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Pesticide residues in food

Report of the 1976 Joint Meeting of the FAO Panel of Experts on Pesticide Residues and the Environment and the WHO Expert Group on Pesticide Residues



Published by FAO and WHO

| | |
|---|-----|
| World Health Organization Technical Report Series | 612 |
| FAO Food and Nutrition Series | 9 |
| FAO Plant Production and Protection Series | 8 |

World Health Organization Geneva 1977

Monographs containing toxicological evaluations and decisions and maximum limits for pesticide residues in food, together with information on identity of the pesticides considered, are issued by FAO under the title:

1976 Evaluations of Some Pesticide Residues in Food (FAO/AGP: 1977/M/5).

Copies can be obtained from the Distribution and Sales Section, FAO, Via delle Terme di Caracalla, Rome 00100, Italy.

ISBN 92 4 120612 8

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PRINTED IN SWITZERLAND

CONTENTS

| | Page |
|--|------|
| 1. Introduction | 7 |
| 2. General considerations | 8 |
| 2.1 Modification of the agenda | 8 |
| 2.2 General principles for allocating ADIs | 8 |
| 2.3 Deficiencies in toxicological data | 9 |
| 2.4 Acquisition and availability of data | 9 |
| 2.5 Presentation of recommended maximum residue limits | 10 |
| 2.6 Maximum residue limits in processed foods | 10 |
| 3. Specific problems | 10 |
| 3.1 Consideration of technical and formulated products | 10 |
| 3.2 Aliesterase-inhibiting compounds | 11 |
| 3.3 Reversible cholinesterase inhibition | 11 |
| 3.4 Chlordimeform | 12 |
| 3.5 Leptophos | 12 |
| 4. Evaluation of data for acceptable daily intake | 13 |
| 4.1 Pesticides evaluated for the first time | 13 |
| 4.2 Pesticides previously evaluated | 15 |
| 5. Evaluation of data for residue limits | 16 |
| 5.1 Pesticides not previously considered for establishment of maximum residue limits | 16 |
| 5.2 Pesticides reviewed in the light of new information | 16 |
| 5.3 Compounds not considered | 17 |
| 6. Comparison of potential daily intakes of pesticide residues with their accept- able daily intakes | 17 |
| 7. Future work | 18 |
| 8. Recommendations | 18 |
| References | 19 |
| Annex 1. Acceptable daily intakes, residue limits, and guideline levels recom- mended at the 1976 Meeting | 22 |
| Annex 2. Further work or information required (or desirable) | 28 |

1976 JOINT MEETING OF THE FAO PANEL OF EXPERTS ON PESTICIDE RESIDUES AND THE ENVIRONMENT AND THE WHO EXPERT GROUP ON PESTICIDE RESIDUES

Rome, 22-30 November 1976

Members of the FAO Panel of Experts on Pesticide Residues and the Environment

- Dr A. F. H. Besemer, Head, Pesticides Division, Plant Protection Service, Ministry of Agriculture, Wageningen, Netherlands
- Professor G. Bressau, Head, Pesticides Unit, Division of Food Chemistry, Federal Health Office, Berlin (West)
- Mr F. Bro-Rasmussen, National Food Institute, Division of Pesticides and Contaminants, Søborg, Copenhagen, Denmark (*Rapporteur*)
- Mr J. G. Cummings, Chief, Chemistry Branch, Registration Division, Office of Pesticide Programs, Environmental Protection Agency, Washington, DC, USA
- Mr J. T. Snelson, Pesticides Co-ordinator, Department of Primary Industry, Canberra, Australia (*Chairman*)
- Dr E. M. Thain, Deputy Director, Tropical Products Institute, London, England

Members of the WHO Expert Group on Pesticide Residues

- Dr V. Beneš, Chief, Toxicology Department, Institute of Hygiene and Epidemiology, Prague, Czechoslovakia (*Rapporteur*)
- Mr D. J. Clegg, Pesticide Section, Toxicological Evaluation Division, Health Protection Branch, Department of National Health and Welfare, Ottawa, Canada (*Vice-Chairman*)
- Professor I. Nir, Department of Clinical Pharmacology, Ministry of Health, Jerusalem, Israel
- Professor F. K. Ohnesorge, Pharmacological and Technological Institute, Düsseldorf, Federal Republic of Germany
- Professor C. Schlatter, Institute of Toxicology, Federal Polytechnic, and University of Zürich, Schwerzenbach, Zürich, Switzerland
- Dr M. van Logten, Laboratory for General Toxicology, National Institute of Public Health, Bilthoven, Netherlands

Observer invited by FAO

- Dr A. J. Pieters, Chairman, Codex Committee on Pesticide Residues, Directorate of Public Health, Foodstuffs Division, Leidschendam, Netherlands

Secretariat

- Dr C. Agthe, Chief, Food Safety, WHO, Geneva, Switzerland
- Dr R. Baron, Health Effects Research Laboratory, Environmental Research Center, United States Environmental Protection Agency, Research Triangle Park, NC, USA (*Temporary Adviser*)
- Dr L. G. Ladomery, Joint FAO/WHO Food Standards Programme, Rome, Italy
- Dr R. Leski, Chemical Residue and Pollution Section, Joint FAO/IAEA Division of Atomic Energy in Agriculture, International Atomic Energy Agency, Vienna, Austria
- Mr A. F. Machin, Senior Research Officer, Central Veterinary Laboratory, Ministry of Agriculture, Weybridge, England (*Consultant*)
- Dr E. Middleton, Food Directorate, Health Protection Branch, Department of National Health and Welfare, Ottawa, Canada (*Temporary Adviser*)
- Dr Orville E. Paynter, Chief, Toxicology Branch, Registration Division, Office of Pesticide Programs, US Environmental Protection Agency, Washington, DC, USA (*Temporary Adviser*)
- Dr E. E. Turtle, Pesticides Specialist, Plant Protection Service, FAO, Rome, Italy (*Joint Secretary*)
- Dr G. Vettorazzi, Scientist, Food Safety, WHO, Geneva, Switzerland (*Joint Secretary*)

1. The first part of the document discusses the importance of maintaining accurate records of all transactions and activities. It emphasizes that this is crucial for ensuring transparency and accountability in the organization's operations.

2. The second part of the document outlines the various methods and tools used to collect and analyze data. It highlights the need for consistent data collection procedures and the use of advanced analytical techniques to derive meaningful insights from the data.

3. The third part of the document focuses on the role of technology in data management and analysis. It discusses how modern software solutions can streamline data collection, storage, and analysis processes, thereby improving efficiency and accuracy.

4. The fourth part of the document addresses the challenges associated with data management, such as data quality, security, and privacy. It provides strategies to mitigate these risks and ensure that the data remains reliable and secure throughout its lifecycle.

5. The fifth part of the document concludes by summarizing the key findings and recommendations. It stresses the importance of ongoing monitoring and evaluation to ensure that the data management processes remain effective and aligned with the organization's goals.

PESTICIDE RESIDUES IN FOOD

Report of the 1976 Joint FAO/WHO Meeting

A Joint Meeting of the FAO Panel of Experts on Pesticide Residues and the Environment and the WHO Expert Group on Pesticide Residues was held in Rome from 22 to 30 November 1976. The Meeting was opened by Mr F. Albani, Director of the Plant Protection and Production Division of the Food and Agriculture Organization on behalf of the Directors-General of the Food and Agriculture Organization and of the World Health Organization. The FAO Panel had already met in preparatory sessions from 17 to 20 November 1976.

In his opening statement, Mr Albani mentioned that recent searching reviews of the objectives, priorities, and findings of FAO and WHO had confirmed the importance of the work of the Joint Meetings of experts. Since the previous Meeting, the title of the FAO group had been changed from "Working Party of Experts on Pesticide Residues" to "Panel of Experts on Pesticide Residues and the Environment". This had been done in compliance with recommendations of an *ad hoc* Governmental Consultation on Pesticides held in Rome in April 1975, and no immediate departure from the past practice of holding regular Joint Meetings in which the occurrence and toxicology of residues in foods were evaluated as a basis for providing advice to Member governments was envisaged.

1. INTRODUCTION

The Joint Meeting was held in pursuance of recommendations made at previous meetings and accepted by 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 (FAO/WHO, 1965a, 1967a, 1968a, 1969a, 1970a, 1971a, 1972a, 1973a, 1974a, 1975a, 1976a) contain information on acceptable daily intakes (ADIs), residue limits, and general principles of evaluation for the various pesticides considered. The supporting documents (FAO/WHO, 1965b, 1965c, 1967b, 1968b, 1969b, 1970b, 1971b, 1972b, 1973b, 1974b, 1975b, 1976b) contain detailed

monographs on these pesticides and include comments on analytical methods.

The present Joint Meeting was convened to consider a further number of pesticides together with requests of both a general and specific nature.

During the Meeting the FAO Panel of Experts was primarily responsible for :

- (a) reviewing data on certain pesticides and their residues ;
- (b) proposing pesticide residue limits and recommending methods of analysis.

The WHO Expert Group was primarily responsible for :

- (a) reviewing toxicological and related data on certain pesticides and their residues ;
- (b) establishing, where possible, ADIs for man for those pesticides.

The Joint Meeting also evaluated potential daily intakes of the pesticides in relation to their ADIs and made a number of general recommendations, some of which were designed to indicate, stimulate, and coordinate lines of research.

2. GENERAL CONSIDERATIONS

2.1 Modification of the agenda

The agenda was modified to permit consideration of fenitrothion, carbaryl, diquat, and phosalone in relation to residue data, and chlor-dimeform and leptophos in the light of potential toxicological hazards.

2.2 General principles for allocating ADIs

Like its predecessors, the Meeting took account of the principles enumerated in the reports of previous Meetings relating to the allocation of ADIs and the formulation of other decisions based on toxicological considerations. In particular, it reemphasized the principles previously laid down for allocating ADIs or temporary ADIs for pesticides. The need for obtaining certain data in order to establish an ADI was reaffirmed. These data include the results of short- and long-term studies. Additional data from special studies on carcinogenicity,

mutagenicity, reproduction teratology, observations in man, etc., as well as information on metabolism, pharmacokinetics, and biochemical effects should also be available. Only in exceptional circumstances may an ADI be established in the absence of long-term studies and certain of the studies mentioned above. A temporary ADI may be allocated in cases where the studies needed for a definite evaluation have not been undertaken or are inadequate, but where there is no concern about the safety of the compound that would preclude the daily intake of small quantities for a limited period of time.

In cases where the information is insufficient for the evaluation of the compound, no ADI can be given, but the absence of an ADI does not necessarily mean that the compound is unsafe. In some cases, however, an ADI is not allocated because the data indicate a major toxicological risk.

2.3 Deficiencies in toxicological data

The Joint Meeting was unable to set ADIs for two newly considered compounds and for three previously considered compounds. In three of these instances no toxicological data were available to the Meeting, whilst in the others the data were inadequate. One temporary ADI was withdrawn in the absence of adequate toxicological data.

The Meeting was, however, able to propose or affirm residue limits, which then had to be designated as guideline levels.

It thus appears that the availability or generation of toxicological data is not on a par with that of residue data, and concern was expressed about this situation.

In addition, there was concern about the guideline levels, and their temporary nature, and the need for a clear distinction between such levels and the maximum residue limits was underlined.

2.4 Acquisition and availability of data

The Meeting reaffirmed that it could not allocate ADIs or establish residue limits on the basis of abstracts or brief summaries of experimental data. To allocate ADIs or establish residue limits, a full review of all the data is necessary.

The Meeting appreciated the large volume of information furnished for its consideration by government agencies, industry, the international Union of Pure and Applied Chemistry, and others. It reaffirmed its policy of reviewing relevant published and unpublished information. The Meeting further referred to FAO and WHO all matters relating to

the acquisition and availability of data and reaffirmed that it would not take into account any information that could not be made available for consideration by all its members.

2.5 Presentation of recommended maximum residue limits

The Committee adhered to the principles laid down in the 1970 and 1974 Joint Meeting Reports (FAO/WHO, 1970a, 1974a), but felt that there was an increasing need for an unambiguous description and uniform presentation of the food items and food groups. In view of the growing number of maximum residue limits it is desirable that a system be developed, preferably before the next Joint Meeting, providing uniformity in the nomenclature of food commodities and groups of food commodities and in their presentation.

In addition it is desirable to compile a dossier accurately indicating in what form different food commodities served as the basis for recommending maximum residue limits, e.g., whether cole crops were used before or after removal of the outer leaves or strawberries with or without the calyx, etc.

2.6 Maximum residue limits in processed foods

The Joint Meeting discussed the question of maximum residue limits for processed foods. It concluded that it should continue to recommend maximum residue limits for some of these foods, e.g., cereal products and vegetable and animal fats, which are important items in international trade. The Meeting recognized that there is a considerable trade in manufactured foods based on fruits, vegetables, cereals, meat, and fish, for example, and that these products can contain pesticide residues derived from the raw materials used. The variety of forms under which the products are offered makes it impossible to recommend residue limits for each of them. In the absence of such limits for processed foods, appropriate limits should be calculated wherever possible on the basis of the limits recommended for raw foods.

3. SPECIFIC PROBLEMS

3.1 Consideration of technical and formulated products

The Committee was concerned about the effects of impurities in technical products. Normally a technical grade compound is initially

evaluated with respect to its toxic properties. The nature and content of impurities in the technical product may influence these properties and may be expected to vary with the method of synthesis or manufacture. It was therefore considered important that the Meeting should have details of the major impurities present in the technical product so that a full toxicological evaluation and an evaluation of the residue data could be carried out.

An additional problem arising in connexion with the testing of technical products is that of the testing of formulations, since substances used in formulations may show toxic effects in their own right, alone or in association with the technical product. Their testing may provide additional supporting data on the toxicological aspects.

Specifically, if the basic toxicity of the active compound is altered by the formulation or by changes in the purity of the technical product in current use, further toxicological studies should be performed with the new product.

3.2 Aliesterase-inhibiting compounds

Short-term feeding studies with organophosphorus insecticides have demonstrated that aliesterase activity in liver and serum may be inhibited at concentrations lower than those that inhibit cholinesterase. The Meeting was unable to assess the relevance of these observations to the determination of a no-effect level.

The Meeting endorsed the opinion expressed in the 1973 and 1975 Joint Meeting Reports (FAO/WHO, 1973a, 1975a), with respect to the usefulness of determining aliesterase inhibition.

3.3 Reversible cholinesterase inhibition

The Meeting drew attention to the fact that the currently used methods for the determination of cholinesterase activity may lead to erroneous conclusions when applied to rapidly reversible cholinesterase inhibitors (e.g., *N*-methyl- and *N,N*-dimethylcarbamates). *In vitro* kinetic studies should be made to elucidate the nature of the reversible inhibition reaction. The results obtained in *in vivo* studies should be interpreted cautiously until more satisfactory methods are available.

In addition, owing to the rapid reversibility of cholinesterase inhibition *in vivo*, important differences in the degree of inhibition may be observed according to the route of administration, e.g., by gavage or in the diet.

3.4 Chlordimeform

It was brought to the attention of the Meeting that the manufacturers of chlordimeform have voluntarily suspended production and marketing of the product for the time being, in the light of preliminary data from studies in progress. In addition, the Meeting was informed about a brief communication to WHO from the National Cancer Institute of the USA relating to the probable effect of 4-chloro-*o*-toluidine, one of the two major metabolites of chlordimeform, in inducing haemangiosarcoma in mice.

In view of the steps taken by the producers and because data were expected to be available by 1978 when re-evaluation was scheduled, the Meeting recommended that the re-evaluation should take place when the full report of the studies becomes available, even if this was before the scheduled time. In the meantime, particularly as the product is not at present available, the Meeting decided to take no action concerning the temporary ADI and related maximum residue limits for chlordimeform.

3.5 Leptophos

The toxicological problem associated with several organophosphorus esters such as tri-*o*-cresylphosphate (TOCP), considered at a previous Meeting (FAO/WHO, 1975a) in the evaluation of leptophos, was briefly discussed in the light of a new report¹ reviewing this compound. The previous Meeting recognized that the potential hazards associated with leptophos were twofold :

- (1) occupational or accidental exposure of individuals to high doses for short periods ; and
- (2) long-term low level exposure and possible build-up of the toxicant to threshold levels leading to ataxia.

Although the first aspect does not come directly under the terms of reference of the Meeting, the toxicological hazard associated with such exposure must be considered, not least because it may affect the evaluation of the hazards from residues in food.

The Meeting observed that no new information relating to such residues had been submitted and that all available data had been discussed

¹ The Report of the Leptophos Advisory Committee to the Administrator, United States Environmental Protection Agency, Washington, DC, 1976 (unpublished document).

at the previous Meeting. The Meeting reaffirmed its previous decision and considered that the scheduled date for the re-evaluation of leptophos—1978—should be maintained.

4. EVALUATION OF DATA FOR ACCEPTABLE DAILY INTAKE

4.1 Pesticides evaluated for the first time

4.1.1 *Organophosphorus pesticides*

Acephate. In short- and long-term studies in rodents and a 2-year study in dogs, the major effects noted were growth depression at high dose levels and cholinesterase depression. The no-effect level based on cholinesterase depression in short-term studies in the rat and dog formed the basis for establishing an ADI. The available data on a study in man provided support for this.

Dialifos. Various short- and long-term studies in rats, mice, dogs, monkeys, hens, cattle, and humans revealed no unusual effects other than cholinesterase depression. Sufficient data were available to allocate an ADI.

Edifenphos. Concern was expressed about the extent of effects on the liver in long-term studies in several species and the absence of a definitive carcinogenicity study. A no-effect level based on the available short-term studies in mice and dogs and long-term studies in the rat formed the basis for estimating a temporary ADI.

Methamidophos. In short- and long-term studies in the dog and the rat, no somatic effects were observed. A no-effect level based on cholinesterase depression in the dog study formed the basis for allocating an ADI. The available data on a study in man provided support for this.

Phosmet. Data were not available to the Meeting. Consideration of this compound was postponed.

4.1.2 *Carbamates*

Carbofuran. Short-term studies in several species and long-term studies in the rat and the mouse were available. A no-effect level in the rat based on the lack of somatic (reproductive) effects served as the basis for the toxicological evaluation. Because of concern about brain cholinesterase depression in the rat, only a temporary ADI was estimated.

Formetanate. Data were not available to the Meeting. Evaluation of this compound was postponed.

Methomyl. Data were not available to the Meeting. Evaluation of this compound was postponed.

Pirimicarb. Long- and short-term studies in rodents and dogs were considered. In dogs, haemolytic anaemia noted following short-term high level administration was not seen in a 2-year study, nor was it seen in rodent studies. The 2-year study in dogs served as the basis for estimating a no-effect level with respect to a haemolytic anaemia. A temporary ADI was established using a high safety factor.

The Committee noted the first observation in a group of animals of a pesticide (pirimicarb) causing a haematological reaction which might be of an immunoreactive nature. In the case observed, the phenomenon occurred only with relatively high doses in a closed inbred colony of dogs. However, it is possible that, by prolonged and constant use of such a pesticide, hypersensitivity may be built up which could eventually lead to an immunological reaction of a haematological or other nature. Immunological and bone marrow studies with this compound should be encouraged to investigate the phenomenon observed and the possibility of its occurrence in other species and with other substances.

4.1.3 Others

Bioresmethrin. Although short-term studies were available, along with several special studies which did not specifically reveal any unusual toxicological effects, the absence of data from long-term studies precluded the Meeting from establishing an ADI.

Cartap. Short- and long-term studies were available in rats and mice and a no-effect level was established. The reduction of weight gain in the female rat was questioned, and concern was expressed as to the absence of studies on a non-rodent species. Teratogenic studies were considered inadequate. A temporary ADI was allocated.

Chlormequat and choline chloride. Choline is a natural constituent of virtually every food and occurs at approximately 1000 mg/kg in many food items. The use of chlormequat/choline chloride mixtures will not significantly affect the level of choline in food commodities and since it was present at normal levels in the diet of the animals on which the toxicity of chlormequat alone was evaluated, a reconsideration of the ADI previously established for chlormequat (FAO/WHO, 1973a) was

not conducted. However, the present studies with this mixture have shown that the addition of choline chloride has led to a reduction in the acute toxic manifestations of chlormequat.

Maleic hydrazide. Data were insufficient to establish a no-effect level in relation to this compound.

Propargite. No data were available to the Meeting. Evaluation of this compound was postponed.

4.2 Pesticides previously evaluated

4.2.1 *Organophosphorus pesticides*

Carbophenothion. Since the additional data required by a previous Meeting were not available and there was no indication of intent to provide these data, the previously allocated temporary ADI was withdrawn.

Pirimiphos-methyl. Studies requested by a previous Meeting had been carried out and were evaluated. The data were sufficient for the establishment of a revised ADI.

Thiometon. Comparative data on metabolism in animals and plants were submitted to the Meeting, as well as a preliminary report on the long-term study in rats and the 2-year study in dogs now in progress. It was decided to continue the temporary ADI and to reconsider the matter at the 1979 Meeting.

4.2.2 *Carbamates*

Carbendazim. Studies required by a previous Meeting were not available, and consideration of this pesticide was accordingly postponed.

4.2.3 *Others*

Captafol. The Meeting was aware of the existence of recent studies on the mutagenicity of this compound. In addition, comments from the manufacturer were brought to the attention of the Meeting. It was therefore decided to assemble the full dossier and submit it, together with the further work previously requested and the comments of the manufacturer, for evaluation at the Meeting in 1977.

Diphenylamine. Additional data desired by a previous Meeting were evaluated. On the basis of Heinz body induction in the mouse, the ADI was revised.

Dodine. The studies requested by a previous Meeting were evaluated. The data were sufficient for a reaffirmation of the temporary ADI, which was established as an ADI.

Paraquat. Additional data presented to the Meeting were evaluated. These made it possible to reaffirm the previously allocated ADI.

5. EVALUATION OF DATA FOR RESIDUE LIMITS

The Meeting evaluated eight pesticides that had not been considered previously. Recommendations made by previous Meetings on other pesticides were reviewed and, in certain cases, amended.

5.1 Pesticides not previously considered for establishment of maximum residue limits

Recommendations for maximum residue limits were made for acephate, carbofuran, cartap, dialifos, edifenphos, methamidophos, and pirimicarb.

In the absence of an ADI it was not possible to recommend maximum residue limits for maleic hydrazide and phosmet, but guideline levels indicating the concentration of residues that could occur from uses of these pesticides, as recommended or authorized by regulatory authorities, were published for the information of regulatory and other interested authorities.

Full details of the evaluation of these compounds are contained in the monographs (FAO/WHO, 1977b) and a summary will be found in Annex 1.

5.2 Pesticides reviewed in the light of new information

The following pesticides were reviewed in the light of information received since the previous Meeting : bioresmethrin, captafol, carbaryl, carbendazim, carbofenothon, chlormequat, diphenylamine, diquat, dodine, fenitrothion, methomyl, paraquat, pirimiphos-methyl, and thiometon.

In the case of bioresmethrin and carbofenothon, information in support of earlier recommendations was reviewed. As no ADI was established for bioresmethrin and that for carbofenothon was withdrawn, earlier recommended limits were recorded as guideline levels.

In response to requests from individual governments, a question on phosalone was dealt with by the Meeting and amendments were made in the light of information supplied.

Certain additions, amendments, or clarifications appear in Annex 1 to this report and in the relevant evaluations (FAO/WHO, 1977b).

5.3 Compounds not considered

Formetanate and propargite were scheduled for evaluation as new compounds by the Meeting. However, insufficient data were received on which to base recommendations.

6. COMPARISON OF POTENTIAL DAILY INTAKES OF PESTICIDE RESIDUES WITH THEIR ACCEPTABLE DAILY INTAKES

The Meeting considered results of calculations made on the potential daily intakes of pesticide residues of most of the compounds toxicologically evaluated. It was possible to undertake these calculations only for compounds for which the proposed residue limits were available early in the Meeting. Such calculations were made for 12 pesticides using food intake figures from five countries in three regions of the world for which food consumption data were submitted to WHO.

The calculations were based on the assumption that the concentrations of pesticide residues in food at the time of consumption were always at the level of the limits recommended by the Joint Meeting and that all food in each class bore these residues at the limit.

The results of this study indicated that with good agricultural practice there was theoretically no possibility that the acceptable daily intakes for the following pesticides might be exceeded: acephate, captafol, cartap, diphenylamine, edifenphos, paraquat, pirimicarb, thiometon. Further work on the reduction of residue levels during storage, processing, and cooking is therefore not essential, and there is no special need to include these pesticides in monitoring studies as long as the residue limits and the acceptable daily intakes remain unchanged.

For one compound—dialifos—on the basis of the above assumptions, the ADI could be exceeded up to four times in one or more of the countries considered. For three compounds—carbofuran, methamidophos, pirimiphos-methyl—the calculations indicated that the ADIs could be exceeded by 5–13 times in the five countries studied.

The Meeting considered that the possibility of exceeding the ADIs for these compounds does not necessarily represent a toxicological problem in view of the assumptions on which the calculations are based. The Meeting recommended that detailed calculations should be prepared, taking into account disappearance figures where known, and that a paper on the subject should be brought before the 1977 Meeting.

7. FUTURE WORK

The following items should be considered by future Joint Meetings :

(1) Pesticides postponed from the previous and present Meetings : carbendazim, daminozide, ethephon, formetanate, and propargite.

(2) Pesticides for which ADIs or maximum residue limits were established only on a temporary basis and that have been listed for review in 1977 : bromophos (FAO/WHO, 1973a, p. 42), chinomethionat (FAO/WHO, 1975a, p. 32), chlorothalonil (FAO/WHO, 1975a, p. 32) cyhexatin (FAO/WHO, 1974a, p. 41), dichlofuanid (FAO/WHO, 1975a, p. 33), 2,6-dichloro-4-nitrobenzamide (FAO/WHO, 1975a, p. 34), dithiocarbamates (FAO/WHO, 1975a, p. 34), fenamiphos (FAO/WHO, 1975a, p. 35), and lindane (FAO/WHO, 1975a, p. 37).

(3) Pesticides that have been listed for re-evaluation in previous reports and evaluations, without dates having been specified.

(4) Certain pesticides listed by the ninth session of the Codex Committee on Pesticide Residues as meriting priority.

8. RECOMMENDATIONS

1. In the interests of public health and agriculture and in view of the needs of the Codex Committee on Pesticide Residues, Joint Meetings on Pesticide Residues should continue to be held annually.

2. Because the full toxicological evaluation of the extensive range of substances involved in the formulation of pesticides is extremely difficult, the Meeting recommended that national authorities should pay careful attention to this problem.

3. To remedy any inconvenience arising from the fact that, since 1972, Annex 1 to each report of a Joint Meeting has contained only additions or amendments made at that meeting, a consolidated Table

containing all current evaluations and recommendations of Joint Meetings should be prepared and published.

4. As a step towards the clear interpretation of existing recommendations by Meetings and to encourage the future standardization of data relating to commodities considered at Meetings, a cumulative list of existing recommendations, outlining any preparation (removal of stalks, trimming of outer leaves, etc.) needed before submitting a sample for analysis, should be prepared and submitted for adoption at a future meeting.

5. A systematic method of presenting recommended maximum residue limits should be developed for consideration at future Meetings.

6. Because of the imbalance between the residue data and the toxicological data for those compounds for which no ADI could be allocated (section 2.3), the generation of the relevant toxicological data should be encouraged as far as possible.

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Annex 1

**ACCEPTABLE DAILY INTAKES, RESIDUE LIMITS, AND GUIDELINE LEVELS RECOMMENDED
AT THE 1976 MEETING**

These figures are additional to, or amend, those recorded in Annex 1 of the reports of earlier Meetings.

Part I lists recommended maximum residue limits. These apply to compounds for which an ADI or temporary ADI has been allocated. Where ADIs or residue limits are temporary, the year in which further data are required is specified in parentheses.

Part II lists guideline levels. These are derived from data relating to residues resulting from uses that are recommended or authorized by national authorities, but they are not supported by ADIs (see FAO/WHO 1976a, p. 42).

PART I. ACCEPTABLE DAILY INTAKES AND MAXIMUM RESIDUE LIMITS

| Pesticide and references to previous evaluations * | Recommended maximum acceptable daily intake (mg/kg body weight) | Commodity | Recommended maximum residue limit (mg/kg) | Remarks |
|--|---|---|---|--|
| acephate | 0.02 | Alfalfa, lettuce, sugar beet leaves Broccoli, Brussels sprouts, cabbage, cauliflower, citrus fruits, tomatoes Cottonseed Potatoes, soybeans, sugar beets Meat and fat of cattle, pigs, sheep, and poultry, milk, eggs | 10 5 2 1 0.1 | Limits are for the parent compound. The metabolite OS-dimethyl phosphor- amidothioate is the insecticide metha- midophos, for which separate recom- mendations are made. |
| captafol 1970b, 1974b, 1975b | 0.05 (1977) | Pineapple (whole fruit) Peanut hulls Peanuts (whole) Wheat Peanut kernels | 10 2 0.5 0.2 0.05 | |

| | | | | | | | |
|---|-----------------|---|----------------|---|---|-----|--|
| carbaryl 1965b, 1967b, 1968b, 1969b, 1970b, 1971b, 1974b, 1976b | 0.01 | Bran | 20 | Limits are now for carbaryl only. Those recommended in 1973 were for free and combined carbaryl, conjugated naphthol, and conjugated methylol carbaryl. Limits cover residues resulting from either pre- or post-harvest uses of carbaryl. The limit for rice is increased to provide for post-harvest application. | | | |
| | | Barley, oats, rice (in husk and hulled), rye, wheat | 5 | | | | |
| | | Wholemeal flour | 2 | | | | |
| | | Wheat flour (white) | 0.2 | | | | |
| carbofuran | 0.003 (1979) | Tobacco (flue-cured) | 50 | Limits are for the sum of carbofuran and 3-hydroxy-carbofuran expressed as carbofuran. | | | |
| | | Alfalfa hay | 20 | | | | |
| | | Hops (dried), alfalfa (fresh), maize fodder (fresh), and other animal feeds not otherwise listed | 5 | | | | |
| | | Brussels sprouts | 2 | | | | |
| | | Sugar beet tops | 1 | | | | |
| | | Cabbage, carrots, potatoes | 0.5 | | | | |
| | | Cauliflower, rice (hulled), soybeans | 0.2 | | | | |
| | | Bananas, coffee (raw beans), fodder beets, grain (barley, maize, oats, sorghum, wheat), lettuce, mustard seeds, oil seeds, onions, peaches, peanuts (kernels), pears, sugar beets (roots), sweet corn (kernels), strawberries, sugar cane, tomatoes | 0.1 ** | | | | |
| | | Meat, fat, and edible offal of cattle, goats, pigs, horses, and sheep, milk | 0.05 ** | | | | |
| | | cartap | 0.05 (1978) | | Hops (dried) | 5 | Limits are for cartap, expressed as the free base. |
| | | | | | Chinese cabbage, tea (green, dried) | 2 | |
| | | | | | Grapes, persimmons, radishes | 1 | |
| | | | | | Cabbage | 0.2 | |
| | | | | | Chestnut (seed including pericarp), ginger, potatoes, rice (hulled), sweet corn | 0.1 | |
| chlormequat | 0.05 | Straw of barley, oats, rye, and wheat | 50 | | | | |
| | | Oats | 10 | | | | |
| | | Wheat | 5 | | | | |

Annex 1 (continued)

| Pesticide and references to previous evaluations* | Recommended maximum acceptable daily intake (mg/kg body weight) | Commodity | Recommended maximum residue limit (mg/kg) | Remarks |
|---|---|--|---|--|
| chlorpyrifos-methyl 1976b | 0.01 | White bread Rice | 0.5 0.1 | The limit for white bread was recommended by the 1975 Joint Meeting but omitted from its report. The residue in rice results from pre-harvest application. This entry amends the commodity description for rice in the 1975 report (1976a), but not the limit. |
| dialifos | 0.003 | Apple pomace (dried) Grape pomace (dried) Citrus pulp (dried) Citrus fruits Apples, pears, raisins Grapes Fat of meat of cattle and sheep, milk (fat basis) Meat and fat of poultry Eggs, pecans | 40 20 15 3 2 1 0.02 ** 0.05 ** 0.01 | Limits are for the sum of dialifos and its oxygen analogue, expressed as dialifos. |
| diphenylamine 1970b | 0.02 | | | Because of deficiencies in the available data relating to residues following current user practice, a possible lowering in the existing recommendation of 10 mg/kg for apples was deferred for review in 1978. |
| diquat 1971b, 1973b | 0.005 | Eggs | 0.01 ** | The ADI refers to diquat dichloride. |
| dodine 1975b | 0.01 | | | The temporary ADI and maximum residue limits recommended by the 1974 Joint Meeting are confirmed and no longer temporary. |

| edifenphos | 0.005 (1979) | Rice (in husk) Rice (hulled) Rice (polished) | 0.2 0.05 0.01 ** | Limits refer to the parent compou |
|------------------------------|-----------------|--|---------------------------------------|---|
| fentirothion 1970b, 1975b | 0.005 | Rice bran Rice (in husk and hulled) Rice (milled) | 20 10 1 | Limits refer to the sum of fenitrothion and its oxygen analogue expressed as fenitrothion. |
| fenthion 1972b | 0.0005 | | | The date (1978) should appear beneath the temporary ADI in the 1975 report (1976a). |
| leptophos 1975b, 1976b | 0.001 (1978) | Cottonseed oil (crude) | 1 | In Annex 1 to the 1975 report (1976a) the entry "cottonseed, oil (crude)" should read "cottonseed, oil (crude)". The limit was correctly recorded as "1 mg/kg". |
| methamidophos | 0.002 | Hops Broccoli, cauliflower, celery, lettuce, tomatoes Brussels sprouts, cabbage, cucumber, eggplant, peaches, peppers, sugar beet leaves Potatoes, rapeseed, cottonseed, sugar beets Meat and fat of cattle, goats, and sheep, milk | 5 2 1 0.1 0.01 ** | Limits refer to the parent compound. |
| paraquat 1971b, 1973b | 0.002 | Sunflower seed Kidney of sheep, cattle, and pigs Dried hops, passion fruit Food commodities of plant origin other than those for which specific recommendations have been made, meat and edible offals other than kidney of sheep, cattle, and pigs Eggs | 2 0.5 0.2 0.05 ** 0.01 ** | Limits are for paraquat ion. ADI is for paraquat dichloride. |
| phosalone 1973b | 0.006 | Cherries | 10 | |

Annex 1 (continued)

| Pesticide and references to previous evaluations* | Recommended maximum acceptable daily intake (mg/kg body weight) | Commodity | Recommended maximum residue limit (mg/kg) | Remarks | |
|---|---|--|---|---|--|
| pirimicarb | 0.004 (1978, 1980) | Chillies | 2 | Limits are for the sum of pirimicarb, demethyl-pirimicarb, and demethyl-formamido-pirimicarb, expressed as pirimicarb. | |
| | | Apples, bell peppers, broccoli, Brussels sprouts, cabbage, cauliflower, celery, cucumber, eggplant, endive, gherkins, lettuce, parsley, tomatoes | 1 | | |
| | | Beans (with pod), blackcurrants, kohlrabi, onions, peaches, plums, raspberries, strawberries | 0.5 | | |
| | | Peas, rapeseed | 0.2 | | |
| | | Beans (without pod) | 0.1 | | |
| | | Beetroot, citrus fruits, parsnips, potatoes, radishes, sugar beet, turnips, wheat grain | 0.05 ** | | |
| | | Peanuts (whole), peanut hulls | 50 | | Limits are for the sum of pirimiphos-methyl, its oxygen analogue, and N-deethyl-pirimiphos-methyl, expressed as pirimiphos-methyl. |
| | | Peanut oil | 10 | | |
| | | Lettuce, mushrooms, olives, peanuts (kernels), spinach | 5 | | |
| | | Apples, Brussels sprouts, cabbage, cauliflower, cherries | 2 | | |
| quintozene 1970b, 1974b, 1975b | 0.007 | Blackcurrants, carrots, cucumbers, gooseberries, peppers, raspberries, spring onions, strawberries, tomatoes | 1 | These limits were recommended by the 1975 Joint Meeting but were incorrectly recorded as "Lettuce, peanuts (kernels)..." 0.3 mg/kg" in the 1975 report (1976a). | |
| | | Beans with pod, cheese, citrus fruits, dates | 0.5 | | |
| quintozene 1970b, 1974b, 1975b | 0.007 | Peas, potatoes | 0.05 ** | These limits were recommended by the 1975 Joint Meeting but were incorrectly recorded as "Lettuce, peanuts (kernels)..." 0.3 mg/kg" in the 1975 report (1976a). | |
| | | Lettuce | 3 | | |
| | | Peanuts (kernels) | 2 | | |

| | | | | |
|---------------------------|-----------------|--|---------------------|---|
| thiometon 1970b, 1974b | 0.005 (1979) | Hops (dried) Apricots, cabbage, celery, chicory, chives, endives, peanuts (whole), parsley, peas (green, including pods), quinces Cottonseed oil, straw of grain crops, fodder beets | 2 0.5 0.1 | Limits are for the sum of thiometon sulfoxide, and its sulfone, expressed as thiometon. |
|---------------------------|-----------------|--|---------------------|---|

PART II. GUIDELINE LEVELS (NO ACCEPTABLE DAILY INTAKES)

| Pesticide and references to previous evaluations * | Commodity | Guideline level (mg/kg) | Remarks |
|--|--|-------------------------------|--|
| carbendazim 1974b | Peanut hay, wheat straw Peanut hulls Peanuts | 2 0.2 0.1 | |
| carbophenothion 1973b 1976b | (see 1973a, p. 26) | | Previously recommended maximum residue limits have been changed to guideline levels since the temporary ADI has been withdrawn. |
| maleic hydrazide | Potatoes Onions | 50 15 | Guideline levels refer to the sum of free and bound unchanged maleic hydrazide and its β -D-glucoside. |
| methomyl 1976b | Pea forage, soybean forage, sorghum forage, barley straw, oat straw, wheat straw Collards, grapes, nectarines, peas (including pods), peaches Asparagus, snap beans Peas (shelled, excluding pods) | 10 5 2 0.5 | The first entry replaces that of " peas, sorghum, and soybean forage, barley oat and wheat straw " in the 1975 report (1976a) and is intended simply to make it clear what commodities are covered. The limit remains the same. |
| phosmet | Forage crops (dry) Apples, fat of cattle meat, peaches Milk and milk products (fat basis) Potatoes | 5 1 0.2 0.02 ** | Limits are for phosmet and its oxygen analogue, expressed as phosmet. |

* The references are to FAO/WHO publications as listed on pp. 19-21.

** Level at or about the limit of determination.

Annex 2

FURTHER WORK OR INFORMATION REQUIRED (OR DESIRABLE)

If a compound has been considered at earlier meetings the requirements listed below replace those stated in earlier reports, unless otherwise indicated.

ACEPHATE

Desirable

1. Further studies to elucidate the metabolic fate of acephate, preferably in non-rodent species.
2. Further studies to elucidate the role of acephate and methamidophos, alone or in combination, in depressing cholinesterase activity.
3. Validation of methods of residue analysis for regulatory purposes (reported to be in progress).

BIORESMETHRIN

Required (before an acceptable daily intake can be allocated)

1. Long-term studies.

CAPTAFOL

Required (by 1978)

1. Further studies to assist the evaluation of histopathological changes in the kidneys and liver of rats.
2. Studies to investigate the lymphocyte-neutrophil shift noted in previous experiments.

Desirable

1. Further studies to investigate the metabolism of the tetrachloroethylthio moiety of captafol.
2. Considerably more information from countries where captafol is used, the aim being to obtain a clear indication of use patterns and resulting residues.

3. Further data on the effects of washing, peeling, and blanching on residue levels in various crops.

4. Information, some of it from studies now in progress, on new methods for the analysis of the parent compound together with the main metabolites in products of animal origin.

5. Results of studies now in progress on the level and nature of captafol residues in meat, milk, poultry, and eggs.

6. Results of studies now in progress on the fate of captafol residues in citrus fruits and citrus pulp.

CARBARYL

Desirable

1. Further studies to elucidate the effects of carbaryl on renal function.

2. Further studies to resolve the differences between the observations of different investigators on reproductive physiology, especially with regard to neuroendocrine and behavioural changes.

3. Details of analytical methods for use in the determination of carbaryl and metabolite residues in raw grain, milled cereal fractions, bread, meat, and milk.

CARBENDAZIM

Required (before an acceptable daily intake can be estimated)

1. Long-term studies to investigate chronic toxicity and carcinogenicity.

2. Reproduction and teratogenicity studies.

3. Metabolism and distribution studies in several animal species.

4. Elucidation of the effect on the liver in female rats and dogs.

5. Information on the nature and level of residues in meat, milk, and eggs, after feeding animals on crops or feedstuffs treated with carbendazim.

Desirable

1. Further studies to determine the effects of high levels of carbendazim on male reproductive organs.

2. Validation of methods of residue analysis for regulatory purposes.

CARBOFURAN

Required (by 1979)

1. Short-term dietary studies in rodents with a view to determining the level causing brain cholinesterase depression *in vivo*.

Desirable

1. Comparative biochemical studies (cholinesterase depression) in rodents to establish the apparently high sensitivity of juveniles compared with adults, as noted in acute toxicity studies.

2. Further studies on reproduction to determine the highest no-effect level.

3. Further information on the level and fate of residues resulting from approved uses of carbofuran on major crops, including those mentioned in Annex 1, and especially on Brussels sprouts.

CARBOPHENOTHION

Required (before an acceptable daily intake can be allocated)

1. Studies to substantiate the marked species difference in sensitivity to plasma cholinesterase depression.

2. An adequate reproduction study.

Desirable

1. Further elucidation of the nature of the terminal residues on crops, particularly as regards the reported possibility of the presence under field conditions of photolysis products.

CARTAP

Required (by 1978)

1. Submission of the details of the studies on metabolism and the identification of metabolites.

2. Teratogenic studies covering the full period of organogenesis.

3. A feeding study in a non-rodent species.

4. Information on the fate of residues in foods of animal origin when treated fodder or plant parts are fed to livestock, including poultry.

5. Effect of cooking on the level and fate of cartap residues.

6. Information on the fate of residues in manufactured tea.

Desirable

1. A paired feeding study in the rat.

CHLORMEQUAT

Required (before maximum residue limits can be recommended)

1. An explanation for the variability of residue levels on grain.
2. An indication of the pre-harvest interval for each type of small grain crop in the various regions where the use of chlormequat is important.
3. Information on the fate of residues in meat following the feeding of animals on straw from treated crops.

DIALIFOS

Desirable

1. Metabolism studies in one or more animal species.
2. Further observations in man.
3. Additional information on national use patterns and supervised residue trials on potatoes, rape, sugar beets, and cotton.
4. Metabolism studies in one or more animal species.
5. Further observations in man.

DIPHENYLAMINE

Desirable

1. Short-term studies with special attention to the formation of Heinz bodies.
2. Data determined by modern gas-liquid chromatography methods on the residues resulting from practices now approved and in use in packing houses.

DODINE

Required (before maximum residue limits can be recommended)

1. A large-scale study to determine whether the feeding of apple pomace and grape pomace to animals contributes residues to meat and milk.

2. Identification of metabolites occurring in crops if the levels shown in the 1976 study are found to be toxicologically significant by WHO.

Desirable

1. Studies of the metabolism of dodine in species other than the rat, preferably guineapigs and/or dogs.
2. Teratological studies in appropriate animal species.
3. Appropriate mutagenicity studies.

EDIFENPHOS

Required (by 1979)

1. Further studies to examine the hepatic involvement observed in several animal species.

Desirable

1. Observations in man (relative to occupational exposure).
2. More information on the residues of edifenphos and its main metabolites on rice in husk at harvest.
3. A method of residue analysis suitable for edifenphos together with its main metabolites.

MALEIC HYDRAZIDE

Required (before an acceptable daily intake can be allocated and maximum residue limits can be recommended)

1. The results of the current carcinogenicity study with rats.
2. A teratogenicity study with the sodium salt or the free acid.
3. Further studies to investigate the possible presence of hydrazine in or on crops.
4. Residue data on other crops for which the use of maleic hydrozide is recommended, including tobacco, carrots and swedes, and similar crops.
5. Data on the fate of maleic hydrazide and its metabolites in livestock and residues in products of animal origin after feeding with commodities containing maleic hydrazide residues, e.g., potatoes.

6. Data on the effect of cooking on residues in potatoes and the effect on residues of different methods of industrial processing in the manufacture of various potato products, e.g., potato chips, dried potatoes, and potato starch. Data on residues in the wastes from these products intended for feeding purposes.

7. Further development of the gas-chromatographic method to make it suitable for regulatory purposes.

8. More information on the carry-over of maleic hydrazide from raw into cured tobacco and into cigarette smoke.

Desirable

1. Studies on the metabolism of the β -D-glucoside of maleic hydrazide.

METHAMIDOPHOS

Desirable

1. Further studies on the teratogenic potential in a suitable species.

2. Further studies to elucidate the contribution of acephate and methamidophos, alone or in combination, in depressing cholinesterase activity.

3. Further information on the level and fate of residues during the cooking and processing of fruit and vegetables.

METHOMYL

Required (before an acceptable daily intake can be allocated and maximum residue limits can be recommended)

1. Submission of full toxicological data.

Desirable

1. Development of an improved analytical method for regulatory purposes.

2. Further information on the decline of methomyl residues in storage or in processing.

3. Further information on national use patterns and residue data from countries other than Australia, Netherlands, and USA.

PHOSMET

Required (before an acceptable daily intake can be allocated and maximum residue limits can be recommended)

1. Submission of full toxicological data.
2. More detailed information on trials, which are believed to have been carried out, on the use of phosmet on fruit and forage crops.

PIRIMICARB

Required (by 30 June 1978)

1. Studies on other species, particularly primates, to define the range of their susceptibility to the haematological changes noted in the dog.
2. Determination of the susceptibility to haemolytic anaemia in the inbred beagle strain used in toxicological studies.
3. Studies to determine fully the reduction in growth noted in several rodent dietary studies.
4. Immunological studies, when appropriate, in animal species other than the dog to investigate still further the significance (and possible range of occurrence) of the haemolytic anaemia associated with pirimicarb.
5. Significance of the hypochromic anaemia associated with rats fed high levels of plant metabolites.

Required (by 1980)

1. A carcinogenic study in an appropriate mammalian species using a currently acceptable protocol.

Desirable

1. A survey of industrially exposed individuals by immunological (or serological) techniques to determine the potential occurrence of antibodies following pirimicarb exposure.
2. More information on residues in grain other than wheat, e.g., barley, oats, rice, maize.

PIRIMIPHOS-METHYL

Desirable

1. Results of studies now in progress on the residues in peanuts and peanut products.
2. Results from commercial trials on other commodities.

THIOMETON

Required (by 1979)

1. Submission of the long-term study in rats now in progress.

Desirable

1. Information on the level and fate of residues in livestock consuming feed containing thiometon residues.