

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

**WORLD HEALTH ORGANIZATION  
TECHNICAL REPORT SERIES**

No. 574

**FAO AGRICULTURAL STUDIES**

No. 97

**PESTICIDE RESIDUES IN FOOD**

**Report of the 1974 Joint Meeting of the FAO  
Working Party of Experts on Pesticide Residues  
and the WHO Expert Committee on  
Pesticide Residues**



Published by  
FAO and WHO



WORLD HEALTH ORGANIZATION

GENEVA

1975

Monographs containing evaluations, acceptable daily intakes, and tolerances for pesticide residues in food, together with information on identity of the pesticides considered, are issued by FAO and WHO under the title :

*1974 Evaluations of Some Pesticide Residues in Food.* (FAO/AGP/74/M/11 ; *WHO Pesticide Residues Series*, No. 4)

ISBN 92 4 120574 1

© FAO and WHO 1975

PRINTED IN SWITZERLAND

# CONTENTS

	Page
1. Introduction . . . . .	7
2. General considerations . . . . .	8
2.1 Principles . . . . .	8
2.2 Considerations on certain testing procedures . . . . .	8
2.3 Observations in man . . . . .	9
2.4 Information needed for toxicological evaluation . . . . .	9
2.5 Classification of and description of commodities in recommendations . . . . .	10
2.6 Metric units . . . . .	10
2.7 Nomenclature of the pesticides evaluated . . . . .	11
3. Specific problems . . . . .	11
3.1 Cholinesterase-inhibiting pesticides . . . . .	11
3.2 Nitrosatable pesticides . . . . .	12
3.3 Amitrole and dithiocarbamates . . . . .	12
3.4 Leptophos . . . . .	13
3.5 DDT . . . . .	13
3.6 Hexachlorobenzene (HCB) . . . . .	14
3.7 Impurities in technical grade pesticides . . . . .	15
4. Evaluation of data for acceptable daily intake . . . . .	16
4.1 Dithiocarbamates . . . . .	16
4.2 Organophosphorus pesticides . . . . .	17
4.3 Others . . . . .	17
5. Evaluation of data for residue limits . . . . .	18
5.1 Receipt of information from various sources . . . . .	19
5.2 Pesticides reviewed in the light of new information . . . . .	19
5.3 Pesticides not previously considered for establishment of maximum residue limits . . . . .	19
5.4 Compounds not considered . . . . .	20
6. Comparison of potential daily intakes of pesticides in diets with their acceptable daily intakes . . . . .	20
7. Future work . . . . .	21
8. Recommendations . . . . .	21
References . . . . .	23
Annex 1. Recommendations concerning acceptable daily intakes and residue limits made at the 1974 Meeting . . . . .	25
Annex 2. Further work or information required (or desirable) . . . . .	31

1974 JOINT MEETING OF THE FAO WORKING PARTY OF EXPERTS  
ON PESTICIDE RESIDUES AND THE  
WHO EXPERT COMMITTEE ON PESTICIDE RESIDUES

Rome, 2-11 December 1974

*Members of the FAO Working Party of Experts on Pesticide Residues :*

- Mr A. Ambrus, Acting Department Head, Central Plant Protection and Quarantine Laboratory, Analytical Department of Pesticides, Budapest, Hungary
- Dr A. F. H. Besemer, Head, Pesticides Division, Plant Protection Service, Ministry of Agriculture, Wageningen, Netherlands
- Dr G. Bressau, Head, Pesticide Laboratory, Federal Health Office, Max von Pettenkofer Institute, Berlin, Federal Republic of Germany
- Mr F. Bro-Rasmussen, Head, Department of Pesticides and Contaminants, National Food Institute, Søborg, Denmark (*Rapporteur*)
- Dr K. A. McCully, Chief, Field Sciences Division, Health Protection Branch, Department of National Health and Welfare, Ottawa, Ont., Canada
- Mr J. T. Snelson, Pesticides Coordinator, Department of Agriculture, Canberra, ACT, Australia (*Chairman*)

*Observer invited by FAO :*

- Dr A. J. Pieters, Chairman, Codex Committee on Pesticide Residues

*Members of the WHO Expert Committee on Pesticide Residues : \**

- Dr E. Astolfi, Professor of Toxicology, University of Buenos Aires, Argentina
- Dr L. R. Axelrod, Environmental Protection Agency, Washington, DC, USA (*Rapporteur*)
- Professor I. Nir, Director, Department of Clinical Pharmacology, Ministry of Health, Jerusalem, Israel
- Professor F. K. Ohnesorge, Chair of Toxicology, Institute of Pharmacology and Toxicology, University of Düsseldorf, Federal Republic of Germany
- Dr E. Poulsen, Director, Institute of Toxicology, National Food Institute, Søborg, Denmark (*Vice-Chairman*)
- Professor Dr L. Rosival, Director, Research Institute of Hygiene, Bratislava, Czechoslovakia
- Professor R. Truhaut, Director, Toxicological Research Centre, Faculty of Pharmaceutical and Biological Sciences, René Descartes University, Paris, France

*Secretariat :*

- Dr R. L. Baron, National Environmental Research Center, Pesticides and Toxic Substances Effects Laboratory, Environmental Protection Agency, Research Triangle Park, NC, USA (*Temporary Adviser*)

---

\* *Unable to attend* : Dr G. Belonožko, All-Union Scientific Institute of Hygiene and Toxicology of Pesticides, Polymers, and Plastics, VNIIGINTOX, Kiev, Ukrainian SSR.

Mr J. Cummings, Pesticides Specialist, UNDP/FAO Project THA 68/526, Bangkok, Thailand (*Consultant*)  
Dr L. G. Lodomery, Food Standards Officer, Food Standards and Control Service, FAO, Rome, Italy  
Dr F. C. Lu, Chief, Food Additives, WHO, Geneva, Switzerland (*Joint Secretary*)  
Mr A. F. Machin, Senior Research Officer, Central Veterinary Laboratory, Ministry of Agriculture, Weybridge, Surrey, England (*Consultant*)  
Dr R. Montesano, Chemical Carcinogenesis Unit, International Agency for Research on Cancer, Lyon, France  
Dr S. D. Murphy, Associate Professor of Toxicology, Harvard University School of Public Health, Boston, MA, USA (*Temporary Adviser*)  
Dr E. E. Turtle, Pesticides Specialist, Plant Protection Service, FAO, Rome, Italy (*Joint Secretary*)  
Dr G. Vettorazzi, Scientist, Food Additives, WHO, Geneva, Switzerland

1. The first part of the document discusses the importance of maintaining accurate records of all transactions. This is essential for ensuring the integrity of the financial statements and for providing a clear audit trail.

2. The second part of the document outlines the various methods used to collect and analyze data. These methods include direct observation, interviews, and the use of statistical models. Each method has its own strengths and limitations, and it is important to choose the most appropriate one for the specific situation.

3. The third part of the document describes the process of data analysis. This involves identifying patterns, testing hypotheses, and drawing conclusions based on the evidence. It is a complex task that requires a high level of skill and attention to detail.

4. The final part of the document discusses the importance of communication in the research process. Researchers must be able to clearly and concisely present their findings to a wide range of audiences, including colleagues, students, and the general public.

5. The document concludes by emphasizing the need for ongoing research and innovation in the field. As new technologies and methods are developed, it is essential to stay up-to-date and to continue to push the boundaries of what is possible.

# PESTICIDE RESIDUES IN FOOD

## Report of the 1974 Joint FAO/WHO Meeting

A Joint Meeting of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Committee on Pesticide Residues was held in Rome from 2 to 11 December 1974. The Meeting was opened by Mr F. Albani, Director of the Plant Production and Protection Division of the Food and Agriculture Organization, on behalf of the Directors-General of the Food and Agriculture Organization of the United Nations and of the World Health Organization. The FAO Working Party had already met in Rome from 27 to 30 November in preparation for the Joint Meeting.

Mr Albani stressed the need of many Member States for expert professional advice on numerous questions relating to pesticides, and especially on pesticide residues. Referring to the World Food Conference of the United Nations recently held in Rome, he mentioned the continuing need for agricultural pesticides in expanding food production. He drew attention to the fact that authorities in developing countries in particular were hoping to find guidance in the recommendations of the Meeting.

### 1. INTRODUCTION

The annual Joint Meeting was held in pursuance of the recommendations made in 1961, at a meeting of a WHO Expert Committee on Pesticide Residues held jointly with the FAO Panel of Experts on the Use of Pesticides in Agriculture, that studies be undertaken 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) contain information on acceptable daily intakes (ADIs) established, on residue limits recommended, and on the methods of analysis suggested for the various pesticides considered. The supporting documents (FAO/WHO, 1965b, 1965c, 1967b, 1968b, 1969b, 1970b, 1971b, 1972b, 1973b, 1974b) 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 requests of both a general and specific nature contained in the report of the Seventh Session of the Codex Committee on Pesticide Residues held from 4 to 9 February 1974.

During the present Joint Meeting the FAO Working Party was primarily responsible for :

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

The WHO Expert Committee was primarily responsible for :

- (a) reviewing toxicological and other relevant data on certain pesticides and their residues ;
  - (b) establishing, where possible, ADIs for man for those pesticides.
- Furthermore, each of these groups of experts made recommendations designed to indicate, stimulate, and coordinate necessary research.

## 2. GENERAL CONSIDERATIONS

### 2.1 Principles

The Meeting discussed a number of principles and guidelines given in previous Joint Meetings, the Seventeenth Report of the Joint FAO/WHO Expert Committee on Food Additives, the report of the WHO Scientific Group on Procedures for Investigating Intentional and Unintentional Food Additives, and the report of the WHO Scientific Group on the Assessment of the Carcinogenicity and Mutagenicity of Chemicals. References to these reports are given on pages 23-24. Some of these principles are emphasized and reiterated in the present report.

### 2.2 Considerations on certain testing procedures

#### 2.2.1 *The need for analysable numbers of animals*

In the toxicological evaluation of several compounds, it proved difficult to interpret long-term studies because there were too few surviving animals at the end of the study for the results to be analysed by appropriate statistical means. The Meeting suggested that experiments should be designed so as to permit valid statistical analysis.

#### 2.2.2 *Data obtained by gavage administration versus feeding*

It was again noted that experimental data from studies where animals are fed a pesticide as part of the feed show obvious differences from data obtained in experiments where the compound is administered by gavage. Reiterating the conclusion reached in 1973 (FAO/WHO, 1974a), the Meet-

ing stated that experiments using gavage cannot replace feeding experiments for the testing of materials found or suspected of being found in food.

### 2.2.3 *Testing of pesticides for mutagenicity*

The Meeting discussed the need for tests to evaluate the mutagenic potential of a pesticide in order to facilitate the allocation of an ADI. The possible mutagenic action of chemicals has been discussed elsewhere (WHO, 1974).<sup>1</sup> The Meeting restated its position (FAO/WHO, 1974a) on the credibility of mutagenicity tests presently available and urged the development of tests capable of yielding data that can be interpreted as representing the human response.

### 2.3 **Observations in man**

The Meeting recognized that the evaluation of the potential hazards of pesticides and the allocation of ADIs for man would be aided by knowledge of the human response to pesticide exposure. (The various types of investigation and observation that can be made in man have been described in detail by a WHO Scientific Group (WHO, 1967).) Such knowledge may in addition be helpful in revising protocols for animal studies to maximize their usefulness in predicting human response. To permit the development of data banks on human response to pesticide exposure, the Meeting suggested that epidemiological studies be designed that could yield data on both acute and chronic effects and accumulation in man. It was recommended that WHO seek the cooperation of the World Federation of Associations of Clinical Toxicology Centers and Poison Control Centers (Lyons, France) and others in developing such data banks.

### 2.4 **Information needed for toxicological evaluation**

The Meeting suggested that WHO should undertake to identify additional sources of data and ongoing and future research efforts in the area of pesticide toxicology. Such sources should be provided with the following information: (a) a list of those pesticides for which data have been inadequate to allocate an ADI, or sufficient only to allocate a temporary ADI, and (b) a list of the data needed for each pesticide for allocating or reassessing ADIs. This same information should be circulated to Member States and appropriate organizations.

---

<sup>1</sup> IARC (1974) *Scientific Publications* No. 10.

## 2.5 Classification of and description of commodities in recommendations

The Meeting considered, in the light of the discussion at the 1970 Joint Meeting (FAO/WHO, 1970a), several documents dealing with the classification and description of foods from the standpoint of residues. A paper distributed by the Codex Committee on Pesticide Residues<sup>1</sup> was felt to be particularly relevant.

Careful consideration was given to the terms used to describe the commodities for which maximum residue limits were recommended. So far as possible, the descriptions adopted for the commodities involved in the residue studies examined by this Meeting take account of :

- (a) commodity descriptions generally used in commerce ;
- (b) the descriptions used in recommendations employed by the Joint FAO/WHO Codex Alimentarius Commission ;
- (c) the terms used by previous Joint Meetings to describe specific commodities.

In certain instances recommendations were made for a group of commodities where the data indicate that the use pattern and residue levels resulting therefrom are generally similar for many of the individual commodities in the group. In instances where the use of the pesticide is limited to specific crops or where the data available were confined to specific crops, recommendations were made for residue limits for those crops.

Some residue limits were recommended for commodities that are subject to further processing, e.g., rice in husk, because these commodities are important in trade. Recommendations were frequently also made for residue limits for the partly or wholly processed commodity, e.g., husked rice and polished rice. This will make it possible to control more effectively the residue levels reaching the consumer.

## 2.6 Metric units

In recent years there has been a general shift to metric units of measurement. Previous Joint Meetings, while recognizing that other systems of measuring and expressing units are still in widespread use, have urged that reported data should be expressed in metric units. The last two Meetings expressed their recommendations for tolerances, practical limits, and guideline levels in mg/kg. Many of the data in the monographs have been converted into and expressed in metric units.

---

<sup>1</sup> *Classification of foods and definition of food groups (CX/PR 74/4)*. Paper prepared by the US Delegation and distributed at the Seventh Session of the Codex Committee on Pesticide Residues, 4-11 February 1974, The Hague, Netherlands.

The present Meeting again considered this question and expressed the view that future Meetings should give their support to the full adoption of metric units. During the present Meeting this could be done only in the appraisals and comments sections of the monographs because so much of the basic information had still been supplied in different units that conversion would not have been practicable.

The Meeting recognized that confusion may arise from expressing both residue or diet levels and daily intake in the same units (mg/kg) and therefore urged care in the use of these terms. Normally, intake should be related to body weight in kilograms and be expressed in mg per kg of body weight.

The Meeting stressed the desirability of a consistent form of presentation of data. Governments, organizations, and industries that supply information for Joint Meetings should be urged to provide it in metric units.

### 2.7 Nomenclature of the pesticides evaluated

The Meeting confirmed the standing practice of referring to pesticides by their ISO common names wherever such names exist. Where no ISO common name exists, the name adopted by a national standards organization may sometimes be used; in such cases the authority for the name should be identified. In cases where a common name has not been adopted by a recognized standards organization, a chemical name may be used. For this purpose and in other references to the chemical name, the IUPAC rules of chemical nomenclature are to be followed wherever possible. In accordance with these principles, the names daminozide, tecnazene, and dicloran<sup>1</sup> were used at the present meeting.

## 3. SPECIFIC PROBLEMS

### 3.1 Cholinesterase-inhibiting pesticides

As suggested by the 1966 Joint Meeting (FAO/WHO, 1967a) and reiterated in the report of the 1972 Meeting (FAO/WHO, 1973a), it would be desirable to determine the usefulness of cholinesterase inhibition and of electroencephalographic criteria for assessing the effects of the cholinesterase-inhibiting pesticides.<sup>2</sup> The Meeting urged that cholinesterase activity in the brain, as well as in erythrocytes and plasma, should in the future be measured during short-term and long-term feeding studies on these compounds.

<sup>1</sup> BSI name for 2,6-dichloro-4-nitrobenzenamine.

<sup>2</sup> Santolucito, J. A. & Morrison, G. (1971) *Toxicol. appl. Pharmacol.*, **19**, 147.

The value of considering other parameters of neurological function and behaviour was also recognized.

### 3.2 Nitrosatable pesticides

A number of *N*-nitroso compounds have been shown to exert a carcinogenic effect in animals. Recent experiments have demonstrated that *N*-nitroso compounds are formed from a number of nitrogen-containing pesticides *in vivo* as well as *in vitro*, and that *in vivo* formation may occur in man.<sup>1</sup> Of the *N*-nitroso compounds formed from certain agricultural pesticides some are known to have a carcinogenic action in rodents.<sup>2</sup> In recent studies such compounds have also been demonstrated to be potent mutagens *in vitro*.<sup>3</sup>

The extent of formation of *N*-nitroso compounds in man, if indeed they are formed, is probably very limited, and it is not yet possible to predict the effect in man of low doses of these substances. It should be borne in mind that man is already exposed in the environment to a variety of other nitrosatable substances and carcinogenic nitrosamines. The Meeting recommended that further research be conducted on the formation of *N*-nitroso compounds from pesticides under conditions and at concentrations that include those to which man might be exposed.

### 3.3 Amitrole and dithiocarbamates

The Meeting took note that thyroid tumours had been produced experimentally with amitrole and with ethylenethiourea, a degradation product of the ethylenebisdithiocarbamates. The Meeting was referred to the report of the WHO Scientific Group on the Assessment of the Carcinogenicity and Mutagenicity of Chemicals (WHO, 1974), which had agreed that, in those cases where adequate knowledge exists of the mechanisms of tumour production, e.g., in the case of hormone-mediated tumour induction, "the data available may permit the logical determination of a tolerance level".

In the cases of amitrole and the dithiocarbamates "no-effect levels" for biochemical and histological changes in the thyroid gland have been demonstrated. Since there is evidence that the antithyroid action of such com-

<sup>1</sup> IARC (1972) *Scientific Publications* No. 3; IARC (1974) *Scientific Publications* No. 9.

<sup>2</sup> Ungerer, O. et al. (1974) *Z. Krebsforsch.*, **81**, 217.

<sup>3</sup> Elespuru, R. K. et al. (1974) *Nature (Lond.)*, **247**, 386; Siebert, D. & Eisenbrand, G. (1974) *Mutation Res.*, **22**, 121.

pounds probably accounts for the thyroid tumours mentioned above, the Meeting felt justified in allocating ADIs with qualifications (see sections 4.1 and 4.3).

### **3.4 Leptophos**

In response to requests for guidance on the introduction and use of this compound in various countries, and in the light of certain reports it had received, the Meeting gave some consideration to the problem of neurotoxicity of leptophos. Clinical signs of poisoning, e.g., ataxia, in hens administered large doses suggested that leptophos may induce a delayed neurotoxic effect similar to that elicited by tris(2-methylphenyl) phosphate (TOCP). No attempt was made to evaluate the possible effect of the aromatic solvent (mainly xylene) and surfactants that were administered simultaneously with leptophos in one study. It was noted that in two studies there was a dose level at which no neurotoxic effects were observed. Further studies were reported to be in progress to ascertain more adequately the magnitude of the problem. In view of the observations reported, the Meeting felt that no satisfactory advice on the use of leptophos as an agricultural insecticide could be provided until these and other data could be fully evaluated. It was proposed that such an evaluation should be undertaken at the next Meeting.

### **3.5 DDT**

DDT insecticides are still widely used because they offer important public health and agricultural benefits. The attention of toxicologists has been focused during recent years on the tumorigenic action of DDT on mouse liver, and this question has been under constant scrutiny by the Joint Meetings since 1967. Data were presented (L. Tomatis & V. Turusov, unpublished observations, 1974) before the present Meeting that demonstrated that mice ingesting 36 mg of DDT per kg of body weight in their feed for 15 weeks developed hepatomas that did not regress. However, no tumours have thus been produced in any other species tested, e.g., rats and hamsters. Furthermore, the limited epidemiological data available give no indication that DDT might be a human carcinogen. A number of people have had intermittent heavy exposure to DDT over a period of some 30 years, which should be sufficient time to produce and observe any increased tumour incidence that might have occurred. There is an urgent need for new epidemiological data that would permit an evaluation of the implications of the results obtained in mice.

### 3.6 Hexachlorobenzene (HCB)

The 1973 Joint Meeting, reviewing the status of HCB, had found that very few of the toxicological data listed as being required by the 1969 Meeting had been received (FAO/WHO, 1974a).

The present Meeting examined recently published reports on tests for mutagenic and teratogenic action,<sup>1</sup> studies of biochemical effects,<sup>2</sup> histopathological studies,<sup>3</sup> tissue disposition studies,<sup>4</sup> and reproduction studies.<sup>5</sup> Although none of these were long-term studies, the results reported permitted the Meeting to reaffirm the previously suggested value of 0.0006 mg per kg of body weight (FAO/WHO, 1970b, 1974a) as a guide for setting upper limits for residues. Since the results of a long-term feeding and carcinogenesis study known to be in progress were not yet available, the Meeting deferred full evaluation for an ADI but allocated a value of 0.0006 mg per kg of body weight as a conditional ADI.

The Meeting expressed concern that some effects attributed to HCB might be due to impurities in the test samples.<sup>6</sup>

It was noted that there is an increasing number of reports of HCB residues in foods, feeds, and human tissues. The sources of these residues are known to include disposal of industrial and municipal wastes, contamination by HCB of other chlorinated pesticides, the approved use of HCB as a seed-dressing, and misuse of HCB-treated seeds in animal feeds. The Meeting urged that :

- (a) support should be given to an international monitoring programme for detecting the sources and extent of contamination ;
- (b) the presence of HCB as an impurity in other pesticides should be monitored and minimized ;
- (c) the recommendations for use of HCB as a seed dressing (FAO/WHO, 1974e) be carefully adhered to ; and
- (d) HCB should be used only as a seed dressing and only when no suitable substitute is available.

<sup>1</sup> Khera, K. A. (1974) *Food Cosmet. Toxicol.*, **12** (in press).

<sup>2</sup> Grant, D. L. et al. (1974) *Environ. Physiol.*, **4**, 159.

<sup>3</sup> Kuiper-Goodman, T. et al. (1974) *Proc. Microsc. Soc. Can.*, **1**, 14 ; Kimbrough, R. D. & Linder, R. E. (1974) *Res. Commun. chem. Path. Pharmacol.*, **8**, 653.

<sup>4</sup> Villeneuve, D. C. et al. (1974) *Environ. Physiol. Biochem.*, **4**, 112 ; Villeneuve, D. C. (1975) *Toxicol. appl. Pharmacol.* (in press) ; Villeneuve, D. C. & Hierlihy, S. L. (1975) *Bull. Environm. Contam.* (in press).

<sup>5</sup> Somers, E. et al. (1973) In : *Pesticides and the environment : a continuing controversy*. North Miami, FL, Symposia Specialists.

<sup>6</sup> Villanueva, E. C. et al. (1974) *J. agric. Food Chem.*, **22**, 916.

Because of the persistent nature of HCB and its widespread occurrence in the environment it must be recognized that, even if all sources of emission could be stopped, some food contamination with HCB will continue for many years. The Meeting therefore urged that the data required by the 1973 Joint Meeting (FAO/WHO, 1974a) be obtained promptly.

### 3.7 Impurities in technical grade pesticides

In connexion with the evaluation of a number of pesticides, there was some discussion of the purity of technical grade materials and the possible influence of known and unknown impurities on the toxicity of the technical grades of the chemicals and of residues resulting from their use. The Meeting drew attention to the fact that very little information on purity had been received about dodine and pirimiphos-methyl, and asked for additional information.

Toxicological studies (both acute and chronic) are generally carried out with technical grade materials produced by commercial-scale processes, and the resulting toxicological data normally take into account the presence of impurities. In view of the experience with 2,3,7,8-tetrachlorodibenzo-[*b,e*][1,4]dioxin and the finding several years ago of trace amounts in samples of 2,4,5-T the Meeting was anxious to avoid similar problems. Admittedly, however, it is most unlikely that small amounts of unknown highly toxic impurities would be detected by chemical analysis of technical grade chemicals or formulations.

The Meeting recognized that specifications such as those issued by FAO and WHO are seldom designed to take account of impurities occurring in technical grade pesticides at the trace level unless the importance of such impurities has already been revealed by biological studies. Such specifications are nevertheless valuable, and it was agreed that manufacturers should be encouraged to conform to them by producing the purest possible grades of pesticides consistent with constraints imposed by cost and scale of manufacture. Constant vigilance is, however, needed to detect reactions in workers at manufacturing plants, spray operators, animals, and plants that could give warning of possible toxic manifestations due to impurities.

The Meeting discussed the feasibility and desirability of providing, in the monographs, information on the steps used in industrial synthesis to aid in the forecasting the possibility that impurities of toxicological significance may be formed during manufacture. While difficulty of ensuring that this information is up to date and of drawing useful conclusions from it was recognized, it was decided that an attempt should be made to include such information in future monographs.

In comparison with information available to the Meeting in earlier years, the information provided more recently on the specifications adopted by manufacturers for their products, including a listing of impurities, has been much more helpful.

#### 4. EVALUATION OF DATA FOR ACCEPTABLE DAILY INTAKE

##### 4.1 Dithiocarbamates

The dimethyl and ethylene bisdithiocarbamates were evaluated by the Joint Meeting in 1965, 1967, and 1970 (FAO/WHO, 1965a, 1968a, 1971a). The following information was listed as being required: studies on possible carcinogenic effects; effects on thyroid function; effects on the reticulo-endothelial and haematopoietic systems; and effects on reproductive physiology. This information has not been made available to the Meeting.

The Meeting recognized that current needs for these pesticides in food production entail their extensive use. Until methods of residue analysis that distinguish between the two groups of dithiocarbamates come into general use, the Meeting decided to allocate a new temporary ADI to all dithiocarbamate fungicides.

For the dimethyl dithiocarbamates (ferbam, thiram, and ziram), the new lower temporary ADI is based on data showing a teratogenic effect with ziram and thiram, and chromosomal aberrations with ziram.<sup>1</sup> Ziram, thiram, and ferbam have also been shown to be nitrosated *in vitro* and *in vivo* and may therefore be capable of forming nitrosamines.<sup>2</sup>

In the case of the ethylene bisdithiocarbamates (mancozeb, maneb, nabam, and zineb), a new lower temporary ADI was allocated on the basis of reports that these fungicides are teratogenic.<sup>3</sup> Furthermore, ethylene-thiourea, a major breakdown and metabolic product of these pesticides (FAO/WHO, 1971b),<sup>4</sup> is teratogenic and mutagenic, and produces thyroid carcinomas and liver tumours in mice and rats.<sup>2, 5</sup>

<sup>1</sup> Antonovič, E. A. et al. (1971) [Toxicity of dithiocarbamates and their fate in warm-blooded animals]. In: *Proceedings on Toxicology and Analytical Chemistry of Dithiocarbamates*, Dubrovnik, pp. 1-143.

<sup>2</sup> IARC (1974) *IARC monographs on the evaluation of carcinogenic risk of chemicals to man*. Vol. 7, *Some antithyroid and related substances, nitrofurans and industrial chemicals*.

<sup>3</sup> Petrova-Vergieva, T. & Ivanova-Chemishanska, L. (1973) *Food Cosmet. Toxicol.*, **11**, 239.

<sup>4</sup> Truhaut, R. et al. (1973) *C.R. Acad. Sci. (Paris)*, **CD1276**, 229.

<sup>5</sup> Graham, S. L. et al. (1973) *J. agric. Food Chem.*, **21**, 321; Šram, R. J. & Beňes, V., unpublished observations, 1974.

There has been a suggestion that with prolonged oral administration zineb, maneb, and ziram induce pathological alterations resembling precancerous changes in the lung of rats.<sup>1</sup>

On the basis of the above findings it was decided to lower the value of the temporary ADI. The new lower temporary ADI is based on a larger safety margin from the no-effect levels specified by the 1970 Meeting (FAO/WHO, 1971a, 1971b, pages 278-279). In extending the temporary ADI for the dithiocarbamates until 1977, the Meeting recommended that the temporary ADIs should be withdrawn if required data are not forthcoming (see section 3.3).

#### 4.2 Organophosphorus pesticides

*Fenamiphos.*<sup>2</sup> Short-term and long-term studies in rats and dogs have revealed no unusual effects, apart from cholinesterase depression. Sufficient data were available to allocate an ADI.

*Fenitrothion.* The results of long-term feeding studies allowed the Meeting to allocate an ADI based upon a level that did not reduce cholinesterase activity. In short-term studies on human volunteers there was a narrow margin between the no-effect dose and a dose resulting in symptoms.

*Pirimiphos-methyl.* The reported slow decline in cholinesterase values following the exposure of rats and dogs to this pesticide raised questions about a study in man showing no effects after a 28-day exposure. Studies in rats and man formed the basis for establishing a no-effect level and allocating a temporary ADI.

#### 4.3 Others

*Amitrole.* A no-effect level for amitrole was observed in long-term and short-term studies in two animal species. The lack of antithyroid effects, as measured by a sensitive biochemical parameter, and the lack of hepatic effects at considerably higher dose levels formed the basis for defining the no-effect level. A conditional ADI was allocated with the proviso that the uses of amitrole be restricted to those where food residues would be unlikely to occur (see section 3.3).

*Chinomethionat.* Additional data, predominantly on reproduction and from a long-term study in rats, were evaluated by the Meeting. A temporary ADI was allocated on the basis of a no-effect level from the long-term study.

---

<sup>1</sup> See footnote 1, page 16.

<sup>2</sup> Proposed ISO name for ethyl 3-methyl-4-(methylthio)phenyl(1-methylethyl)-phosphoramidate.

*Chlorothalonil*. The significance of kidney changes found on detailed microscopic examination was not resolved. A temporary ADI was allocated on the basis of low-level feeding studies.

*2,4-D*. 2,4-D was reconsidered by the Meeting in the light of recently published experimental data. On the basis of this information there is no indication to change the previously allocated ADI for man (0-0.3 mg per kg of body weight).

A survey of "dioxin" content in 2,4-D has shown that the manufacturing process for 2,4-D in itself obviates the possibility of the formation of "tetra, hexa, and octadioxin" but does not rule out the occurrence of other impurities.

*Daminozide*. Sufficient data were not available to allocate an ADI.

*Dichlofluanid*. A temporary ADI was allocated on the basis of no-effect levels in rat and dog feeding studies and a three-generation rat reproduction study.

*2,6-Dichloro-4-nitrobenzenamine (dicloran)*. No-effect levels based on in two species formed the basis for allocating a temporary ADI. The occurrence of an ocular disturbance in dogs has been reported and further studies are needed to resolve this issue.

*Dinocap*. Dinocap was reconsidered by the Meeting on the basis of two new metabolism studies in ducks. These studies did not, however, satisfy Joint Meeting data requirements (FAO/WHO, 1970a) for an ADI. The Meeting emphasized that additional studies with a variety of dose levels and a larger number of ducks were needed to establish the exact dosage of dinocap that does not produce cataracts.

Significant data were not available to allocate an ADI for man.

*Dodine*. A no-effect level was estimated from 2-year studies in rats and dogs, although concern was expressed over the lack of metabolic data. A temporary ADI based on the no-effect level in the dog was allocated.

*Tecnazene*. Insufficient significant data were available to allocate an ADI.

The decisions of the Meeting on the toxicological evaluation of these pesticides are summarized in Annex 1.

## 5. EVALUATION OF DATA FOR RESIDUE LIMITS

The Meeting reviewed and, in certain cases, amended recommendations made previously. Seven pesticides that had not been considered by previous Meetings were also evaluated.

### **5.1 Receipt of information from various sources**

Very few governments submitted information directly, and in most instances the amount of information was small. Although many useful and relevant data were supplied by manufacturers of compounds evaluated for the first time, submissions by industry were largely deficient in residue data on compounds for re-evaluation. In some instances members were aware of the existence of information that had not been made available for evaluation. The Meeting therefore urged that every effort should be made to seek the cooperation of governments, industry, and others to ensure that complete data relating to all compounds reviewed at the Meetings are made available.

### **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: chlorpyrifos; 2,4-D; dichlofluanid; dinocap; ethylene bisdithiocarbamates; fenitrothion; hexachlorobenzene; and mancozeb. In addition, a number of questions concerning the following compounds, referred from the Seventh Session of the Codex Committee on Pesticide Residues (FAO/WHO, 1974c), were considered in the light of available information and such information as was supplied by governments: aldrin/dieldrin, azinphos-methyl, binapacryl, bromophos, captan, captafol, chlordane, cyhexatin,<sup>1</sup> dichlorvos, dicofol, endosulfan, endrin, heptachlor, lindane, phosphamidon, pyrethrins, and quintozone. Certain additions, amendments, and clarifications appear in Annex 1 to this report and in relevant monographs (FAO/WHO, 1975b).

### **5.3 Pesticides not previously considered for establishment of maximum residue limits**

Recommendations for maximum residue limits were made for amitrole, chinomethionat, chlorothalonil, dichlofluanid, 2,6-dichloro-4-nitrobenzenamine (dicloran), dodine, fenamiphos, and pirimiphos-methyl.

In the case of amitrole, recommendations designed to reduce the risk of contamination of food were made.

In the absence of an ADI, it was not possible to recommend tolerances for leptophos, but guidelines indicating the level of residues resulting from recommended uses of this insecticide were published for the information of regulatory and other interested authorities.

---

<sup>1</sup> Proposed ISO name for tricyclohexylhydroxystannane (tricyclohexyltin hydroxide).

Full details of the evaluation of these compounds are contained in the monographs (FAO/WHO, 1975b) and a summary of the recommended values is provided in Annex 1.

#### 5.4 Compounds not considered

Daminozide, tecnazene, dimethyl dithiocarbamates (ferbam, thiram, and ziram), and bisdithiocarbamates (maneb, metiram, nabam, and zineb) were scheduled for evaluation at the Meeting. However, no useful data on which to base recommendations were received. Additional efforts should be made to seek and obtain information so that these compounds can be considered at a future meeting. In the case of daminozide, the Meeting noted that, owing to the lack of raw materials, production might have to cease for several years. The manufacturers had proposed that the compound should not be considered for the time being.

Questions on three compounds, diazinon, piperonyl butoxide, and [1,1'-biphenyl]-2-ol (*o*-phenylphenol), were referred from the Codex Committee on Pesticide Residues in 1974 (FAO/WHO, 1974c) but were not dealt with by the Meeting. They were referred to the next Joint Meeting.

### 6. COMPARISON OF POTENTIAL DAILY INTAKES OF PESTICIDES IN DIETS WITH THEIR ACCEPTABLE DAILY INTAKES

The Meeting considered the results of a study—an extension of earlier studies—undertaken in accordance with the recommendations of previous Meetings (FAO/WHO, 1969a, 1970a, 1971a, 1972a). The potential intakes of all pesticides for which ADIs and residue limits had previously been recommended, together with those dealt with at this Meeting, were calculated on the basis of more up-to-date food consumption data from five countries. Details of the methods used for calculating the potential intakes are given in the report of the 1969 Joint Meeting (FAO/WHO, 1970a).

The calculated "potential daily intakes" of the pesticides evaluated at this Meeting were reviewed. For chlorothalonil, dicloran, dodine, and fenamiphos, there was not even a theoretical possibility that the acceptable daily intakes might be exceeded. For fenitrothion and pirimiphos-methyl a recalculation based on available information on the disappearance of residues during processing and cooking before consumption showed that the potential daily intakes calculated in this way might marginally exceed the acceptable daily intakes.

It is therefore felt that any available data showing the effect of storage, transport, and processing on the nature and level of residues should be used to permit a closer estimation of the potential intake. For those chemicals that resist degradation, monitoring the actual levels in the diet would be particularly desirable.

## 7. FUTURE WORK

The following items should be considered at the 1975 or future Joint Meetings :

1. Pesticides for which ADIs or residue limits have been withheld or established only on a temporary basis and that have been listed for review in 1975. They are bromophos-ethyl, chlordimeform, coumaphos, disulfoton, fenthion, leptophos, methidathion, monocrotophos, omethoate, parathion-methyl, piperonyl butoxide, quintozone, trichlorfon, and pyrethrins.

2. Pesticides evaluated at previous meetings for which information is deficient, or which otherwise require re-evaluation.

3. Evaluation of the following pesticides : bioresmethrin and cyanofenphos.<sup>1</sup>

4. Compounds put forwards for evaluation and other matters to be referred to the Joint Meeting by the Codex Committee on Pesticide Residues at its Eighth Session, scheduled for March 1975.

5. Reconsideration of recommendations for : aldrin-dieldrin ; 2,4-D (see item (4) on page 24 of the report of the 1973 Meeting) ; hexachlorobenzene (see item (6) on page 24 of the report of the 1973 Meeting) ; dithiocarbamate fungicides (maneb, metiram, nabam, propineb, zineb, ferbam, thiram, and ziram) (for evaluation for residue limits) ; benomyl ; carbendazim ;<sup>2</sup> and thiophanate-methyl.

## 8. RECOMMENDATIONS

1. In the light of the need of research workers, government officials, members of the Codex Alimentarius Commission, and others for full and early knowledge of the matters discussed at Meetings, the Directors-General are requested to review procedures for the publication of reports and mono-

---

<sup>1</sup> Proposed ISO name for *O*-(4-cyanophenyl) *O*-ethyl phenylphosphonothioate.

<sup>2</sup> Proposed ISO name for methyl 1*H*-benzimidazol-2-ylcarbamate.

graphs with a view to decreasing the length of time between Meetings and the issue of these publications.

2. To provide more time for the collection of data from various sources and for the consideration of these data by the appropriate specialists, an agenda for the next Meeting listing the compounds to be considered should be issued immediately after the present Meeting. For similar reasons, the Codex Committee on Pesticide Residues should be asked to propose its priorities so as to enable longer periods of notice before each future Joint Meeting of work required on particular pesticides.

3. When attempting to re-evaluate certain pesticides about which sufficient information had not been available at previous sessions, the Meeting once again found that necessary research, to which attention had previously been drawn, had not been carried out. This is particularly true with respect to pesticides no longer covered by patent rights. As this information is essential to obtaining assurance concerning the safety of these products, some of which are used on a large scale and will be needed for currently planned increases in world food production, the Meeting strongly recommended that new and vigorous efforts, coordinated on an international basis, should be made to provide financial support for such research.

4. In some instances where lack of information precluded full evaluation, members knew of the existence of data that had not been placed before the Meeting. They drew attention to the need for more comprehensive collection and collation of such information. In view of the acknowledged importance of pesticides in the production and protection of foods as reflected in the resolutions of the World Food Conference, the Director-General of FAO is requested to give every possible consideration to strengthening the facilities available for soliciting and collating information existing in archives of governments, industry, and other institutions, and otherwise to provide the support that is essential to the full evaluation of pesticides.

5. In view of the value of observations of the effects of pesticides in man (see section 2.3), it is recommended that WHO seek the cooperation of the World Federation of Associations of Clinical Toxicology Centers and Poison Control Centers and other organizations in developing the relevant data banks.

6. As noted in section 2.4 of this report, it is proposed that WHO should take various steps to acquire the additional information needed for the evaluation of certain pesticides.

## REFERENCES

- FAO/WHO (1958) *Procedures for the testing of intentional food additives to establish their safety for use. Second report of the Joint FAO/WHO Expert Committee on Food Additives. FAO Nutrition Meetings Report Series, No. 17 ; Wld Hlth Org. techn. Rep. Ser., No. 144*
- FAO/WHO (1961) *Evaluation of the carcinogenic hazards of food additives. Fifth report of the Joint FAO/WHO Expert Committee on Food Additives. FAO Nutrition Meetings Report Series, No. 29 ; Wld Hlth Org. techn. Rep. Ser., No. 220*
- FAO/WHO (1962) *Principles governing consumer safety in relation to pesticide residues. Report of a meeting of a WHO Expert Committee on Pesticide Residues held jointly with the FAO Panel of Experts on the Use of Pesticides in Agriculture. FAO Plant Production and Protection Division Report No. PL/1961/11 ; Wld Hlth Org. techn. Rep. Ser., No. 240*
- FAO/WHO (1964) *Evaluation of the toxicity of pesticide residues in food ; report of a Joint Meeting of the FAO Committee on Pesticides in Agriculture and the WHO Expert Committee on Pesticide Residues. FAO Meeting Report, No. PL/1963/13 ; WHO/ Food Add./23 (1964)*
- FAO/WHO (1965a) *Evaluation of the toxicity of pesticide residues in food ; report of the Second Joint Meeting of the FAO Committee on Pesticides in Agriculture and the WHO Expert Committee on Pesticide Residues. FAO Meeting Report, No. PL:1965/ 10 ; WHO/FOOD Add./26.65*
- FAO/WHO (1965b) *Evaluation of the toxicity of pesticide residues in food. FAO Meeting Report, No. PL:1965/10/1 ; WHO/Food Add./27.65*
- FAO/WHO (1965c) *Evaluation of the hazards to consumers resulting from the use of fumigants in the protection of food. FAO Meeting Report, No. PL:1965/10/2 ; WHO/ Food Add./28.65*
- FAO/WHO (1967a) *Pesticide residues in food. Joint report of the FAO Working Party on Pesticide Residues and the WHO Expert Committee on Pesticide Residues. FAO Agricultural Studies, No. 73 ; Wld Hlth Org. techn. Rep. Ser., No. 370*
- FAO/WHO (1967b) *Evaluation of some pesticide residues in food. FAO : PL/CP/15 ; WHO/Food Add./67.32*
- FAO/WHO (1968a) *Pesticide residues. Report of the 1967 Joint Meeting of the FAO Working Party and the WHO Expert Committee. FAO Meeting Report, No. PL:1967/ M/11 ; Wld Hlth Org. techn. Rep. Ser., No. 391*
- FAO/WHO (1968b) *1967 evaluation of some pesticide residues in food. FAO/PL:1967/ M/11/1 ; WHO/Food Add./68.30*
- FAO/WHO (1969a) *Pesticide residues in food. Report of the 1968 Joint Meeting of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Committee on Pesticide Residues. FAO Agricultural Studies, No. 78 ; Wld Hlth Org. techn. Rep. Ser., No. 417*
- FAO/WHO (1969b) *1969 evaluations of some pesticide residues in food. FAO/PL:1968/ M/9/1 ; WHO/Food Add./69.35*
- FAO/WHO (1970a) *Pesticide residues in food. Report of the 1969 Joint Meeting of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Group on Pesticide Residues. FAO Agricultural Studies, No. 84 ; Wld Hlth Org. techn. Rep. Ser., No. 458*

- FAO/WHO (1970b) *1969 evaluations of some pesticide residues in food*. FAO/PL:1969/M/17/1 ; WHO/Food Add./70.38
- FAO/WHO (1971a) *Pesticide residues in food. Report of the 1970 Joint Meeting of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Group on Pesticide Residues*. FAO Agricultural Studies, No. 87 ; Wld Hlth Org. techn. Rep. Ser., No. 474
- FAO/WHO (1971b) *1970 evaluations of some pesticide residues in food*. AGP:1970/M/12/1 ; WHO/Food Add./71.42
- FAO/WHO (1972a) *Pesticide residues in food. Report of the 1971 Joint Meeting of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Committee on Pesticide Residues*. FAO Agricultural Studies, No. 88 ; Wld Hlth Org. techn. Rep. Ser., No. 502
- FAO/WHO (1972b) *1971 evaluations of some pesticide residues in food*. AGP-1971/M/9/1 ; WHO Pesticide Residues Series, No. 1
- FAO/WHO (1973a) *Pesticide residues in food. Report of the 1972 Joint Meeting of the FAO Working Party of Experts on Pesticide Residues and of the WHO Expert Committee on Pesticide Residues*. FAO Agricultural Studies, No. 90 ; Wld Hlth Org. techn. Rep. Ser., No. 525
- FAO/WHO (1973b) *1972 evaluations of some pesticide residues in food*. AGP:1972/M/9/1 ; WHO Pesticide Residues Series, No. 2
- FAO/WHO (1974a) *Pesticide residues in food. Report of the 1973 Joint Meeting of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Committee on Pesticide Residues*. FAO Agricultural Studies, No. 92 ; Wld Hlth Org. techn. Rep. Ser., No. 545
- FAO/WHO (1974b) *1973 evaluations of some pesticide residues in food*. AGP:1973/M/9/1 ; WHO Pesticide Residues Series, No. 3
- FAO/WHO (1974c) *Report of the Seventh Session of the Codex Committee on Pesticide Residues*. (Unpublished document ALINORM 74/24)
- FAO/WHO (1974d) *Toxicological evaluation of certain food additives with a review of general principles and of specifications*. FAO Nutrition Meetings Report Series, No. 53 ; Wld Hlth Org. techn. Rep. Ser., No. 539
- FAO/WHO (1974e) *The use of mercury and alternative compounds as seed dressings. Report of a Joint FAO/WHO meeting*. FAO Agricultural Studies, No. 95 ; Wld Hlth Org. techn. Rep. Ser., No. 555
- FAO/WHO (1975a) *Pesticide residues in food. Report of the 1974 Joint Meeting of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Committee on Pesticide Residues*. FAO Agricultural Studies, No. 97 ; Wld Hlth Org. techn. Rep. Ser., No. 574
- FAO/WHO (1975b) *1974 evaluations of some pesticide residues in food*. AGP:1974/M/11 ; WHO Pesticide Residues Series, No. 4 (in press)
- WHO (1967) *Procedures for investigating intentional and unintentional food additives. Report of a WHO Scientific Group*. Wld Hlth Org. techn. Rep. Ser., No. 348
- WHO (1974) *Assessment of the carcinogenicity and mutagenicity of chemicals. Report of a WHO Scientific Group*. Wld Hlth Org. techn. Rep. Ser., No. 546

Annex 1

RECOMMENDATIONS CONCERNING ACCEPTABLE DAILY INTAKES AND RESIDUE LIMITS  
MADE AT THE 1974 MEETING

These recommendations are additional to, or amend, those recorded in Annex 1 of the report of the 1972 Meeting (FAO/WHO, 1973a) as well as those recorded in Annex 1 of the report of the 1973 Meeting (FAO/WHO, 1974a).

Temporary recommendations are denoted by superscripts <sup>a</sup>, <sup>b</sup>, or <sup>c</sup>, indicating that further work is to be made available not later than 30 June in the year 1975, 1976, or 1977 respectively.

Further explanatory notes are given at the end of this table (see page 30).

Pesticides and references <sup>1</sup>	Maximum acceptable daily intake (mg/kg body weight)	Commodity	Residue limits (mg/kg)		Remarks
			Tolerances (practical limits indicated as (P))	Guideline levels <sup>2</sup>	
aldrin 1967b, 1968b	0.0001				See also dieldrin.
amitrole 1975b	0.00003	Raw agricultural commodities of plant origin	0.02 *		Conditional ADI: uses of amitrole should be restricted to those where food residues would be unlikely to occur.
binapacryl 1970b, 1975b	0.0025	Cherries	0.5		
captafol 1970b, 1974b, 1975b	0.05 <sup>b</sup>	Apricots Plums	15 <sup>b</sup> 10 <sup>b</sup>		Figures relate only to parent compound.

## Annex 1 (continued)

Pesticides and references <sup>1</sup>	Maximum acceptable daily intake (mg/kg body weight)	Commodity	Residue limits (mg/kg)		Remarks
			Tolerances (practical limits indicated as (P))	Guideline levels <sup>2</sup>	
Chinomethionat (oxythioquinox) 1968b, 1975b	0.003 c	Papayas (whole fruit)	5.0 c		
		Apples, citrus fruits (kernels), avocado, raw cereals, cucumbers, currants (black, red, white), grapes, gherkins, gooseberries, papaya (pulp), Macadamia nuts (kernels)	0.1 c 0.02* 0.05* 0.01*		
chlorothalonil 1975b	0.03 c	Meat			
		Milk			
chlorpyrifos 1973b, 1975b	0.0015	Peaches	30 c		
		Currents (black, red, white)	25 c 15 c		
cyhexatin 1971b, 1974b, 1975b	0.007 c	Celery			
		Blackberries, cherries, chicory sprouts, collards, endive, kale, lettuce (head), raspberries, peppers	10 c		
2,4-D 1971b, 1972b, 1975b	0.3	Beans (green including pod), broccoli, Brussels sprouts, cabbage, cauliflower, cranberries, cucumbers, melons, onions, oranges, pumpkins, squash, tomatoes	5 c		
		Carrots, sweet corn, sugar beets	1 c		
chlorpyrifos 1973b, 1975b	0.0015	Lima beans, peanuts (whole)	0.5 c		
		Peanuts (kernels), potatoes	0.1 c		
cyhexatin 1971b, 1974b, 1975b	0.007 c	Citrus fruit (whole)	0.3		
		Apples, pears, tea (dry, manufactured), tomatoes	2 c 1 c		
2,4-D 1971b, 1972b, 1975b	0.3	Gherkins			
		Cucumbers, melons, bell peppers (glass-house use only)	0.5 c		
2,4-D 1971b, 1972b, 1975b	0.3	Meat	0.2		
		Milk and milk products (fat basis)	0.05 (P)*		
2,4-D 1971b, 1972b, 1975b	0.3	Citrus fruit	2		
		Potatoes	0.2		
		Milk	0.05*		

Tolerances are expressed as the parent compound excluding organic degradation products and inorganic tin. Formerly listed as tricyclohexyl hydroxide or as tricyclohexyl hydroxystannate.

				Recommendations apply to the parent compound.
dichloruanid 1970b, 1975b	0.3 c	Currents (red, black, white), grapes, raspberries Lettuce, strawberries Apples, cucumbers, peaches, pears Tomatoes, beans (green with pod), cherries	15 c 10 c 5 c 2 c	
dichlorvos 1967b, 1968b, 1970b, 1971b, 1975b	0.004	Vegetables (except lettuce)	0.5	See FAO/WHO, 1973a, Annex 1, Remarks.
2,6-dichloro-4-nitrobenzenamine (dicloran) 1975b	0.03 c	Cherries, peaches Apricots, carrots, grapes, lettuce, plums, raspberries, strawberries Blackberries, currants (red, white, black) Beans (French) Gherkins, tomatoes	15 c 10 c 5 c 2 0.5	
dicofof 1969b, 1971b, 1975b	0.025	Fruits (except strawberries) Vegetables (except cucumbers, gherkins, tomatoes) Cucumbers, gherkins Strawberries, tomatoes	5 5 2 1	
dieldrin 1967b, 1968b, 1969b, 1970b, 1971b	0.0001	Fruits (other than citrus)	0.1 u	
dinocap 1970b, 1975b	No ADI	Apples, apricots, blackberries, boysenberries, cantaloupes, cucumbers, grapes, honeydew melons, muskmelons, peaches, pears, pumpkins, raspberries, squash, strawberries		Revised temporary ADI, which applies to the parent compounds or to the sum of residues of all compounds present.
dithiocarbamates, dimethyl ferbam, thiram, and ziram) 1965b, 1968b, 1971b, 1973a	0.005 c		0.1 *	
dithiocarbamates, ethylene bis-(mancozeb, maneb, and zineb, including zineb derived from nabam plus zinc sulfate) 1965b, 1968b, 1971b, 1975a	0.005 c			Revised temporary ADI, which applies to the parent compounds or to the sum of residues of all compounds present.



ferbam 1965b, 1968b, 1971b, 1975a	0.005 <sup>c</sup>	Cauliflower, cocoa beans, eggplant, pears, peppers, rice (polished), soybeans (dry)	0.1	Revised temporary ADI.
hexachlorobenzene 1970b, 1974a, b, 1975a, b	0.0006	Cucumbers, meat, fat of meat, milk, milk products, onions, potatoes	0.05 *	
leptophos 1975b	No ADI	Broccoli, Brussels sprouts, cabbage, lettuce, tomatoes Crude cottonseed oil Cottonseed, cottonseed meal Potatoes Maize: field corn (kernels), sweet corn (kernels and cobs, husks and silks removed)	2 1 0.2 0.1 0.05	Conditional ADI. Previous residue limits (1974a) con- firmed.
mancozeb 1968b, 1971b, 1975a	0.005 <sup>c</sup>	Beans (with pod) Apples, pears Celery, lettuce Tomatoes Carrots, maize: sweet corn (cob and kernels, husks and silks removed) Potatoes, banana (pulp)	3 <sup>c</sup> (0.1) 2 <sup>c</sup> (0.02) 2 <sup>c</sup> (0.01) * 1 <sup>c</sup> (0.05) 0.2 <sup>c</sup> (0.01) * 0.05 <sup>c</sup> (0.01) *	Revised temporary ADI. Residue limits should be based on and determined by measurement of the ethylendiamine moiety, and of ethyl- enethiourea (ETU). Limits for ETU are also recommended and appear in brackets. Neither limit should be exceeded in a given sample.
maneb 1965b, 1968b, 1971b, 1975a	0.005 <sup>c</sup>			Revised temporary ADI.
nabam 1965b, 1968b, 1971b, 1975a	0.005 <sup>c</sup>			Revised temporary ADI.
oxythioquinox — See chinomethionat				
phosphamidon 1965b, 1967b, 1969b, 1970b, 1973b, 1975b	0.001	Beans, broccoli, Brussels sprouts, cabbage, carrots, celery, green peppers, peas, spinach, cherries, peaches, plums, strawberries	0.2	Tolerances are for the sum of phos- phamidon and its desethyl derivative, expressed as phosphamidon.
pirimiphos-methyl 1975b	0.005 <sup>b</sup>	Bran (wheat, rice) Wheat, rye, rice (in husk) Barley, maize, oats Wholemeal flour (wheat, rye)	20 <sup>b</sup> 10 <sup>b</sup> 7 <sup>b</sup> 5 <sup>b</sup>	

## Annex 1 (continued)

Pesticides and references <sup>1</sup>	Maximum acceptable daily intake (mg/kg body weight)	Commodity	Residue limits (mg/kg)		Remarks
			Tolerances (practical limits indicated as (P))	Guideline levels <sup>2</sup>	
pyrethrins 1967b	0.04	Rice (hulled), wheat flour (white) Bread (wholemeal), rice (polished) Bread (white) Meat, milk, eggs	2 <sup>b</sup> 1 <sup>b</sup> 0.5 <sup>b</sup> 0.05 * <sup>b</sup>		Previously recommended tolerances confirmed and no longer temporary.
quintozene 1970b, 1974b, 1975b	0.001 <sup>a</sup>	Peanut kernels	1		The temporary tolerance for mushrooms, recommended in 1969 and 1973, is withdrawn.
tecnazene 1975b	No ADI	See remarks			
thiram 1965b, 1968b, 1971b, 1975a	0.005 <sup>c</sup>				Revised temporary ADI.
zinab 1965b, 1968b, 1971b, 1975a	0.005 <sup>c</sup>				Revised temporary ADI.
ziram 1965b, 1968b, 1971b, 1975a	0.005 <sup>c</sup>				Revised temporary ADI.

1. References are to FAO/WHO publications (see list of references on p. 23). Dates of publication refer to the first complete or completely revised monograph or to important mentions of the compound in a report. Where a monograph has been completely revised mention is not necessarily made of any earlier ones.

2. Guideline levels are included to assist administering authorities, even though ADIs have not been established for the individual products, or temporary ADIs established at an earlier date have been withdrawn. The levels recommended are those that need not be exceeded if good practices are followed.

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.

**ALDRIN/DIELDRIN**

**Required** (before July 1975)

1. Information on use patterns in fruit growing and residues arising therefrom in countries where such uses are approved.

**AMITROLE**

**Desirable**

1. Long-term feeding studies in a sufficient number of rats and mice with low levels of amitrole of known composition and purity.
2. Studies to elucidate the possible relationship between the effects of amitrole on the thyroid and on the liver.
3. Studies to show that the analytical methods determine not only the parent compound but biologically active metabolites.
4. Studies to develop a specific method sensitive to 0.005 ppm.

**AZINPHOS-METHYL**

**Desirable**

1. Residue data for other crops, including grapes, for which insufficient data were available to establish tolerances or amend tolerances recommended at the 1973 and 1974 Joint Meetings.

**CAPTAN**

**Desirable** (in addition to the information listed in FAO/WHO, 1974a)

1. Further data on residues arising from approved uses of captan on apples and pears.

## CHINOMETHIONAT

### **Required** (by July 1977)

1. Studies to identify and evaluate the toxicity of metabolites.
2. A method of analysis that determines the 2,3-dithiolo-6-methyl-quinoxaline metabolite.

### **Desirable**

1. Studies on the relationships between observed liver enlargement and reduced microsomal enzyme activity.
2. Studies of metabolism in non-rodent species of animal.
3. Observations in man.
4. Information on the lower limit of determination of chinomethionat in various crops with the use of Vogeler's method.

## CHLORDANE

### **Desirable** (in addition to the information listed in FAO/WHO, 1971a)

1. Information from governments on use patterns.
2. Information from countries other than the USA on residues resulting from approved uses.

## CHLOROTHALONIL

### **Required** (before July 1977)

1. Additional studies to resolve lower dose limit for kidney effects in the rat.
2. Determination of growth reduction in pups relative to dietary ingestion or secretion into maternal milk.
3. Data on residues of chlorothalonil and the 4-hydroxy metabolite in crops that may be fed to animals.
4. The results of feeding studies on dairy cattle, understood to be in progress, to determine the level and nature of residues in milk and tissues.

### **Desirable**

1. Observations in man.
2. Residue data for food moving in commerce.
3. Further information on the effects of processing, including household cooking, on residues.

## 2,4-D

### **Desirable** (in addition to the information listed in FAO/WHO, 1972a)

1. Information on the storage and fate of 2,4-D in food animals.
2. Information on the fate of 2,4-D in soils and residue data on crops grown on contaminated soil.
3. Development of extraction procedures to determine total 2,4-D residues including 2,4-D (free acid), 2,4-dichlorophenol, and their conjugates.

## DICHLLOFLUANID

### **Required** (by 1977)

1. Studies on absorption and distribution in various organs and excretion of dichlofluanid in the rat.
2. Information on the pharmacokinetic properties of the dichlorofluoromethylthio moiety.

### **Desirable**

1. Metabolism studies on dichlofluanid.
2. Results of current studies on the pathway of degradation, especially the fate of the fluorine-containing moiety of the molecule in and on plants.
3. Further residue data from supervised trials to resolve certain inconsistencies or to provide new information on blackberries, gooseberries, loganberries, mulberries, raspberries, currants, hops, kohlrabi, leaf brassica, melons, onions, paprika, wheat, and barley.
4. Further residue data for raw agricultural products moving in commerce.
5. Further evaluation of the analytical method of Becker for regulatory purposes.

## 2,6-DICHLORO-4-NITROBENZENAMINE (DICLORAN)

### **Required** (before July 1977)

1. Further studies on the ocular disturbance observed in dogs to confirm and clarify this effect.
2. Information on fate in livestock animals (since plant material containing dicloran residues may be fed to animals).

### **Desirable**

1. Information on the effect of dicloran on hepatic microsome systems in several species.
2. Further observations in man.
3. Further information on the fate of residues during storage, transport, and processing of fruit and vegetables.
4. Information on the transfer of residues from grapes to wine and on their possible influence on wine processing.
5. Further information on soil residues and their possible uptake into subsequent crops.
6. Further data to clarify inconsistencies in the residue levels found in different berries.

## DICOFOL

### **Desirable**

1. Results of residue studies to indicate the level of residues in various fruits and vegetables following currently approved use patterns.

## DINOCAP

### **Required** (in addition to the information listed in FAO/WHO, 1970a)

1. Information on the nature of dinocap residues.
2. Residue data from countries other than the USA and Canada.
3. The development and evaluation of a specific residue method suitable for regulatory purposes.

## DITHIOCARBAMATES

### **Required** (before July 1977)

1. See section 4.1 of this report.

2. For ethylene bis dithiocarbamates :
  - (a) Residue studies in which the ethylenediamine moiety and ethylenethiourea (ETU) are separately determined.
  - (b) Further studies on the fate of residues during the preparation and processing of foods with particular reference to their conversion to ETU.

#### DODINE

##### **Required** (by 1976)

1. Metabolic studies of dodine in animals and plants.

##### **Desirable**

1. Teratogenicity studies in appropriate animal species.
2. Fate of residues in apple and grape pomace when fed to dairy cows.
3. Supervised trials on various crops in countries other than the USA.
4. Further details on residues arising in supervised trials on peaches and grapes, and during wine processing.

#### ENDOSULFAN

##### **Desirable** (in addition to the information listed in FAO/WHO, 1972a)

1. Additional residue studies in which total residues of  $\alpha$ -endosulfan,  $\beta$ -endosulfan, and endosulfan sulfate are measured and related to the agricultural practices in those countries with registered uses.

#### FENAMIPHOS

##### **Required** (before July 1977)

1. Further data on which to judge the residues in or on potatoes and tomatoes.
2. Adequate residue data on which to base recommendations for limits for other crops (e.g., beans, cucumbers, lettuce, peppers, and strawberries).

##### **Desirable**

1. Information on brain cholinesterase and behavioural studies in animals exposed to low levels for extended periods.
2. Observations in man.

3. Additional studies on the potentiation effects with other organo-phosphorus pesticides.

4. Residue data for raw agricultural products moving in commerce.

5. Further residue data for different crops from supervised trials in accordance with good agricultural practice, including data on rates and frequencies of application; soil, foliar, or other treatment; and preharvest intervals, especially for broccoli and tangerines.

#### FENITROTHION

##### **Desirable**

1. Further observations in man.

2. Results from studies now in progress on the effect of cooking on fenitrothion residues in rice.

3. Further studies to determine the fate of residues during the cooking of other cereal products from wheat and rye.

4. Information on the level and fate of residues following postharvest use on oats, barley, and rye.

#### FOLPET

##### **Desirable** (in addition to the information listed in FAO/WHO, 1974a)

1. Information on the nature, level, and fate of residues following washing, blanching, storage, and thermal processing of treated crops.

2. Residue data obtained by newer methods of analysis on the main commodities for which tolerances have been recommended.

3. Information on the fate of residues in soil.

4. Further data on the quantities of degradation products in relation to residues of the parent compound.

5. Results of metabolism studies currently planned.

#### LEPTOPHOS

##### **Required** (before July 1975)

1. Residue data on other major crops for which usage recommendations are made, including rice, other small grains, fruit, sugarcane, and sugarbeet.

2. Additional residue data from countries other than the USA.

3. Residues in those parts of agricultural crops that are used either as such or as agricultural waste for feeding purposes following normal agricultural practices.

## LINDANE

### Required (before July 1977)

1. A long-term carcinogenicity study.

### Desirable (in addition to the information listed in FAO/WHO, 1974a)

1. Supervised trials on vegetables in countries where lindane is widely used.

## PIRIMIPHOS-METHYL

### Required (before July 1976)

1. Additional studies whereby no-effect levels for decreased pregnancy rates and for hydronephrosis in offspring can be clearly established.
2. Further studies to clarify the liver injury in dogs observed in 90-day studies.

### Desirable

1. Observations of longer duration in man.
2. Information from studies now in progress on other stored commodities including nuts, peanuts, and dried fruit.
3. Information on residues in fruit and vegetables following approved uses.
4. Further information on the level and fate of residues in food at the point of consumption following the use of pirimiphos-methyl for the control of various pests in stored products.

## TECNAZENE

### Required (before an ADI and residue limits can be recommended)

1. Adequate toxicological data.
2. Full information on specifications for the chemical and the formulated products (including impurities, e.g., HCB), present use patterns, residue data from supervised trials, fate of residues in crops other than potatoes and in soils, etc.