticides are not included in this list)

| | |
|---|---|
| AChE | acetylcholinesterase |
| ADI | Acceptable Daily Intake |
| TADI | Temporary Acceptable Daily Intake |
| ai | active ingredient |
| approx. | approximate |
| at. wt. | atomic weight |
| b.p. | boiling point |
| bw | body weight |
| c | centi - ($\times 10^{-2}$) |
| °C | degree Celsius (centigrade) |
| CCPR | Codex Committee on Pesticide Residues |
| cm | centimetre |
| CNS | central nervous system |
| cu | cubic |
| DL | racemic (optical configuration, a mixture of dextro- and laevo-; preceding a chemical name) |
| EC | emulsion concentrate |
| ERL | extraneous residue limit |
| $F_1$ | filial generation, first |
| $F_2$ | filial generation, second |
| f.p. | freezing point |
| FAO | Food and Agriculture Organization of the United Nations |
| g | gram |
| µg | microgram |
| GAP | good agricultural practice |
| G.I. | gastro-intestinal |
| GPC | gel-permeation chromatography |
| GLC | gas-liquid chromatography |
| h | hour(s) |
| ha | hectare |
| Hb | haemoglobin |
| i.m. | intramuscular |
| i.p. | intraperitoneal |
| IR | infrared |
| i.v. | intravenous |
| JMPR | Joint Meeting on Pesticide Residues (Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues) |
| k | kilo- ($\times 10^3$) |
| kg | kilogram |
| l | litre |
| $LC_{50}$ | lethal concentration, 50% |

| | |
|---|---|
| LD | lethal dose |
| $LD_{50}$ | lethal dose, median |
| m | metre |
| mg | milligram |
| $\mu$m | micrometre (micron) |
| min | minute (s) |
| ml | millilitre |
| MLD | minimum lethal dose |
| mm | millimetre |
| M | molar |
| mo | month(s) |
| m.p. | melting point |
| MRL | Maximum Residue Limit (This term replaces "tolerance") |
| TMRL | Temporary Maximum Residue Limit |
| N | normal (concentration) |
| no. | number |
| NOEL | no-observed-effect level |
| NOAEL | no-observed-adverse-effect level |
| o | ortho (indicating position in a chemical name) |
| 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.) |
| s.c. | subcutaneous |
| SD | standard deviation |
| SE | standard error |
| sp./spp. | species (only after a generic name) |
| sp gr | specific gravity |
| sq | square |
| t | tonne (metric ton) |
| TADI | Temporary Acceptable Daily Intake |
| tert | tertiary (in a chemical name) |
| THS | thyroid-stimulating hormone |
| TLC | thin-layer chromatography |
| TMRL | Temporary Maximum Residue Limit |
| UV | ultraviolet |
| v/v | volume ratio (volume per volume) |
| WHO | World Health Organization |
| wk | week |
| WP | wettable powder |
| wt | weight |
| wt/vol | weight per volume |
| w/w | weight per weight |
| yr | year |
| < | less than |
| $\leq$ | less than or equal to |
| > | greater than |
| $\geq$ | greater than or equal to |
| * | at or about the limit of determination |

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* First evaluation

# PESTICIDE RESIDUES IN FOOD

## Report of the 1988 Joint FAO/WHO Meeting of Experts

### 1. Introduction

A joint meeting of an 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 1988. The meeting was opened by Dr C.H. Bonte-Friedheim, Assistant Director-General, FAO, on behalf of the Directors-General of FAO and WHO. The FAO Panel had met in preparatory sessions from 15 to 17 September.

The meeting was held in pursuance of recommendations made by previous meetings and accepted by the governing bodies of FAO and WHO that studies should be undertaken jointly by experts to evaluate possible hazards to 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 for man (ADIs), maximum residue limits (MRLs) and general principles of evaluation for the various pesticides considered. The supporting documents 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 of 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 man for the pesticides. The recommendations of the joint meeting, including requests for further research and information, are proposed for use by Member Governments of the respective agencies and other interested parties.

Dr Bonte-Friedheim also informed the meeting of the death of Professor Gerhard Bressau of the Federal Republic of Germany in June 1988 and expressed his deep regret. He called for a minute of silence in his memory. Professor Bressau, a pesticide chemist of international reputation, had made very valuable contributions to the work of the Joint Meetings for many years.

## 2. GENERAL CONSIDERATIONS

### 2.1 PRINCIPLES FOR THE SAFETY ASSESSMENT OF PESTICIDE RESIDUES IN FOOD

As stated in section 2.4 of the 1987 JMPR report, a document to consolidate and update the methodology used by the WHO Expert Group on Pesticide Residues at Joint FAO/WHO Meetings on Pesticide Residues is being developed. The working title of this document is "Principles for the Safety Assessment of Pesticide Residues in Food". The International Programme on Chemical Safety (IPCS) is sponsoring the preparation of this document, with the active participation and support of the Canadian Health Protection Branch. A draft of this document is being modified in response to comments. It is anticipated that a final draft will also be reviewed by the WHO Expert Group of the 1989 JMPR, after which it will be published by WHO.

### 2.2 GUIDELINES FOR PREDICTING DIETARY INTAKE OF PESTICIDE RESIDUES

The meeting considered the above-mentioned document (WHO/EHE/FOS/88.2) which it recognized as a refinement of previous approaches to the estimation of dietary exposure to pesticide residues. The meeting noted the cautionary statements regarding use of the proposed approach involving Theoretical Maximum Daily Intake (TMDI), Estimated Maximum Daily Intake (EMDI) and Estimated Daily Intake (EDI).

The meeting was informed that the necessary indices of food consumption were being developed so that TMDI and EMDI calculations could be undertaken for international consideration. It was noted that EDI estimates would remain a national matter. Recognizing that TMDI calculations would yield misleading estimates of dietary exposure to pesticide residues, the meeting recommended that TMDI calculations should not be undertaken until suitable EMDI calculations could also be performed. Previous JMPR Evaluations contain much information on residues in food as consumed in addition to that on residues in raw agricultural commodities.

The meeting also recommended the more systematic development of such data which were needed for any more realistic estimation of pesticide residue intake. (See Section 2.3.)

### 2.3 GUIDELINES FOR DEVELOPING DATA ON PESTICIDE RESIDUES IN FOOD AS CONSUMED

The meeting noted that the CCPR ad hoc Working Group on the Development of Residue Data and Sampling had expressed the opinion that information on the effects of preparation, processing and cooking on pesticide residues was vital in obtaining an accurate estimate of the dietary intake of pesticide residues (Alinorm 89/24, para 218) and had drafted guidelines on the subject. Following discussion at the CCPR it was agreed that, after taking into account comments from countries, a revised draft of the above guidelines should be handed over to the JMPR for further development as the subject of the Guidelines was relevant to estimates of dietary intake and to FAO work on registration requirements.

The meeting received the draft guidelines and considered that FAO should finalise them within the framework of the FAO International Code of Conduct on the Distribution and Use of Pesticides so that they can be published in the appropriate guideline.

## 2.4 DEFINITIONS OF GOOD AGRICULTURAL PRACTICE (GAP) AND MRL

The 20th Session of the CCPR (1988) held detailed discussions on the definitions of good agricultural practice (GAP) and MRL and agreed to send the proposed definitions (Alinorm 87/24, Appendix V) to governments and the JMPR for comments.

The meeting agreed that the proposed definitions were complex and need to be expressed more simply. There were also some points which needed correction.

GAP

For the purposes of the JMPR, a suitable working definition would be:

"Good agricultural practice in the use of pesticides (GAP) includes the nationally *authorised safe uses of pesticides under actual conditions, necessary for effective* and reliable pest control. It encompasses a range of levels of pesticide applications up to the highest authorised use, applied in a manner which leaves a residue which is the smallest amount practicable."

Explanatory note:
Authorised safe uses include nationally registered or recommended uses, which take into account public and occupational health and environmental safety considerations. (See definition of registration in FAO International Code of Conduct on the Distribution and Use of Pesticides.)

Actual conditions include any stage in the production, storage, transport, distribution and processing of food commodities and animal feed.

MRL

The meeting agreed with the proposed definition but suggested some changes to the explanatory note, as follows:

1. Renumber, so that para (2) is no longer governed by the phrase "Codex MRLs, ..... derived from:" and becomes a second note.

2. Para (1) a): delete "and estimation of an acceptable daily intake (ADI)".

3. Para (1) b) should be changed to describe more accurately the estimations made by the JMPR. All pertinent residue data are reviewed, not only data from supervised trials reflecting national good agricultural practices. It is important that data from supervised trials conducted at the highest nationally recommended, authorised or registered use are included in the reviews.

   Para (1) b) should therefore be changed as shown below, where the changes are underlined.

4. Para (2), now Explanatory Note (2): delete "which" in line 3.

The revised note now reads as follows:

Explanatory Notes:
(1) Codex MRLs, which are primarily intended to apply in international trade, are derived from estimations made by the JMPR following

a) toxicological assessment of the pesticide and its residue
b) review of residue data from supervised trials including those reflecting national good agricultural practices. Data from supervised trials conducted at the highest nationally recommended, authorised or registered uses are included in the review. In order to accommodate variations in national pest control requirements, Codex MRLs take into account the higher levels shown to arise in such supervised trials, which are considered to represent effective pest control practices.

(2) Consideration of the various dietary residue intake estimates and determinations both at the national and the international level in comparison with the ADI, should indicate that foods complying with Codex MRLs are safe for human consumption.

## 2.5 RECOMMENDATIONS OF PREVIOUS JOINT MEETINGS

The meeting reviewed the recommendations of the Joint Meetings held from 1978 to 1987 to determine whether any that had not been satisfied should still remain in force. Of the 37 recommendations made during this period, the meeting identified the three listed below which it considered to be in this category. These are also repeated, together with the recommendations of the present meeting, in section 5.

Previous recommendations

1981

2. WHO should investigate the possibility of providing a mechanism for independent assessment of disputed pathological findings.

1982

5.2 The meeting discussed the value and availability of the toxicological information in respect of public health, environmental toxicology and industrial medicine and recommended that the Directors-General of FAO and WHO, in consultation with the Manager of IPCS, should review existing procedures for the publication of the reports and evaluations of the JMPR to improve their accessibility.

1985

5.7 Because some of the oncogenicity studies in mice reviewed by the meeting did not include haematology determinations, the meeting recommends that haematology determinations in future oncogenicity studies in mice should be performed at least at termination.

## 2.6 ADIs AND TEMPORARY ADIs

The meeting considered its use of ADIs and temporary ADIs. It agreed that future Joint Meetings should not allocate temporary ADIs for new compounds. Further, it anticipated that an ADI will not be allocated in the absence of an adequate data base.

Relevant data that become available on previously reviewed compounds will be considered. ADIs will then be confirmed, revised or withdrawn.

Generally, a monograph should be published whenever data are evaluated.

## 2.7 EXPRESSION OF RESIDUE LIMITS

The values used to express residue limits were defined at the JMPR in 1973. They relate to the accuracy that could be expected in the determination of the original tolerances.

In its deliberations, the meeting considered the errors involved in both sampling and analysis of samples.

Maximum residue levels based on geometrical progression appeared more logical by virtue of the fact that the percentage error in residue analysis is not constant but increases with decreasing concentration. Below 0.01 mg/kg levels approach the limit of determination of pesticides in foods, while above 1 mg/kg owing to improved accuracy, values of 10, 15, 20 and 25 mg/kg have greater statistical value. Therefore, it is the range between 0.1 and 10 mg/kg that is of principal interest in establishing values for limits.

Given that shortcomings in accuracy can be considered as the sum of the analytical (systematic) and sampling errors, the Horowitz equation, derived from collaborative studies, provides a relation between concentration and error (coefficient of variation). The following concentrations, in mg/kg, have the coefficients of variation shown in parentheses: 0.001 (45%), 0.01 (32%), 0.1 (23%), 1.0 (16%), 10 (11%) and 100 (8%).

These can be considered as the minimum errors relating to analytical procedures, since they are associated with collaborative interlaboratory studies. In practice, errors in routine analytical laboratories will be greater. Assuming an error of $\pm 2$ standard deviations, one arrives at the values given in Annex III, which suggest that the values

0.01, 0.04, 0.1, 0.2, 0.5, 1.0, 2.0, 3.0, 5.0, 10, 15, 20, 30 mg/kg

are adequate to cover the range of levels 0.01 to 30 mg/kg.

Very few reliable data are available on the errors associated with sampling, which will be additive and vary with the crop and analyte. At best, sampling error can be judged equal to the analytical error, and would serve to expand the ranges in Annex III. Given this, the above values can be slightly changed to:

0.01, 0.05, 0.1, 0.2, 0.5, 1.0, 2.0, 3.0, 5.0, 10, 15, 20, 30 mg/kg

These intervals are in fact very similar to those suggested by the JMPR in 1973. In order to complete this review, it is necessary to obtain more accurate data on interlaboratory analytical studies as well as on the sampling errors involved in various matrices.

The meeting at this time recommends the continued use of the existing MRL intervals, pending the outcome of the request for more data, particularly those associated with sampling errors.

## 2.8 MATTERS REFERRED TO THE JMPR BY THE CCPR - PROCEDURES

The meeting reviewed the relationship between the JMPR and the CCPR and noted that, sometimes, the recommendations of the JMPR on MRLs, residue descriptions and related matters were not acceptable to one or more countries and on occasion this has resulted in matters being referred back to the JMPR by the CCPR.

The meeting emphasised that recommendations could only be based on information available to the JMPR and that requests or suggestions from the CCPR for changes in recommendations should always be accompanied by a clear statement of the reason for the referral, and must be supported by the data necessary for the JMPR to (re-)consider the issue.

The meeting requested that the secretariats of the JMPR and CCPR should consider the mechanism and timetable required to achieve the above in all relevant cases of referrals.

## 2.9 REPORT OF THE 20TH SESSION OF THE CODEX COMMITTEE ON PESTICIDE RESIDUES (ALINORM 89/24)

The meeting noted the report of the 20th Session of the CCPR, in particular items drawn to the attention of the JMPR. Several of these were considered at the meeting and are dealt with in the appropriate sections of this report, as follows.

1. General Items:

- Reconsideration of adherence to an approximately geometrical progression (0.1, 0.2, 0.5, 1 etc.) when recommending MRLs (para. 18); see 2.7.

- Consideration of draft revised definitions of GAP and MRL (Alinorm 89/24, Appendix V) proposed by the CCPR at its 20th Session (para. 22); see 2.4.

- The JMPR was requested to indicate the individual commodities on which its estimates of group MRLs are based (para. 56).

- The JMPR was requested to consider the document "Guidelines for developing data on pesticide residues in food as consumed" (para. 219); see 2.3.

2. Questions on the following individual compounds:

- benalaxyl (paras. 170, 173); see 4.3
- bendiocarb (para. 142). The question could not be considered owing to lack of data.
- bromide ion (para. 53); see 4.6
- carbendazim (para. 82); see 4.7
- chlorpyrifos (para. 65). The question could not be considered owing to lack of data.
- cyhexatin (para. 81); see 4.10
- deltamethrin (paras. 137, 141); see 4.12
- dimethipin (para. 162); see 4.14
- dimethoate (para. 70); see 4.15
- etrimfos (para. 126); see 4.17
- ethylenethiourea (paras. 105, 106); see 4.16
- fenitrothion (para. 72). The question could not be considered owing to lack of data.
- flucythrinate (paras. 165, 167); see 4.20
- glyphosate (paras. 181, 183, 184); see 4.21
- imazalil (para. 111). The question could not be considered owing to lack of data.

- methomyl (para. 94); see 4.26
- omethoate (para. 77); see 4.28
- permethrin (para. 123) The question could not be considered owing to lack of data.
- 2-phenylphenol (para. 78). The question could not be considered owing to lack of data.
- phosmet (para. 103); see 4.32
- prochloraz (paras. 151, 152); see 4.34
- thiodicarb (para. 168); see 4.35
- triadimefon (paras. 133, 134); see 4.40
- vinclozolin (paras. 186, 188); see 4.42

- the request to predict dietary intakes for permethrin (para 125), pirimiphos-methyl (para 90), triazophos (para 155) and vamidothion (para 85) could not be satisfied because neither information on diets nor a mechanism for making the calculations has been fully developed.