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Report of the 1976 Joint FAO/WHO Meeting

Technical Report Series
612

World Health Organization Geneva 1977

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Rome, 22–30 November 1976

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PESTICIDE RESIDUES IN FOOD

Report of the 1976 Joint FAO/WHO Meeting

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

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

1. INTRODUCTION

The Joint Meeting was held in pursuance of recommendations made at previous meetings and accepted by governing bodies of FAO and WHO that studies should be undertaken jointly by experts to evaluate possible hazards to man arising from the occurrence of residues of pesticides in foods.

The reports of previous Joint Meetings (FAO/WHO, 1965a, 1967a, 1968a, 1969a, 1970a, 1971a, 1972a, 1973a, 1974a, 1975a, 1976a) contain information on acceptable daily intakes (ADIs), residue limits, and general principles of evaluation for the various pesticides considered. The supporting documents (FAO/WHO, 1965b, 1965c, 1967b, 1968b, 1969b, 1970b, 1971b, 1972b, 1973b, 1974b, 1975b, 1976b) contain detailed

monographs on these pesticides and include comments on analytical methods.

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

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

(*a*) reviewing data on certain pesticides and their residues ;

(*b*) proposing pesticide residue limits and recommending methods of analysis.

The WHO Expert Group was primarily responsible for :

(*a*) reviewing toxicological and related data on certain pesticides and their residues ;

(*b*) establishing, where possible, ADIs for man for those pesticides.

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

2. GENERAL CONSIDERATIONS

2.1 Modification of the agenda

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

2.2 General principles for allocating ADIs

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

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

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

2.3 Deficiencies in toxicological data

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

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

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

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

2.4 Acquisition and availability of data

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

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

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

2.5 Presentation of recommended maximum residue limits

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

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

2.6 Maximum residue limits in processed foods

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

3. SPECIFIC PROBLEMS

3.1 Consideration of technical and formulated products

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

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

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

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

3.2 Aliesterase-inhibiting compounds

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

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

3.3 Reversible cholinesterase inhibition

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

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

3.4 Chlordimeform

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

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

3.5 Leptophos

The toxicological problem associated with several organophosphorus esters such as tri-*o*-cresylphosphate (TOCP), considered at a previous Meeting (FAO/WHO, 1975a) in the evaluation of leptophos, was briefly discussed in the light of a new report [1] reviewing this compound. The previous Meeting recognized that the potential hazards associated with leptophos were twofold:

(1) occupational or accidental exposure of individuals to high doses for short periods; and

(2) long-term low level exposure and possible build-up of the toxicant to threshold levels leading to ataxia.

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

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

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