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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**

Rome, 8-15 December 1969



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**1969 JOINT MEETING OF THE FAO WORKING PARTY OF EXPERTS
ON PESTICIDE RESIDUES AND THE
WHO EXPERT GROUP ON PESTICIDE RESIDUES**

Rome, 8-15 December 1969

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PESTICIDE RESIDUES IN FOOD

Report of the 1969 Joint FAO/WHO Meeting

A Joint Meeting of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Group on Pesticide Residues was held in Rome, 8-15 December 1969. The meeting was opened by O.E. Fischnich, Assistant Director-General on behalf of the Directors-General of the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO). The FAO Working Party of Experts on Pesticide Residues had already met 3-7 December 1969 in Rome in preparation for the joint meeting.

1. INTRODUCTION

This annual Joint Meeting of pesticide experts was convened at a time of ever-increasing public concern regarding the safety of pesticides to man and his environment. After carefully reviewing the available data, the Meeting agreed that while there are still some unresolved questions about the effect of certain pesticides on human health, these pesticides must nevertheless be used for the foreseeable future. Care must be taken to use them in such a way as to avoid hazard to man and, as far as possible, the contamination of the environment. This reaffirms a conclusion reached at a Joint Meeting of an FAO Panel of Experts on the Use of Pesticides in Agriculture and the WHO Expert Committee on Pesticide Residues in 1961 (FAO/WHO, 1962a). This first Joint Meeting had recommended that studies be undertaken to evaluate these hazards on the basis of the toxicological and other pertinent data on those pesticides known to leave residues in food, even when used in accordance with good agricultural practice.

Subsequently, joint meetings of the FAO Committee on Pesticides in Agriculture and the WHO Expert Committee on Pesticide Residues were held in 1963 and 1965. The reports of these meetings (FAO/WHO, 1964; FAO/WHO, 1965a), which were concerned primarily with establishing acceptable daily intakes, and the supporting documents (FAO/WHO, 1965b and c) were then considered by the FAO Working Party on Pesticide Resi-

dues with a view to recommending tolerances and appropriate methods of analysis for certain pesticides used on cereals (FAO, 1966).

To minimize the delay in establishing acceptable daily intakes, tolerances and methods of analysis for additional pesticides, joint meetings of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Committee on Pesticide Residues (referred to hereafter as "Joint FAO/WHO Meetings on Pesticide Residues") were held in 1966, 1967 and 1968. In the reports of these meetings (FAO/WHO, 1967a, 1968a and 1969a), the established acceptable daily intakes and recommended tolerances for a number of pesticides are given. The supporting documents (FAO/WHO, 1967b, 1968b and 1969b) contain detailed monographs on the pesticides which were considered and include comments on analytical methods.

The present Joint Meeting of the FAO Working Party of Experts and the WHO Expert Group on Pesticide Residues 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 Fourth Session of the Codex Committee on Pesticide Residues held in October 1969 (FAO/WHO, 1969c).

During the present Joint Meeting the FAO Working Party undertook:

1. to review relevant data on certain pesticide residues;
2. to propose pesticide residue tolerances and, where appropriate, practical residue limits;
3. to recommend methods of analysis for pesticide residues.

The WHO Expert Group undertook:

1. to review toxicological and related data on certain pesticides;
2. to establish, where possible, acceptable daily intakes for man of those pesticides.

Furthermore, each of these groups made recommendations designed to initiate, stimulate and coordinate necessary research.

2. GENERAL CONSIDERATIONS

2.1 Modification of the agenda

All the pesticides mentioned in Section 6, "Future Work," in the report of the 1968 Joint Meeting (FAO/WHO, 1969a) were considered except for thiabendazole: the relevant data on this pesticide were received too late for evaluation. Among the compounds referred to this

meeting by the Codex Committee on Pesticide Residues (see Section 5.1), bromide ion, carbaryl, chlordane, DDT, dichlorvos, dieldrin, ethion, heptachlor, hydrogen phosphide, lindane, malathion, parathion, piperonyl butoxide and pyrethrins had been considered at a previous meeting. A number of fumigants were placed on the agenda as suggested by the 1968 meeting. Special consideration was given to carbaryl and DDT because of the new data which had become available since they were previously evaluated.

2.2 Definitions

The glossary published as Appendix 1 to the report of the 1967 Joint Meeting on Pesticide Residues (FAO/WHO, 1968a) was noted and the meeting agreed to continue using the terms defined therein. In addition, the definitions of "conditional acceptable daily intake" and "tentative negligible daily intake" were agreed upon. (See Section 2.3 and Appendix IV.)

2.3 Principles adopted

As with previous meetings, this meeting took account of the principles enumerated in the first and second reports of the Joint Meetings of the FAO Committee on Pesticides in Agriculture and the WHO Expert Committee on Pesticide Residues (FAO/WHO, 1964; FAO/WHO, 1965a) and also those set out in the Second, Fifth, Eleventh and Twelfth reports of the Joint FAO/WHO Expert Committee on Food Additives (FAO/WHO, 1958; FAO/WHO, 1961; FAO/WHO, 1968c; and FAO/WHO, 1969d) and in the report of the WHO Scientific Group on Procedures for Investigating Intentional and Unintentional Food Additives (WHO, 1967).

The general principles concerning the evaluation of metabolites, as stated in the Report of the 1968 Joint Meeting, were reaffirmed and extended as follows:

The acceptable daily intake (ADI) applies to the pesticide, together with its metabolites if the main metabolites present in the residues in the edible portions of farm animals, animal products or plants are identical with the main metabolites in experimental animals. The metabolites must also be present in the same order of magnitude.

If the main metabolites in and on plants and animals are not identical, or if they are identical but not of the same order of magnitude, then the ADI applies only to the original pesticide, and separate studies on the main metabolites in the residues may be necessary for assessment of their toxicological properties.

In the evaluation of the toxicological and related data the Meeting took account of these principles and criteria for establishing ADIS or temporary ADIS when appropriate. Furthermore, the Meeting agreed to establish "conditional ADIS" following toxicological evaluation of certain compounds in order to limit their use except where there are no satisfactory substitutes. A similar practice has been adopted for a number of substances by the Joint FAO/WHO Expert Committee on Food Additives (FAO/WHO, 1968c, 1969d).

In evaluating the toxicological data on many pesticides, questions arose on the possible carcinogenicity, mutagenicity or teratogenicity of some of these compounds and on the interpretation of the relevance to man of some experimental animal results regarding these effects. Where a dose-response relationship in a teratogenicity test was found, the Meeting felt an evaluation could be given. Where problems of mutagenicity arise the meeting agreed with the views stated in the report of the WHO Scientific Group on Procedures for Investigating Intentional and Unintentional Food Additives (WHO, 1967).

The question of possible carcinogenicity of some pesticides was discussed at great length and it was agreed that there was no conclusive evidence for or against the carcinogenicity of those pesticides considered. The Meeting strongly urged that consideration be given to the question of dose-response for carcinogens and of possible threshold levels. A definite requirement in the assessment of carcinogenicity should be that experimental procedures follow the rules put forward in the Fifth Report of the Joint FAO/WHO Expert Committee on Food Additives (FAO/WHO, 1961) and in the report on Carcinogenicity Testing published by the International Union against Cancer (IACC). The Meeting then recommended that WHO should convene an appropriate meeting generally to evaluate the significance of carcinogenic effects of chemicals in experimental animals for assessing the potential risk of these chemicals to man.

In evaluating evidence on residues of the various pesticides, information on patterns of use, on supervised trials, on methods of analysis, and on the fate of residues during storage and processing was considered: any available evidence on the occurrence of residues in foods in commerce or at the time of consumption was also taken into account.

2.4 Variability of composition of certain pesticides

During the course of their discussions, the Meeting frequently encountered problems stemming from inadequate information on the composition of certain technical grade pesticides and associated contaminants. Also of concern was the fact that some pesticides are produced by dif-

ferent manufacturers; thus the composition of technical products may vary, particularly with respect to contaminants. The Meeting noted with satisfaction the programme of the FAO Working Party of Experts on the Official Control of Pesticides (Section B: Specifications) to develop and publish specifications for agricultural pesticides and formulations thereof and felt that this programme would greatly assist in the solution of these problems.

2.5 Methods of analysis

The Meeting decided that for each compound for which a tolerance or practical residue limit is recommended an effort would be made to advise on the method most suitable for use by regulatory analysts: attention would be drawn to the method of choice, and indications of the sensitivity of the methods mentioned would be given in each case where possible.

The Meeting reviewed a report from the Fourth Meeting of the Commission on Pesticide Residue Analysis of the International Union of Pure and Applied Chemistry (IUPAC, 1970) which contained the following recommendations relating to multiresidue methods for organochlorine pesticide residues:

“(i) That as an interim measure this Commission on Pesticide Residue Analysis should adopt the Mills procedures as defined and explained in the FDA Pesticide Analytical Manual, Volume 1, 1968, as multidetection¹ methods which are suitable for recommendation to FAO, Codex Alimentarius and other interested parties.

It is also recommended that further consideration be given to the recommendations of at least one alternative multidetection method.

- (ii) That the Section attempt to promote the further development and orderly improvement of the Mills, and other adopted methods.
- (iii) That research on the development of confirmatory tests which are compatible with adopted methods should be encouraged.
- (iv) That the Section publicize and emphasize the importance of expertise and experience on the part of the residue analyst applying any of these multidetection techniques, particularly in view of the possible presence of interfering substances such as the poly-chlorobiphenyl compounds.”

¹ The term “multidetection” is understood to mean multiresidue.

These recommendations were acceptable to the Meeting in the light of present knowledge, and it was agreed that they should be forwarded to the Codex Committee on Pesticide Residues. Recommendations relating to methods for residues of organophosphorus pesticides, fumigants and organomercurials were also received from IUPAC and discussed, but they were not ready for forwarding at this time.

Details of a gas chromatographic method for residues of phosphamidon and its des-ethyl derivative were reviewed in response to the request contained in the report of the 1968 Joint Meeting (FAO/WHO, 1969a). It was agreed that the procedure would be satisfactory. (See monograph addendum on phosphamidon, FAO/WHO, 1970.)

2.6 DDT

Current concern over the potential hazard from DDT is based on (1) its ubiquity, (2) its persistence in the environment and the effect on some wildlife, (3) its retention in living organisms, (4) its capacity to be transferred to and to be retained in the foetus, and (5) the existence of some experimental evidence of its capacity to induce tumours in experimental animals. The relevance to human health of information, particularly on the last aspect, was considered at the meeting.

Although the available experimental data do not provide sufficient information to allow a definite evaluation of the potential carcinogenicity of DDT, they do strongly indicate that DDT ought to be extensively tested. In fact the 1967 Joint Meeting on Pesticide Residues (FAO/WHO, 1968a) had already recognized the need for further studies. Following this recommendation, work was initiated by WHO and the International Agency for Research on Cancer (IARC). Progress reports on the present state of the experiments were reviewed but the final results were not expected to be available until 1971.

A definite decision on the potential hazard of DDT to man could not be taken at this meeting. However, because the hazard to man from DDT had not been ruled out, it was emphasized that uses of DDT should be limited to those situations where there were no satisfactory substitutes. While the Meeting stressed the desirability of introducing alternative compounds and alternative methods of control, it recognized the vital role that DDT and some other organochlorine pesticides play in the food production and protection programmes of many countries because of their low costs, user safety, lack of suitable substitutes and safety in their storage and transport. For example, it was estimated that DDT and other organochlorine compounds represented considerably more than half the total insecticides used in the agriculture of developing countries. Main-

tenance, development and any expansion of the essential protection of food and fibre by alternative chemicals would be beyond the financial resources of many countries at the present time and could involve the introduction of new risks for which users and others were not yet prepared. Indeed, in terms of food supply and welfare of expanding populations, the continuing and controlled use of DDT and some other organochlorine pesticides was essential in the present state of knowledge.

The Meeting noted that total diet studies carried out in a few countries where DDT was widely used had revealed that the intakes of DDT and its metabolites were well below the ADI established at this Meeting. In addition, the replacement of persistent organochlorine insecticides by alternatives was being increasingly dictated by problems of pest resistance. In several countries, use patterns and scales of use of DDT were under review, with likely reductions in residue levels in many food crops. The Meeting therefore expressed a requirement for new information on amended use patterns in various countries, with details of residue levels resulting from supervised trials and practical usage, in order to reconsider the recommendations for temporary tolerances.

2.7 Fumigants

Extensive data on the effects of inhalation of fumigants and in some cases on their fate in the body are generally available in experimental animals and in man. These data, which have been used in establishing maximum permissible concentrations for occupational exposure as time-weighted averages, could also be adapted to provide a no-effect level for oral administration. This evaluation should take into account the possibilities that continuous ingestion may occur and that certain groups of consumers (e.g. children, pregnant women, old people, individuals with illness or impaired physiological functions) may be more sensitive than the adult workers who are generally submitted to medical control. To use these data for this purpose, precise information is needed on the extent of absorption of each fumigant through the lungs, possibly through the skin and by the oral route when animals are exposed to the vapour. It should also be recognized that for some fumigants the fate in the body may be different with various routes of absorption.

For these reasons some oral feeding studies of at least a 90-day duration are required. Such studies have been undertaken in only very few cases. In addition, insufficient information is available on the reaction products of fumigants with food, including the toxicity of such products and their influence on nutritive value. For the reasons given above, with the exception of hydrogen cyanide, for which an ADI was established in

1965 (FAO/WHO, 1965c), acceptable daily intakes for unchanged fumigants cannot be established at this time.

The Meeting reviewed the data pertaining to the occurrence of residues from the use of methyl bromide and ethylene dibromide in foods and agreed that there would be a continuing need to consider residues of bromine occurring as inorganic bromide. Nevertheless, the occurrence of residues of the fumigants in unreacted form in certain foods has been reported, and some of the older data on this subject do not clearly differentiate residues in organic form from those occurring in the food as inorganic bromide. It was therefore decided to review the position of residues of these two fumigants, together with those from carbon disulfide, carbon tetrachloride, ethylene dichloride and ethylene oxide, at a future meeting when results should be available following the use of recently developed sensitive analytical methods for measuring residues of these compounds (IUPAC, 1970). However, it was recommended that no further consideration be given to trichloroethylene at present because the compound is rarely used as a fumigant and no residues of it have been found in food commodities moving in commerce.

2.8 Fungicides used for seed treatment

Some of the most widely used fungicides for the protection of seed and seed grain such as organomercurial compounds and hexachlorobenzene are highly toxic to man as has been demonstrated through several incidents of mass poisoning where treated grain was improperly used for human consumption. Furthermore, unintentional residues of these fungicides have appeared in food crops, in animals and in animal products. The Meeting, therefore, stressed the need for safer substitutes and urged governments and others concerned to give high priority to research for such substitutes.

2.9 Environmental contamination

The Meeting noted the understandable concern over the contamination of the environment from certain uses of persistent pesticides and made recommendations with respect to DDT and seed treatment chemicals (see Sections 2.6 and 2.8).

No recommendations could be made for practical residue limits in fish because adequate information on residue levels in fish in commercial channels was not available. Member countries are strongly urged to provide information from surveys and residue studies on fish as soon as possible. In the absence of such data the tolerance for DDT in fish was withdrawn.

2.10 Matters relating to the establishment of ADIs

The Meeting reemphasized that the magnitude of the safety factor used in establishing the ADI depends on a number of considerations, one of which is the varying susceptibility in toxicity among species. For this reason adequate biochemical and toxicological data from observations in man are of prime importance and could allow the use of considerably smaller safety factors, with obvious consequential advantages (WHO, 1967).

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

The Meeting considered a preliminary study undertaken in accordance with the recommendations of the previous meeting (FAO/WHO, 1969a). In this study (details of which are given in Appendix III) calculations were made of theoretical intakes of twenty-four pesticides in four countries for which average food consumption figures had been compiled by FAO. The computer programme already developed by WHO for food additives was employed in the study.

These calculations were based on the assumptions that the residue levels in food at the time of consumption were the same as the tolerance recommendations of the Joint Meeting for all the crops for which tolerances or practical residue limits are given and that all food in each class bore these residues to the limit of the tolerance. Only in a few isolated cases (e.g. malathion and hydrogen cyanide) were data available on the degree of disappearance in processing, in which event appropriately lower values were used.

The results of this intake study indicate that the acceptable daily intakes for the following pesticides are not being exceeded at this time: chlorobenzilate, chloropropylate, coumaphos, crufomate, dimethoate, diphenyl, fenchlorphos, hydrogen cyanide and parathion. Further work on the reduction of residue levels during storage, processing and cooking is not essential, and there is no need to include them in monitoring studies as long as the tolerance figures and the acceptable daily intakes for them remain unchanged.

On the other hand, heptachlor and phosphamidon are borderline and warrant further studies at this stage. Based on the same assumptions, there is a potential for the acceptable daily intake to be exceeded with azinphos-methyl, chlordane, diazinon, dicofol, endosulfan, lindane, malathion and a greater potential with carbaryl, DDT, dieldrin, dioxathion, ethion and parathion-methyl. Available information on the disappear-

ance of residues during storage, processing and cooking prior to consumption should be used in a reassessment of these compounds. Where adequate information is not available for this purpose, work should be initiated to obtain the necessary data on disappearance prior to consumption. In such work priority should be assigned to those compounds where the calculated theoretical intake exceeds the acceptable daily intake by the largest amount. If such studies indicate that the residue levels at the time of consumption will result in a calculated theoretical intake which does not exceed the acceptable daily intake, no further work needs to be done at this time. If there still remains a potential for exceeding the acceptable daily intake, however, then residue determinations in total diet and other monitoring studies should be concentrated on the levels of those particular compounds in foodstuffs. These studies should be done in many countries and on a continuing basis.

The results obtained in this study indicate that it is useful to calculate the potential daily intake of pesticide residues using average food consumption figures for individual countries as compiled by FAO. Furthermore, these results indicate that the use of average food consumption figures, instead of high consumption figures (ninth decile), could change the temporary nature of the tolerances recommended for some of these pesticides, provided that the other required information was supplied.

4. EVALUATION OF DATA FOR ACCEPTABLE DAILY INTAKES

Because a definite decision on the potential hazard of DDT to man cannot be taken now, it was decided to change the ADI to a conditional ADI in order to limit its use except where there are no satisfactory substitutes. Furthermore, new information on the toxicology of DDT dictated a reduction in the ADI to the level established in 1963 (FAO/WHO, 1964) (see Section 2.6).

In considering the following fumigants: carbon disulfide, carbon tetrachloride, ethylene dibromide, ethylene dichloride, methyl bromide and trichloroethylene, it was found that insufficient information was available on feeding studies in animals or on the possible formation of toxic reaction products in treated food commodities. Therefore the meeting decided it was inadvisable to establish even temporary ADIs for these compounds. Recent analytical evidence that residues from fumigants containing bromine may not merely be inorganic bromide (see Section 2.7) was also noted.

For binapacryl, diphenylamine and ethoxyquin, ADIs were established, while the already existing ADI for 2-phenylphenol, established by the Joint FAO/WHO Expert Committee on Food Additives in its sixth report

(FAO/WHO, 1962b) was reaffirmed, although further animal experiments including studies on reproduction and metabolism were considered desirable. For binapacryl, further studies on metabolism in rats and other animal species were considered to be very desirable. Additional reproduction studies in rats should be performed with ethoxyquin to elucidate the effect on survival rate of the offspring.

In the group of structurally related compounds, captafol, captan, and folpet, great emphasis was placed upon the studies of metabolism, of reproduction and of possible teratogenicity. Although data from experiments in several animal species were available, the Meeting considered it advisable to require further studies and to establish only temporary ADIs for these compounds.

Because of the apparent erratic effect of quintozone on the growth of rats and some effects on bone marrow and liver observed in groups of dogs fed high-dose levels, only a temporary ADI could be established. Studies to explain these effects and carcinogenicity studies in two species of animals were considered necessary.

Although the available information on experiments with fenitrothion in rodents indicates a lower toxicity than that of the structurally similar compound parathion-methyl, in the absence of reproduction and teratogenicity data, it was possible to establish only a temporary ADI. There is also a lack of information on the composition of the technical product as manufactured in various countries.

The Meeting reevaluated the ADI for carbaryl in the light of new information. Indications of adverse effects on the reproductive physiology of several animal species and signs of influence on kidney function in studies in man and different animal species required further studies to be made, and the Meeting therefore established a temporary ADI at a lower level than the ADI established in 1967. Information is also required on the composition of the technical product as manufactured in different countries.

For hexachlorobenzene the available data were considered insufficient to recommend any type of ADI. On the other hand, investigations have shown that the use of this compound as a seed dressing had resulted in occurrence of unintentional residues in food commodities moving in international trade, thus creating a need for a toxicological evaluation prior to recommending practical residue limits. Under existing circumstances and pending the availability of a suitable substitute, the Meeting agreed to recommend a "tentative negligible daily intake" based upon a no-effect level in a short-term experiment in rats (see Appendix IV).

The Meeting could not establish an ADI for formothion or thiometon because of insufficient data especially from long-term studies in suitable animal species. In evaluating dinocap, no ADI could be established, as

the available data on the composition of the technical product and its toxicity were considered incomplete. Similarly, the Meeting considered the available data on dichlofluanid insufficient to establish an ADI.

The daily intake values established by the Meeting are listed in Appendix I.

5. EVALUATION OF DATA FOR TOLERANCES AND PRACTICAL RESIDUE LIMITS

The Meeting reviewed and in certain cases amended recommendations previously made on some pesticides. Some pesticides that had not been previously considered were also reviewed.

5.1 Matters referred to the Joint Meeting by the Codex Committee on Pesticide Residues

The Fourth Session of the Codex Committee on Pesticide Residues at its meeting in Arnhem, 3-14 October 1969, referred to the Joint Meeting a number of questions concerning the following substances: bromide ion, carbaryl, chlordane, DDT, dichlorvos, dieldrin, ethion, heptachlor, hydrogen phosphide, lindane, malathion, parathion, piperonyl butoxide and pyrethrins. Where data were available, certain amendments, additions or clarifications were made. See Appendix I and the relevant monographs (FAO/WHO, 1970).

5.2 Pesticides reviewed in the light of new information

The following pesticides were reconsidered in the light of information which had been received since the previous meeting: captan, carbaryl, carbon disulfide, carbon tetrachloride, DDT, ethylene dibromide, ethylene dichloride, ethylene oxide and organomercurials.

Recommendations and amendments were made for captan, carbaryl and DDT (see Appendix I and the relevant monographs).

5.3 Pesticides considered for the first time

Recommendations for tolerances or for practical residue limits were made for binapacryl, captafol, diphenylamine, ethoxyquin, fenitrothion, folpet, hexachlorobenzene, 2-phenylphenol and quintozone. (These recommendations are summarized in Appendix I.) In the absence of ADIS,

however, it was not possible to make recommendations for dichlofluanid, dinocap, formothion and thiometon. (Full details of their evaluation are contained in the monographs and a summary of the additional information required is contained in Appendix II.)

6. FUTURE WORK

It was suggested that the following items should be considered at a future meeting:

1. The compounds in the modified Priority V group listed in Appendix X of the report of the fourth session of the Codex Committee on Pesticide Residues (FAO/WHO, 1969c), namely: chlormequat, diquat, endrin, fentin acetate, fentin chloride, fentin hydroxide, paraquat and thiabendazole.
2. Review of compounds for which the ADIs and/or tolerances or practical residue limits expire in 1970 and also dieldrin for which new data have recently become available.
3. Matters that may be referred to the Meeting by the 1970 Codex Committee on Pesticide Residues.
4. Review and examination of the results of further studies on the calculation of potential intakes of pesticides in diets and their relationships with ADIs, in accordance with the recommendation, 7.1.2. These results should then be compared with the intake figures derived from total diet studies.
5. In accordance with the recommendations of Section 2.7, the review of fumigants otherwise due in 1970 should be delayed until the 1971 Joint Meeting.
6. Residues from the use of systemic fungicides should be reviewed at a future meeting.

7. RECOMMENDATIONS

The recommendations made at the 1968 Joint Meeting (FAO/WHO, 1969a) were reiterated and the following additional recommendations were made. Recommendations concerning particular pesticides are included in Appendix II and the monographs (FAO/WHO, 1970).

7.1 Recommendations to FAO and WHO

7.1.1 In accordance with the recommendation of the 1968 Joint Meeting and in the interests of public health and agriculture, further joint meetings on pesticide residues should be convened annually.

7.1.2 The study of the relationship between intake, tolerance and ADI should continue with those pesticides for which the pilot study showed that there was a theoretical possibility for exceeding the ADI. This study should be extended to include additional countries as well as the pesticides reviewed in 1969. The study should take into consideration information now available on the disappearance of residues during storage and processing prior to consumption, together with information indicating the specific food commodities to which the tolerances apply. Any information on the percentage of food commodities bearing residues should also be taken into account.

7.1.3 A meeting of experts in the fields of toxicology and carcinogenicity should be convened by WHO to consider the question of threshold levels and dose response with respect to the carcinogenic potential of some pesticides.

7.1.4 During the course of studies at this and at previous meetings, deficiencies have been encountered in information particularly concerning pesticides that have been in use for a long time or which, for some other reason, are not covered by patent rights and which are not actively promoted by commercial interests. The relevant deficiencies in information are outlined in the monographs concerned with the individual pesticides. However, with these compounds it seems unlikely that the necessary research will be undertaken unless it is initiated by official bodies and supported by public funds. In particular, it is suggested that FAO should explore the possibilities of obtaining funds for supporting such work on an international basis.

7.1.5 The Meeting reiterated its recommendation that consideration should be given to the publication of a single volume containing all the pesticides evaluated up to and including the 1969 meeting.

7.2 General recommendations

7.2.1 Information should be provided on the fate of pesticide residues in food during storage and processing prior to consumption. Such information will provide better means of estimating actual intakes from foods which contain known residues at the raw stage. Data obtained from laboratory work and from measurements made on samples subjected to

processing including cooking, both commercially and in the home, are valuable for this purpose. In this connexion, information regarding rates of hydrolysis under different pH and temperature conditions would be useful.

7.2.2 Adequate data should be provided whenever feasible from observations of the effects of pesticides in man. Such data are of primary importance in establishing ADIs and could allow the use of a considerably smaller safety factor than that used with data obtained from experimental animals.

7.2.3 Because some compounds currently in use as seed protectants are highly toxic to man and their uses can result in the occurrence of unintentional residues, the need to develop safer substitutes was emphasized. In the meantime, every effort should be made to reduce the contamination of commercial grain and animal feeds to the minimum and to undertake surveys to ensure that directions are being observed by farmers and others concerned with the handling of treated seeds.

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Appendix I

INDEX TO DOCUMENTATION AND SUMMARY OF RECOMMENDATIONS
CONCERNING ACCEPTABLE DAILY INTAKES, TOLERANCES, AND
PRACTICAL RESIDUE LIMITS AS OF DECEMBER 1969 ¹

	FAO/ WHO publica- tion (See Ref- erences)	Maxi- mum accept- able daily intake (mg/kg body weight)	Tolerance (ppm)	Practical residue limits (ppm)	Remarks
Blank spaces indicate no recommendations made					
acrylonitrile	1965c				
aldrin	1967b, 1968b	0.0001			Also see diel- drin.
allethrin	1965b				
arsenic (as cal- cium or lead arsenate)	1969b				
azinphos-methyl	1969b	0.0025	Apricots, grapes . . . 4 c Other fruit . 1 c Vegetables . 0.5 c		
BHC (mixture of isomers)	1969b				
binapacryl	1970	0.0025 1.0	Peaches, cher- ries 1 Apples, pears, grapes . . . 0.5 Plums 0.3 Nectarines . 0.2		
bromide (inorgan- ic form, deriv- ed from bro- mine -containing fumigants and other sources)	1969b, 1970 Previ- ously consid- ered under ethylene dibro- mide or methyl bromide		Spices, herbs. 400 b Raw cereals, wholemeal flour 50 Dried figs . . 250 b Dried raisins, dried dates. 100 b Dried peaches 50 b Dried prunes 20 b Other dried fruit 30 b Avocados . . 75 b Citrus fruit, strawberries Other fresh fruit 20 b		Tolerance for dried eggs sus- pended at 1969 Meeting pending review and clarifica- tion in 1971. Recommendations relate ex- clusively to inorganic bro- mide. Toler- ances not rec- ommended for unchanged fu- migrant. ● Current work on status of res- idues in vari- ous products to be reviewed in 1971.

¹ For further details concerning the recommendations, consult the original documents referred to in first column. Explanatory notes are given at the end of this table.

APPENDIX I (continued)

	FAO/ WHO publica- tion (See Ref- erences)	Maxi- mum accept- able daily intake (mg/kg body weight)	Tolerance (ppm)	Practical residue limits (ppm)	Remarks
calcium arsenate	1969b		Blank spaces indicate no recommendations made		
captafol	1970	0.05 d	Pecches . . . 15 d Cherries (sour) . . . 10 d Cherries (sweet) . . . 2 d Tomatoes . . . 5 d Melons (whole) . . . 2 d Cucumbers (whole) . . . 1 d Apricots . . . 0.5 d Plums 0.2 d		Recommendations relate only to parent substance. Referred to as difolatan on p. 18 of FAO/WHO 1969a.
captan	1970 (See Re- marks)	0.125 d	<ul style="list-style-type: none"> ● Apples, cherries 40 d ● Pears 30 d ● Apricots . . . 20 d ● Citrus, peaches, plums, rhubarb, tomatoes . . . 15 d ● Strawberries, raspberries, cranberries, cucumbers, lettuce, green beans, peppers . . . 10 d ● Raisins 5 d 		● Monograph in 1965b becomes obsolete.
carbaryl	1967b, 1968b, 1969b, 1970	0.01 d	<ul style="list-style-type: none"> ● Raspberries, blackberries, boysenberries, peaches, nectarines, asparagus, okra, leafy vegetables (except Brassica), nuts (whole), olives (fresh) . . . 10 d ● Citrus, strawberries, blueberries . . . 7 d ● Apples, bananas (pulp), grapes, beans, peas (including pod), brassica, tomatoes, peppers, eggplant, poultry 5 d ● Cucurbits (including melons) . . . 3 d ● Rice 2.5 d 		Earlier tolerances reviewed at 1969 Meeting in light of Codex comments. Tolerance on whole milk temporarily withdrawn (see monograph).

APPENDIX I (continued)

	FAO/ WHO publi- cation (See Ref- erences)	Maxi- mum accept- able daily intake (mg/kg body weight)	Tolerance (ppm)	Practical residue limits (ppm)	Remarks
carbaryl			Blank spaces indicate no recommendations made		
			<ul style="list-style-type: none"> ● Cottonseed (whole), sweet corn (kernels), nuts (shelled), olives (processed), meat of cattle, goats and sheep 1 d Potatoes 0.2 d 		
carbon disulfide	1965c, 1968b				At 1969 Meeting decided to re-view these fu-migants in 1971 in the light of work with new ana-lytical methods.
carbon tetrachloride	1965c, 1968b	0.01			
chlorbenside	1965b				To be measured as alpha plus gamma chlo-r-dane. Tol-erances apply only to residues from soil treat-ments.
chlordane	1968b, 1970	0.001	<ul style="list-style-type: none"> ● Root vegeta-bles (except car-rots), leafy and stalk vegeta-bles 0.3 a Cuburbits, pineapple 0.2 a Sugar beets, pod vegeta-bles (whole pods, ber-ries, toma-toes, ● Eggplant, pep-pers, pimen-tos, sweet corn, popcorn 0.1 a 	Raw cereals . 0.1 a	
chlorfensan	1965b	0.01			Erroneously omitted from Annex 2 of Ref. 1969a.
chlorobenzilate	1969b	0.02	<ul style="list-style-type: none"> Apples, pears (whole fruit) 5 c Citrus (whole) 1 c Almonds, wal-nuts (with-out shells) 0.2 c Melons canta-loupes 1 c 		
chloropicrin	1965c				
chlorpropham	1965b				
chloropropylate	1969b	0.01	<ul style="list-style-type: none"> Apples, pears, citrus (whole fruit) 3 c Tomatoes, can-taloupes 1 c 		

APPENDIX I (continued)

	FAO/WHO publication (See References)	Maximum acceptable daily intake (mg/kg body weight)	Tolerance (ppm)	Practical residue limits (ppm)	Remarks
			Blank spaces indicate no recommendations made		
chlorthion	1965b				
coumaphos	1969b	0.005c	Eggs (shell-free) Meat, including poultry (on fat basis)	0.05 c 0.5 c	To be determined as coumaphos and oxygen analogue and expressed as coumaphos.
crufomate	1969b	0.1	Whole milk Meat (fat basis)	0.05 c 1 c	
DDT	1967b, 1968b, 1969b, 1970	0.005 (See Remarks)	Apples, pears, peaches, apricots, small fruit (except strawberries), vegetables (except root), meat or poultry (on fat basis) Nuts (shelled) strawberries, root vegetables Cherries, plums, citrus and tropical fruit	Whole milk . . . 0.05 Milk products (fat basis) . . 1.25 Eggs (shell-free) . . 0.5 7 1 a 3.5 a	<ul style="list-style-type: none"> ● ADI is "conditional." ● Tolerance on fish withdrawn at 1969 Meeting. Limits apply to DDT, DDD and DDE singly or in combination.
demeton	1965, 1968b	0.0025			
diazinon	1965b, 1967b, 1968b, 1969b	0.002	Peaches, citrus, cole crops and leafy vegetables Other fruit and vegetables Meat (fat basis)	0.7 a 0.5 a 0.75 a	
dichlofluanid	1970				
dichlorvos	1967b, 1968b, 1970	0.004	Raw cereals Cereal products (milled and for human consumption), fresh vegetables Fruit (other than citrus)	2 a 0.3 a 0.1 a	<ul style="list-style-type: none"> Content of dichloroacetaldehyde (DCA) to be reported where possible. ● 1968 recommendation for "canned and frozen vegetables" withdrawn at 1969 Meeting.

APPENDIX I (continued)

	FAO/ WHO publi- cation (See Ref- erences)	Maxi- mum accept- able daily intake (mg/kg body weight)	Tolerance (ppm)	Practical residue limits (ppm)	Remarks
			Blank spaces indicate no recommendations made		
dicolol	1969b	0.025	Fruit, hops, vegetables, tea (from particular estate) for blending only 5 c Tea (blended) 1 c		
dieldrin	1967b, 1968b, 1969b, 1970	0.0001	Fruit (other than citrus) ● Asparagus, broccoli, brussels sprouts, cab- bage, car- rots, cauli- flower, cu- cumber, egg- plant, horse- radish, let- tuce, onions, parsnips, pep- pers, pimen- tos, potatoes, radishes and radish tops . 0.1 c Citrus, rice . 0.05 c	Raw cereals. 0.02 c Eggs (shell-free basis) . 0.1 c Milk products (fat ba- sis) . . 0.125 c Meat (fat basis) . 0.2 c Whole milk . 0.005 c	Practical residue limit shell-free egg is equiva- lent to 0.25 ppm in egg yolk. Limits ap- ply to aldrin and dieldrin singly or to- gether and expressed as dieldrin.
difolatan (See captafol)					
dimethoate	1968b	0.02	Tree fruit (including citrus) . . . 2 a Tomatoes and peppers . . 1 a Other vege- tables . . . 2 a		Residues to be determined as dimethoate and its oxygen ana- logue and ex- pressed as di- methoate.
dimethrin	1965b				
dinocap	1970				
dioxathion	1969b	0.0015	Pome fruit . 5 c Grapes . . . 2 c Citrus fruit . 3 c Meat, exclud- ing poultry (fat basis) . 1 c		Residues of cis and trans iso- mers of princi- pal active in- gredient to be determined and expressed as sum of both.
diphenyl	1967b, 1968b	0.125	Citrus fruit . 110		
diphenylamine	1970	0.025	Apples . . . 10		
dithiocarbamates dimethyl (ferbam, thiram and ziram)	1965b 1968b	0.025 b			Applied to par- ent compound and to sum if more than one present.

APPENDIX I (continued)

	FAO/WHO publication (See References)	Maximum acceptable daily intake (mg/kg body weight)	Tolerance (ppm)	Practical residue limits (ppm)	Remarks
Blank spaces indicate no recommendations made					
dithiocarbamates ethylene bis (mancozeb, maneb, and zineb, including zineb derived from nabam plus zinc sulfate)	1965b, 1968b	0.025 b			Applies to parent compound and to sum if more than one present.
DNOC	1965b				
endosulfan	1968b, 1968b	0.0075	Fruit, vegetables	2 b	To be measured and reported as total endosulfan A and B and endosulfan sulfate.
endrin	1965b				
ethion	1969b, 1970	0.00125	Grapes	2 c	● The proviso "at slaughter" for meat made at 1968 Meeting withdrawn.
			Other fruit	1 c	
			Vegetables	0.5 c	
			Tea (from particular estate) for blending only	7 c	
			Tea, blended	1 c	
			● Meat (fat basis)	2.5 c	
ethoxyquin	1970	0.06 d	Apples, pears	3 d	
ethylene dibromide	1967b, 1968b				Analytical method should differentiate between residues, as original compound or as inorganic bromine. ● New data on residues in foods to be included in 1971 review, (see entry for bromide).
ethylene dichloride	1965c, 1968b				
ethylene oxide	1965c, 1969b				
fenchlorfos	1969b	0.01	Whole milk	0.04 c	Residues of fenchlorfos and oxygen analogues to be determined and expressed as fenchlorfos.
			Egg yolk	0.05 c	
			Meat (fat basis)	7.5 c	

APPENDIX I (continued)

	FAO/ WHO publi- cation (See Ref- erences)	Maxi- mum accept- able daily intake (mg/kg body weight)	Tolerance (ppm)	Practical residue limits (ppm)	Remarks
ferbam	1965b, 1968b	0.025 b	Blank spaces indicate no recommendations made		See dithiocarba- mates.
fenitrothion	1970	0.001 d	Apples, cher- ries, grapes, lettuce . . . 0.5 d Red cabbage, tea (green at harvest) . . . 0.3 d Tomatoes . . . 0.2 d Cocoa . . . 0.1 d	Milk prod- ucts (fat basis) . 0.5 d Meat or fat of meat 0.03 d Milk (whole) 0.002 d	
folpet	1970	0.16 d	Currants (fresh) . . . 30 d Grapes, blue- berries . . . 25 d Cherries, rasp- berries . . . 15 d Apples, citrus Tomatoes, strawberries 5 d Cucumber, cantaloupe (whole), wa- ter melon (whole), onion . . . 2 d		Recommendations apply only to parent compound.
formothion	1970		Strawberries. 0.3 a Black cur- rants . . . 2.0 a		Residues present as dimethoate to be covered by recommen- dations for di- methoate.
heptachlor	1967b, 1968b, 1969b, 1970	0.0005	Cole crops and other leafy vegeta- bles, root veg- etables (other than potatoes, carrots, ● sugar beets). 0.1 a	Whole milk . 0.005 a Milk products (fat ba- sis) . . 0.125 a Meat (fat ba- sis) . . 0.2 a Raw cereals. 0.02 a Vegetables (except carrots) 0.05 a Carrots. 0.1 a	Residues of hep- tachlor and its epoxide to be determined and expressed as heptachlor. Tol- erances apply to residues from applica- tion to seed and soil only.
hexachloroben- zene	1970	(See Re- marks)		Fat of cattle, sheep, goats, and poultry 1 d	Tentative negli- gible daily in- take of 0.0006 mg/kg body weight estab- lished. (For 1973 review, see mono- graph.)

APPENDIX I (continued)

	FAO/ WHO publi- cation (See Ref- erences)	Maxi- mum accept- able daily intake (mg/kg body weight)	Tolerance (ppm)	Practical residue limits (ppm)	Remarks
hexachloroben- zene (cont'd)			Blank spaces indicate no recommendations made		
				Eggs (shell- free) . 1 d Milk products 0.3 d Raw wheat . 0.05 d Cereal products (from wheat), milk (whole). 0.01 d	
hydrogen cyanide	1965c, 1969b	0.05	Raw cereals . 75 Flour 6		
hydrogen phosphide	1967b, 1968b, 1970	Not nec- essary (See Re- marks)	● Flour and other milled cereal prod- ucts, break- fast cereals Dried vegeta- bles, spices . 0.01 Raw cereals . 0.1		● "Only items to be cooked" deleted from previous rec- ommendations. Subject to re- strictions in use (FAO / WHO, 1968, page 17) residues not detectable at time of con- sumption.
lead (as arsenate)	1969b				
lindane	1967b, 1968b, 1969b,	0.0125	Raw cereals . 0.5 a Vegetables . 3 a Cranberries, cherries, grapes, plums and straw- berries . . . 3 a	Whole milk . 0.004 a Eggs (yolk) . 0.2 a Milk products (fat ba- sis) . . 0.1 a Meat (fat basis) 2 a ● Poultry (fat basis) 0.7 a	Referred to as "gamma BCH" prior to 1967. ● Recommendation concerning poultry er- roneously omit- ted from Table in Annex 2 of 1969a.
malathion	1967b, 1968b, 1969b	0.02	Raw cereals, nuts, dried fruits . . . 8 Whole meal and flour from rye and wheat . . . 2 Citrus fruit . 4 Leafy vegeta- bles 6		● Tolerances for "fruit" and "other vege- tables" sus- pended at 1969 Meeting pend- ing review and clarification in 1970.

APPENDIX I (continued)

	FAO/ WHO publi- cation (See Ref- erences)	Maxi- mum accept- able daily intake (mg/kg body weight)	Tolerance (ppm)	Practical residue limits (ppm)	Remarks
			Blank spaces indicate no recommendations made		
mancozeb	1968b	0.025 b			See dithiocarba- mates.
maneb	1965b, 1968b	0.025 b			See dithiocarba- mates.
methoxychlor	1965b	0.1			
methyl bromide	1967b, 1968b				See entry under "bromide (inor- ganic)" for rec- ommendations pertaining to inorganic bro- mide residues from methyl bromide.
mevinphos	1965b				
MGK 264	1968b				
nabam	1965b, 1968b	0.025 b			See entries for " dithiocarba- mates " and " zineb. "
organomercurial compounds	1968b, 1967b			1968b page 208 suggests possible figures	FAO / WHO, 1967b mono- graph is en- titled " phenyl mercury ace- tate. " No objection to use as seed dressings and on apples up to petal fall.
orthophenylphe- nol (See 2-phe- nylphenol)					
oxydemeton- methyl	1968b, 1969b	With- drawn at Meeting in 1968 (Ref. 1969b)			Previous to 1968b referred to as demeton - S - methyl - sulfoxide.
oxythioquinox	1969b				(Renamed qui- nomethionate.)
parathion	1965b, 1968b, 1970	0.005	Vegetables (except car- rots) 0.7 a ● Peaches, apri- cots, citrus 1 a ● Other fresh fruit 0.5 a		● Reexamina- tion of data at 1969 Meeting showed that tolerance rec- ommendations for two groups of fruit had been recorded wrongly in pre- vious reports.

APPENDIX I (continued)

	FAO/ WHO publi- cation (See Ref- erences)	Maxi- mum accept- able daily intake (mg/kg body weight)	Tolerance (ppm)	Practical residue limits (ppm)	Remarks
Blank spaces indicate no recommendations made					
parathion-methyl	1969b	0.001 c	Fruit, cole crops, cucur- bits 0.2 c Other vege- tables 1 c Cottonseed oil 0.05 c		
phenyl mercury acetate					(See organomer- curial com- pounds)
2-phenylphenol (and sodium salt)		1.0	Cantaloupes (whole) 120 Pears 25 Carrots, peaches 20 Sweet pota- toes, apples, plums (in- cluding fresh prunes) 15 Citrus, cucum- bers, pep- pers, cantal- oupes (edi- ble portions), pineapple, tomatoes 10 Cherries, nec- tarines 3		Residues express- ed as 2-phenyl- phenol. Referred to as orthophenyl- phenol on p. 18 of FAO / WHO 1969a.
phosphamidon	1965b, 1967b, 1969b	0.001	Raw cereals 0.1 c Apples, pears 0.5 c Citrus fruit 0.4 c Other fruit, cole crops 0.2 c Tomatoes, let- tuce, cucum- bers, water- melons 0.1 c		Residues to be determined by cholinesterase inhibition and results express- ed as phosphamidon.
phosphine					(See hydrogen phosphide.)
piperonyl butoxide	1967b, 1968b, 1970	0.03 c	Raw cereals 20 c Fresh fruit and vegeta- bles, dried fruit and veg- etables, oil- seeds, tree nuts 8 c ● Dried codfish 1 c		● Only data for codfish examined at 1969 Meeting.
propham pyrethrins	1965b 1967b, 1968b, 1970	0.04 c	Raw cereals 3 c Fresh fruit and vegeta- bles, dried fruit and veg- etables, oil- seeds, tree nuts 1 c ● Dried codfish 0.1 c		● Only data for codfish examin- ed at 1969 Meeting.

APPENDIX I (concluded)

	FAO/ WHO publi- cation (See Ref- erences)	Maxi- mum accept- able daily intake (mg/kg body weight)	Tolerance (ppm)	Practical residue limits (ppm)	Remarks
quinomethionate	1969b		Blank spaces indicate no recommendations made		Listed in 1969b as oxythioqui- nos, subsequent- ly renamed.
quintozene	1970	0.001 d	Mushrooms 10 d Peanuts (whole) 5 d Bananas (whole) 1 d Lettuce, pea- nuts (ker- nels) 0.3 d Beans (navy), potatoes 0.2 d Tomatoes 0.1 d Cottonseed 0.03 d Broccoli, cab- bage 0.02 d Bananas (pulp), beans (other than navy), peppers (bell) 0.01 d		
thiometon	1970				See dithiocarba- mates.
thiram	1965b, 1968b	0.025 b			
toxaphene	1969b				● 1969 Meeting decided not nec- essary to con- tinue to study this compound. (See Section 2.7 this report.)
trichloroethylene	1969b				
triphenyltin	1965b				Also called fen- tin compounds. (Including zineb derived from nabam plus zinc sulfate.) See dithiocarba- mates.
zineb	1965b, 1968b				
ziram	1965b, 1968b	0.025 b			See dithiocarba- mates.

EXPLANATORY NOTES

- Reference entries in the first column are to first complete or completely revised monograph. Succeeding date references are to addenda to first reference. Where a monograph has been completely revised no mention is made of any earlier obsolete ones. The complete list of references appears on page 16.
- Compounds with FAO/WHO, 1970 publication references, if not accompanied by references to earlier monographs, were considered at the 1969 Meeting for the first time.
- Entries preceded by bullets ● relate to additions or to changes made at the 1969 Meeting concerning compounds considered at previous meetings.
- The suffixes a, b, c, and d in columns 2, 3 and 4 indicate "temporary." The results of work required should be made available:

a — not later than 30 June 1970	c — not later than 30 June 1972
b — not later than 30 June 1971	d — not later than 30 June 1973
- Unless otherwise indicated, the tolerances and practical residue limits should apply as soon as practicable after harvest to the raw agricultural products moving in commerce and prior to processing.
- With commodities entering international trade the tolerances are applicable at the point of entry into a country or as soon as practicable thereafter.

**FURTHER WORK OR INFORMATION: NEEDS ESTABLISHED
AT 1969 MEETING**

The items included in this Appendix are additional to those included in Annex 3 of the Report on the 1968 Joint Meeting (FAO/WHO, 1969a).

BINAPACRYL

Desirable

1. Further work on the absorption and the excretion rates in rats or other species.
2. Reproduction and teratogenicity studies in a nonrodent mammalian species.
3. More studies on possible cataract formation in animals.
4. Further information on the unidentified fraction of the technical product.
5. Residue data from countries other than the United States of America.
6. The development and evaluation of a GLC method suitable for regulatory purposes.

CAPTAFOL

Required before 30 June 1973

1. Studies to elucidate the effects seen in the teratogenic experiments.
2. Data from countries other than the United States of America on the required rates and frequencies of application, preharvest intervals and the resultant residues.
3. Data on residue levels in raw agricultural commodities moving in commerce.
4. Data on the effect of washing, peeling and blanching on the residue levels of various crops.
5. Elucidation of the histopathology of the kidney and liver in the rat.

Desirable

1. Metabolic studies to provide further information on the absorption and distribution after oral administration and to identify the metabolites found in animal tissues.
2. Collaborative studies to establish a regulatory method for captafol in the presence of captan and folpet.

CAPTAN

Required before 30 June 1973

1. Further teratogenicity studies in nonhuman primates.
2. Further studies on metabolism especially on the trichloromethylthio moiety.
3. Residue data for other crops, including blueberry, figs, hops, sweet potato and spinach.
4. Residue data from countries other than the United States of America.

Desirable

1. The effects of feeding a low-protein diet on the chronic toxicity of captan.
2. The development and evaluation of a GLC method, distinguishing captan from captafol and folpet, suitable for regulatory purposes.

CARBARYL

Required before 30 June 1973

1. Clarification of the effect upon reproductive physiology in several species of animal.
2. Further studies to establish a no-effect level with respect to kidney dysfunction in animals and/or man.

DDT

Required before 30 June 1971

1. Results of the carcinogenicity studies which are currently in progress.
2. Information on any officially acceptable uses on agricultural commodities, together with residues resulting from pertinent trials.

DICHLOFLUANID

Required (before an acceptable daily intake or tolerances can be established)

1. Further information on the absorption and metabolism of the compound, particularly with regard to the fate of the fluorine-containing portion of the molecule.
2. A long-term feeding study in the rat including a histological examination of all major organs.
3. A 1 to 2-year feeding study in a nonrodent mammalian species.
4. Information on the composition of the technical dichlofluanid, including the impurities.
5. More detailed information on the nature and magnitude of terminal residues in plants including data on the fluorine-containing moiety of the molecule.
6. Information about possible degradation mechanism of the molecule by the action of sulphhydryl compounds in vitro and in vivo.
7. Data on the required rates and frequencies of application, preharvest intervals and the resultant residues from different countries, especially on those crops which

have shown inconsistency of residue data. Data on degradation products of dichlofluanid, if important in magnitude or toxicologically, should be included.

8. Data on residue levels in raw agricultural products moving in commerce.

9. Qualitative and quantitative data on fate of residues in washing, blanching and storing and thermal processing of treated crops.

10. Data concerning the possible occurrence of the parent compound in wines produced from treated grapes.

Desirable

1. Metabolism in animal species other than the rat.
2. Metabolic studies and other observations in man.
3. Information on the fate of the compound in soil.
4. Evaluation of the analytical methods by collaborative studies for regulatory purposes.

DINOCAP

Required (before an acceptable daily intake or tolerances can be established)

1. Additional studies with more animals to establish the exact dosage of dinocap which does not produce cataracts.
2. Extension of the chronic toxicity experiment in dogs or other nonrodent mammalian species.
3. Metabolic studies including determination of phenols in the blood.
4. Information on the compounds included in dinocap and assurance of a standardized technical product.
5. Investigation aimed at clarifying physiological lesions with regard to cellular respiratory control.
6. Reproduction studies in animals.
7. Information is required on the nature of terminal residues, including the identity of the substances giving peaks by the GLC method of examination.
8. Residue data are required from countries other than the United States of America.

Desirable

The development and establishment of a GLC method for the determination of residues of the active ingredients.

DIPHENYLAMINE

Desirable

1. Experiments to determine if methaemoglobin is formed in animals.
2. Short-term studies using an adequate number of rats.
3. Additional metabolic studies in nonrodent mammalian species.
4. The results of the carcinogenicity study in mice which is currently in progress.

ETHOXYQUIN

Desirable

1. Additional reproduction studies to investigate the effect on survival rate of offspring of rats.
2. A method of analysis for apples and pears suitable for regulatory purposes.
3. Composition and purity of this compound as manufactured in several countries and the amount of ethoxyquinmonomer in the products from various manufacturers.

FENTROTHION

Required before 30 June 1973

1. Reproduction and teratogenicity studies in animals, preferably in nonhuman primates.
2. Adequate long-term studies in rodent and nonrodent mammalian species.
3. Data on residue levels in raw agricultural commodities moving in commerce and in total diet studies.
4. Data on disappearance of residues during storage, processing and cooking.
5. Data on rate of residue decline in rice and preharvest interval.
6. Before use as a grain protectant, data on persistence of residues in storage of the grains concerned and definitive data on residues in bread are needed.
7. Data on occurrence of 4-nitro-3-methylphenol residues and their significance toxicologically.
8. Information on ingredients in technical products produced by several manufacturers.

Desirable

1. Observations in man.
2. Evaluation of gas chromatographic methods for regulatory purposes.

FOLPET

Required before 30 June 1973

1. Long-term studies of sufficient duration to test for possible carcinogenic effects.
2. Additional studies on the effects of the compound on reproductive physiology
3. Further studies on metabolism, especially on the trichloromethylthio moiety.
4. Further data on the nature of terminal residues in plants as well as on the magnitude of the degradation product: magnitude in relation to the parent compound or toxicological importance.
5. Further data on the degradation mechanisms of folpet.
6. Data on the necessary rates and frequencies of application, preharvest intervals, and the resultant residues, from countries other than the United States of America.

7. Data on residue levels in raw agricultural products moving in commerce.
8. Qualitative and quantitative data on fate of residues in washing, blanching, storing and thermal processing of the treated crops.

Desirable

1. Information on the fate of the compound in soil.
2. Evaluation of the analytical methods by collaborative studies taking into account the possible presence of structurally related compounds, e.g. captan and captafol.

FORMOTHION

Required (before an acceptable daily intake or tolerances can be established)

1. Short-term studies in a nonrodent mammalian species with cholinesterase determination.
2. Long-term studies in rats.
3. Information on ingredients in technical products produced by several manufacturers.
4. Data on animal metabolism and residues in meat and milk of animals consuming agricultural products treated in accordance with good agricultural practice.
5. Data on disappearance of residues during storage, processing and cooking.
6. Data on residue levels in raw agricultural commodities moving in commerce and in total diet studies.

Desirable

1. Metabolic studies in nonrodent mammalian species.
2. Observations in man.
3. Evaluation of a gas chromatographic method for residue analysis and for regulatory purposes.

HEXACHLOROBENZENE

Required (before an acceptable daily intake or tolerances can be established)

1. Metabolic studies in animals including identification of the toxic product or products excreted in milk.
2. Short-term studies in nonrodent mammalian species and long-term studies especially in relation to the effect on bone marrow.
3. Reproduction studies in rats.

Required before 30 June 1973 (for 1973 review of Practical Residue Limits)

1. Data from countries other than Australia on residues in raw agricultural commodities.
2. Data from surveys of residues in commodities moving in international trade.

Desirable

1. Analytical procedures capable of distinguishing HCB (hexachlorobenzene) from BHC (benzenehexachloride) isomers and which are suitable for use in laboratories engaged in general regulatory work.
2. Collaborative studies on analytical methods capable of recovering and identifying HCB residues in the above food commodities.

LINDANE

Required (before 30 June 1970)

1. Data on the occurrence of lindane as a practical residue in milk and milk products.
2. Information on the necessity of applying lindane directly to animals, together with data on the residues resulting from such applications.

MALATHION

Required (before 30 June 1970)

1. Information on the residues in fruit and vegetables following uses in accordance with good agricultural practice in different countries.
2. Information on the minimum periods likely to pass between application and/or harvesting and the time the tolerance is to be applied in different countries.

2-PHENYLPHENOL AND ITS SODIUM SALT

Desirable

1. A reproduction study in experimental animals.
2. Metabolic studies in experimental animals and man.
3. Long-term studies using a larger number of animals.
4. Data on residue levels in raw agricultural commodities moving in commerce.
5. Data on residues in food at the time of consumption.
6. Results of collaborative studies of chromatographic methods of analysis.

PYRETHRINS AND PIPERONYL BUTOXIDE

Required before 30 June 1972

In addition to "Further Work" included in FAO/WHO 1967b and 1968b, experience and residue data from similar trials with dried fish in other countries.

QUINTOZENE

Required before 30 June 1973

1. Carcinogenicity studies in two species of animals.
2. Studies to explain the cause of growth depression in rats and the effect on liver and bone marrow in dogs.

3. Further studies on the metabolism and on the metabolites, particularly pentachloroaniline.
4. Data from countries other than the United States of America on the required rates and frequencies of application, preharvest intervals and the resulting residues.
5. Information on residues in edible animal tissues and in animal products resulting from the feeding of plant products (including forage) treated with quintozene in accordance with normal agricultural practice.
6. Information on the frequency and level of quintozene residues in food commodities in commerce.
7. Information on the level of metabolites, particularly pentachloroaniline in plants and animals.

Desirable

1. Development of analytical methods for greater sensitivity and evaluation for regulatory purposes.
2. Information on the residue levels in root crops, especially carrots, grown in soil treated previously with quintozene in crop rotation.

THIOMETON

Required (before an acceptable daily intake or tolerances can be established)

1. Long-term studies in animals.
2. Cholinesterase inhibition studies to establish a no-effect level.
3. Information on the content of the technical product and assurance of standard composition.
4. Data on residue levels in raw agricultural commodities moving in commerce and in total diet studies.
5. Data on rate of disappearance during storage, processing and cooking.
6. Information on composition of technical products, including impurities.
7. Data on animal metabolism and residues in meat and milk of animals consuming agricultural products treated in accordance with good agricultural practice.

Desirable

1. Adequate information on metabolism.
2. Investigation on cholinesterase inhibition in man.
3. A gas chromatographic method for analysis of residues of thiometon and its metabolites suitable for regulatory purposes.

Appendix III

METHODS USED IN THE WHO PILOT STUDY FOR CALCULATING POTENTIAL INTAKES OF PESTICIDES IN DIETS

1. Selection of the pesticides under consideration

Both acceptable daily intakes and tolerances or practical residue limits in certain foods for 28 pesticides have now been established by the Joint FAO/WHO Meetings on Pesticide Residues. For the pilot study on calculated potential intake, 24 of these compounds were considered. The other four, namely bromide ion, dichlorvos, piperonyl butoxide and pyrethrins were not considered in this pilot study because tolerances vary according to the nature of the commodity under consideration (e.g. dried and frozen vegetables), and to compute the potential intake will require a special breakdown of the food intake data. Of the 24 compounds considered, the tolerances are generally applicable at the time of harvest or at the point of entry into international trade and no separate tolerance figures are given for processed foods.

2. Food classification

Food items were grouped together using a classification similar to that used by the United States Food and Drug Administration, when publishing official tolerances. However, some modifications were necessary to enable the classification to be applicable on a worldwide basis, and therefore use was also made of the classification used in the food balance sheets compiled by FAO.

3. Use of food balance sheets and food consumption data

The tolerances for the pesticides under consideration are generally applicable to the raw materials, and therefore the most useful information for computing potential pesticide intakes was obtained from the food balance sheets compiled by FAO. These tables provide "disappearance data" for a number of items or classes of foods. From this information it is possible to obtain a measure of the total consumption of a food commodity including the food item in all forms. Because these food balance sheets often only give a figure which refers to a general class of foods, access to more complete data was necessary. For one country, Country 1, in the Americas, very complete data were available on the intake of various foods. These data were obtained from a food survey conducted in the country in question. In order to enable a computerized calculation to be possible it was necessary to adjust

food survey data to give figures which corresponded to figures for the general class of food given in the food balance sheets. In some cases the consumption figure used for a food item was only a rough estimate because of the lack of details regarding how much of a specific food occurs in a processed commodity (e.g. pineapple in "mixed fruit").

The procedure of adjusting food survey figures to equal food balance sheet figures was possible in an organized and consistent fashion in the case of Country 1 which had the most complete food survey data. Fairly good food survey data were also available from Country 2 in Europe; less complete food survey data were also available from Country 3 in Asia and Country 4 in the Americas. The same procedure was used to adapt the food survey data to the food balance sheets in these other three countries, but where the figures were too incomplete to give a figure for a specific food item, the figure was estimated by apportionment from the data obtained for Country 1. In a few cases this procedure was modified slightly to allow for differing dietary patterns in each country.

Appendix IV

GLOSSARY

The definitions in this glossary were accepted by the Meeting for use in the report and the associated monographs (FAO/WHO, 1970). They are as adopted at the 1967 Joint Meeting (FAO/WHO, 1968a), except "regulatory method of analysis" and "referee method of analysis" which were added at the 1968 Meeting (FAO/WHO, 1969b) and "conditional acceptable daily intake" and "tentative negligible daily intake" which were added at the 1969 Meeting.

Pesticide residue

A pesticide residue is a residue in or on a food of any chemicals used for the control of pests. The term also includes derivatives of such chemicals. The amounts are expressed in parts by weight of the chemical and/or derivative per million parts by weight of the food (ppm).

Explanatory note

In interpreting this definition it is proposed to include the consideration of any substance which may, at a given time, be known to be derived from the product and which may be held to influence the toxicology of the residue. Residues from unknown sources (i.e. background residues) will be considered as well as those from known uses of the chemical in question. The term pesticide will be held to include any constituent of a pesticide used for the control of pests during the production, transport, marketing or processing of food or which may be administered to animals for the control of insects or arachnids in or on their bodies. It will not apply to antibiotics or other chemicals administered to animals for other purposes, such as to stimulate their growth or to modify their reproductive behaviour; nor will it apply to fertilizers or, at least for the present, to other substances used to influence the rate of growth of plants (other than herbicides).

Negligible residue

A negligible residue is an amount of a pesticide residue that is regarded as toxicologically insignificant.

Unintentional residue

An unintentional residue is one which occurs in a food as a result of circumstances *not* designed to protect the food against pest attack.

Explanatory note

For this purpose the range of pesticide uses is as indicated under "pesticide residue." The food should be specified in each case and the term includes products such as milk and meat from treated animals. Furthermore, the residue may be acquired at any stage in the growing, harvesting, distribution, marketing or processing of the food. The unintentional residue also includes a residue of a chemical which occurs in nature as part of the environment but which cannot be distinguished from residues due to the use of pesticides. Residues sometimes described as "incidental," "accidental" or "background" residues are included within this term.

Practical residue limit

The practical residue limit is the maximum unintentional residue (see definition) allowed in a specified food.

Explanatory note

A practical residue limit is the level of pesticide residue above which a regulatory action may be taken. It applies to a specific commodity and pesticide for which no *tolerance* has been established. Observation of a residue level above the "limit" may be presumptive evidence of violation of good agricultural practice; values below the "limit" are presumed to result from incidental effects, including possibly isolated effects, from other approved use of the pesticide.

Acceptable daily intake

The acceptable daily intake of a chemical is the daily intake which, during an entire lifetime, appears to be without appreciable risk on the basis of all the known facts at the time. It is expressed in milligrammes of the chemical per kilogramme of body weight (mg/kg).

Explanatory note

For this purpose "without appreciable risk" is taken to mean the practical certainty that injury will not result even after a lifetime of exposure. Furthermore, for a pesticide residue the acceptable daily intake is intended to give a guide to the maximum amount that can be taken daily in the food "without appreciable risk" to the consumer. Accordingly, the figure is derived as far as possible from feeding studies in animals and/or in man. The studies are usually conducted with the pesticide chemical itself. However, if the residues of a pesticide are known to consist of more than one chemical which may influence the toxicology of the residue (see definition of "pesticide residue"),

information on the toxicology of the residual chemicals and, where appropriate, their acceptable daily intakes have to be taken into account when assessing the risks. (See Section 2.3 of this Report for further information concerning the inclusion of metabolites.) Acceptable daily intakes are always subject to revision at any time in the light of new information.

Conditional acceptable daily intake

A conditional acceptable daily intake is one which is established for a pesticide in order to limit its use to those situations where no satisfactory substitutes are available.

Temporary acceptable daily intake

A temporary acceptable daily intake is one which is recommended for a limited period.

Explanatory note

A specified period is provided to enable additional biochemical, toxicological or other data to be obtained, as may be required for establishing an ADI. (See "Further Work Required.") In such cases any recommendation will normally involve the application of a safety factor, the size of which will be dependent upon the nature of the toxicity of the compound, but which will be larger than that normally used in estimating acceptable daily intakes. In all cases the positions will be reviewed not later than the first meeting following the specified date.

Tentative negligible daily intake

A tentative negligible daily intake is allocated to a pesticide when unintentional residues of it occur in food and when at least a short-term toxicity study is available. The short-term study, however, will have yielded insufficient information to establish even a temporary acceptable daily intake.

For discussion of a case in point see the paragraph on hexachlorobenzene, page 11.

Tolerance

A tolerance is the maximum concentration of pesticide residue that is permitted in or on food at a specified stage in the harvesting, storage, transport, marketing or preparation of the food, up to the final point of consumption. The concentration is expressed in parts by weight of the pesticide residue per million parts by weight of the food (ppm).

Temporary tolerance

A temporary tolerance is one that is valid for a limited time, which is specified in each case.

Explanatory note

Such tolerance recommendations are made under two conditions: (1) when they are derived from temporary ADIS, and (2) when they are derived from an ADI but the residue data is inadequate for firm tolerance recommendations.

The second class includes cases where information on losses of residue during storage, handling and preparation is inadequate and where calculations based on such inadequate figures and on appropriate food consumption data reveal a theoretical possibility that acceptable daily intakes could be exceeded. In cases of this kind, temporary tolerances are recommended only after information on the actual occurrence of residues in food, obtained from total diet and similar studies, has been considered and after assurance has been obtained that acceptable daily intakes are not likely to be exceeded. The information considered includes the results from subjective sampling and/or from objective sampling, including total diet studies, in various countries and particularly in places where pesticides are most widely used. In all cases the position will be reviewed not later than the first meeting following the specified date.

Good agricultural practice

Good agricultural practice is the recommended usage of a pesticide which is necessary and essential for the control of a pest under all practical conditions, bearing in mind any toxicological hazard involved.

Explanatory note

The "recommended usage" complies with the procedures, including the formulation, dosage rates, frequency of application and preharvest intervals recommended by appropriately trained specialists; it is the usage that has been registered, approved or otherwise accepted for the purpose by the relevant official department and which is normally included on the label. Such recommended methods of application should be based on supervised trials and other experimental work and should take into account such variations in climate, in crop husbandry and in incidence of pests as may occur under practical conditions from time to time in the various places in which the pesticide may be used. For this purpose good agricultural practice shall be held to include practice in the control of pests during the storage, transport, marketing and processing of foods.

Total diet studies

A total diet study is one designed to show the pattern of pesticide residue intake by a person consuming a typical diet.

Explanatory note

To make total diet studies, random samples of food are usually purchased in representative population centres in the country or district concerned and weighed out in the proportions in which they are consumed in the total diet. The weighed portions are then washed, cooked or otherwise prepared in the normal way for table presentation

and then mixed to give a number of predetermined food group samples comprising, for example, cereals, green vegetables, root crops, fruits and preserves, fats, meats and milk. These groups are chosen with the intention of minimizing the subsequent analytical problems; they also serve to identify the areas of the diet which contribute most to total residue present. The foods are purchased and prepared under expert supervision with the requirements of the studies in mind, but otherwise they resemble as far as possible the normal character of the total diet. Water and beverages are included.

Each food group sample, prepared as above, is analysed for various residues. This may involve several different analyses for each group. The exact analytical procedure may vary from group to group. In addition, from experience, it may become possible to omit certain analyses for some groups. Thus, the different groups will not necessarily be subject to exactly the same analytical procedure. Similar studies have also been described as "market basket studies."

Subjective sample

A subjective sample is one taken after a known or suspected use of a pesticide on a crop.

Explanatory note

Subjective samples include those taken during the early stages of the introduction of a pesticide into practical application when it is desirable to ascertain the residues occurring after known methods of application in the field, as well as those taken in circumstances where there are reasons to suspect that good agricultural practices have not been properly followed. Such samples may relate to crops from specific sites or from districts or countries where particular pesticides are known, or suspected, to have been used. Subjective sampling, rather than total diet studies, is sometimes used to assess the actual danger to consumers, particularly where the sampling and analytical facilities are limited; it enables the facilities to be concentrated on those categories of food intake considered to offer the greatest risks. Subjective sampling also enables certain of the analytical difficulties encountered in total diet studies to be avoided.

Objective sample

An objective sample is a random or impartial sample.

Explanatory note

The samples taken during total diet intake studies fall into this category.

Regulatory method of analysis

A regulatory method is one used for the determination of residues in the course of the administration of legislation relating to the subject.

Explanatory note

For this purpose, it is often necessary to identify the nature of the residue as well as to determine its level. Subject to any expression of requirements in the particular law, the accuracy, precision and sensitivity of a regulatory method need be sufficient only to demonstrate clearly whether a tolerance level has been exceeded. Usually regulatory methods are not specified in pesticides legislation, and at any given time there may be a number of methods available for a particular purpose.

Referee method of analysis

A referee method is one that has been specified, or agreed upon, for use in the event of a dispute.

Explanatory note

Referee methods are mainly required to settle disputes concerning the level of a residue, but procedures for identification of a residue may sometimes have to be included in such methods. Referee methods lay special emphasis on accuracy and precision, even if this may involve equipment and experience not normally available in laboratories undertaking regulatory work. Nevertheless some regulatory methods are suitable for use as referee methods, although their evaluation by interlaboratory comparisons is desirable before they are adopted as such.

Further work required

Further work required is work which must be done and properly reported before acceptable daily intakes and/or tolerances can be recommended or confirmed.

Explanatory note

In certain instances, although acceptable daily intakes have been established, further work has been considered to be essential to remove doubts about the toxicological significance of some experimental observations. Results of the further work required should be made available not later than the specific date mentioned, after which the compound will be reevaluated. The reevaluation may be done at an earlier meeting if relevant information should become available.

Further work desirable

Further work desirable is work which, when properly reported, would be expected to provide additional assurance that recommended acceptable daily intakes and/or tolerances are adequate for the protection of the health of the consumer.

