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PRINCIPLES GOVERNING CONSUMER SAFETY IN RELATION TO PESTICIDE RESIDUES

**Report of a Meeting
of a WHO Expert Committee on Pesticide Residues
held jointly with the
FAO Panel of Experts on the Use of Pesticides
in Agriculture**

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WORLD HEALTH ORGANIZATION

GENEVA

1962

**MEETING
OF A WHO EXPERT COMMITTEE ON PESTICIDE RESIDUES
HELD JOINTLY WITH THE
FAO PANEL OF EXPERTS ON THE USE OF PESTICIDES
IN AGRICULTURE**

Rome, 9 - 16 October 1961

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PRINCIPLES GOVERNING CONSUMER SAFETY IN RELATION TO PESTICIDE RESIDUES

Report of a Meeting of a WHO Expert Committee on Pesticide Residues held jointly with the FAO Panel of Experts on the Use of Pesticides in Agriculture

In 1959 the FAO Panel of Experts on the Use of Pesticides in Agriculture¹ reviewed some major problems on the use of pesticides and made a number of recommendations for further studies in this field. One recommendation was that FAO, jointly with WHO, should study :

- (1) the hazard to consumers arising from pesticide residues in and on food and feedstuffs ;
- (2) the establishment of principles governing the setting up of pesticide tolerances ;
- (3) the feasibility of preparing an International Code for the toxicological and residue data required in achieving the safe use of a pesticide.

In order to implement this recommendation, a joint meeting between a WHO Expert Committee on Pesticide Residues and the FAO Panel of Experts was held in Rome from 9 to 16 October 1961.

In their letters to members of this joint Meeting, the Directors-General of FAO and WHO stated that the Meeting should consider, among other matters, principles for establishing tolerances for pesticide residues in food. In addition to carrying out this assignment, the Meeting also undertook to outline principles of consumer safety and to give guidance on how these principles might be put into practice.

GENERAL CONSIDERATIONS

1. Pesticides are indispensable to the farmer in his fight against pests and diseases. Without their use, many foods could not be produced economically or perhaps at all, and the yield of all crops could be seriously

¹ FAO (1959) Meeting Report No. 1959/3 (mimeographed).

reduced. For example, without pesticides, present production in the USA of potatoes, apples, citrus fruits, and cotton would be reduced by 50% and meat, milk and wool by at least 25%. The effective control of tsetse flies would undoubtedly open vast areas in Central Africa for full agricultural use.

2. Pesticides vary widely in the degree of possible hazard they present to users, consumers of treated crops, farm animals, wild life and the public. The Meeting was concerned only with the possible hazards to human and animal consumers. It acknowledged the need for studies on the hazards to operators and to wild life and was pleased to note that the aspects concerning the safety of the operator have already received, and continue to receive, the attention of WHO and ILO and of nature conservationists concerned, internationally, with the problem of protecting wild life against the effects of pesticides.

3. A wide range of pesticide chemicals is needed for the control of pests and diseases on many types of food throughout the world. Frequently, the use of a pesticide for a specific purpose does not lead to a residue. In recording its belief in the basic principle that, as far as possible, food should be pure, the Meeting recognized that, because of the necessity of using pesticides, residues may occur. It therefore considered what measures should be taken to ensure that, if a residue is present, it will not harm the consumer. The Meeting noted the particular question of the applications of pesticides to stored food following harvest and emphasized the importance of using, if possible, compounds that leave either no residue or unquestionably harmless residues.

4. In those areas where pests have developed resistance to pesticides, high dosage rates have to be used to obtain adequate control. The Meeting, although aware of the extreme importance of the problem of resistance, considered it to be one for discussion elsewhere.

5. The Meeting recognized that some pesticides such as sulfur present no real problem because, in world-wide experience over many years, they have shown themselves to be without serious hazard to man. It was recognized that no residue problem is presented by the use of pesticides on ornamental plants and nursery stock, or on crops which are not used for human or animal consumption at any stage.

6. In this Report the Meeting outlines the general educational and legal means by which it considers pesticides may be controlled for the protection of the consumer and describes some requirements for defining safety and for specifying regulations. Care has been taken to distinguish between (1) *acceptable daily intake*, (2) *permissible level*, and (3) *tolerance*, because confusion of these terms has frequently led to difficulty.

Definitions

7. The terms used in this Report are defined thus :

(1) *Residue* : A pesticide chemical, its derivatives and adjuvants in or on a plant or animal. Residues are expressed as parts per million (ppm) based on the fresh weight of the sample.

(2) *Food factor* : The average fraction of the total diet made up by the food or class of foods under discussion. Details of the diet of a country may be obtained from the FAO Food Balance Sheets or other similar data.

(3) *Acceptable daily intake* : The daily dosage of a chemical which, during an entire lifetime, appears to be without appreciable risk on the basis of all the facts known at the time. "Without appreciable risk" is taken to mean the practical certainty that injury will not result even after a lifetime of exposure. The *acceptable daily intake* is expressed in milligrams of the chemical, as it appears in the food, per kilogram of body weight (mg/kg/day).

(4) *Permissible level* : The permissible concentration of a residue in or on a food when first offered for consumption, calculated from the *acceptable daily intake*, the *food factor*, and the average weight of the consumer. The *permissible level* is expressed in ppm of the fresh weight of the food.

(5) *Tolerance* : The permitted concentration of a residue in or on a food, derived by taking into account both the range of residues actually remaining when the food is first offered for consumption (following good agricultural practice) and the *permissible level*. The *tolerance* is also expressed in ppm. It is never greater than the *permissible level* for the food in question and is usually smaller.

THE CONTROL OF THE USE OF PESTICIDES

8. In its Report, the FAO Panel of Experts on the Use of Pesticides in Agriculture¹ recorded briefly its discussion on the legislative control of residues. It recognized the difficulties related to this problem and noted that a number of countries had already taken measures, of a varied nature, towards their solution.

9. Nevertheless, a common pattern is discernible. Firstly, there is informal consultation between manufacturers and research and government departments concerned. Secondly, guidance, preferably of a detailed nature, is given to farmers on how to use pesticides so that any residues ultimately

¹ FAO (1959) Meeting Report No. 1959/3 (mimeographed).

present in the food do not offer a hazard to consumers. Thirdly, punitive means exist to deal, if necessary, with farmers who, in ignorance or defiance of that advice, so misuse a pesticide that unnecessarily high residues remain in the food.

This common pattern can be put into effect in a number of ways as described in the four methods in paragraph 10, and it is for each country to decide the method most suitable to its own conditions and resources. Four requirements are basic to them all. They are: (1) qualified official agricultural advisers who know the agricultural practice of the country, the chief crops and the pests and diseases of those crops, and who have an adequate working knowledge of the different types of available pesticides; (2) analytical facilities for determining any residues on a crop grown, treated and harvested in that country; (3) toxicological advice on the amount of a pesticide that may be consumed daily in the human diet without effect on the consumer; and (4) finally, and most important of all, joint consultation by all authorities, agricultural, health, analytical and nature conservation, at all times to agree on the conditions for the use of a pesticide before that use is implemented. Knowledge of the national diet is essential.

10. Whichever method is adopted, it is advisable for the authorities to obtain a preliminary evaluation of the effectiveness of a pesticide in their country before it is used commercially. Residue data should be obtained at the same time, and often the manufacturer who wishes to introduce the product may be in a position to make the necessary analyses.

Method 1. The importation and/or manufacture and use of selected pesticides are entirely controlled by government authorities. Firms are allowed to manufacture or import only certain pesticides. These are used only by the agricultural department on the advice of its qualified advisers. It is desirable that samples of treated foods be analyzed for residue content and that this analysis be continued until the authorities are satisfied that they have adequate knowledge of the residue level occurring in the food.

Method 2. The importation and/or manufacture of selected pesticides continues under government control. Their use on behalf of the government is extended to farmers who have been trained for this purpose and who will use them to the satisfaction of the advisory agricultural and health officials. Confirmation of correct use by residue analysis should be obtained if possible.

Method 3. Generally, there need be no hindrance to the importation and/or manufacture of pesticides, but all products offered for sale must be registered. The purpose of registration is to ensure, as far as possible, that the product will be effective and safe if used according to the directions

on the label. The sale and use of pesticide products are limited to selected farmers. The selection will be made on the advice of competent authorities who must be satisfied that the farmer will use the pesticide as advised. This procedure will in effect have a restricting action on the range of pesticides manufactured or imported. Confirmation of correct use by residue analysis may be considered necessary in certain cases.

Method 4. All pesticide products are registered for sale, but the sale and use of the more toxic products are further controlled or even prohibited. With the exception of the requirement for registration, the sale and use of the less toxic pesticides are otherwise unrestricted. Official detailed advice on the correct use of pesticides is issued, and measures for dealing with those who misuse the products are available. Adequate analytical facilities must be available for residue determinations.

11. The official advice on the correct use of a pesticide should include information on one or more of the following : (1) the edible crops to which its use is restricted ; (2) the maximum dose per application ; (3) the maximum number of applications ; (4) the last date of application (in the case of winter crops) ; and (5) the minimum interval between last application and harvesting. This advice should appear on the label of the product and should be a condition of registration. All label claims and instructions for use should be as agreed by the competent authorities. Special attention should be paid to the labelling of seed grain treated with pesticides, such as the organomercurials and hexachlorobenzene, which are present at concentrations that will make the consumption of the grain harmful to man and farm animals. Official advice should also be disseminated through the advisory services and by means of advisory leaflets, trade journals and manufacturers' literature. (The advice should also refer to operator precautions and the protection of farm animals, wild life and the public.)

12. To be effective, punitive measures against those who fail to observe the official advice should be on a mandatory basis. The measures may be based either on *tolerances* or on minimum intervals between last application and harvesting. Examples of the former are the systems established in the United States, Canada, Australia and New Zealand ; of the latter, the laws in Austria, Belgium and France.

13. From the descriptions above, it is evident that, with limited funds available for the purpose, more satisfactory results would be achieved by spending these funds on an advisory service to the farmer on the use of pesticides, and on officials for checking that pesticides are being used correctly, than on extensive random sampling and analysis of food from the market. This course would permit the authorities to concentrate their available analytical facilities, devoted to enforcement, on foods which may be overtreated with pesticides as the result of unusual conditions.

TOXICOLOGICAL INVESTIGATION

14. The aims of toxicological investigation are to ascertain : (1) the amount of a pesticide to which man and farm animals can be exposed daily for a lifetime without injury ; (2) the nature of injuries which will result if an excess is absorbed ; (3) means for detecting subclinical effects before they become injurious ; (4) therapeutic measures for the treatment of injuries ; (5) information which will allow workers to utilize the pesticide safely.

15. These aims can be achieved only by the intelligent efforts of experienced qualified investigators who are not rigidly bound to follow a schedule of required procedures. The procedures must be determined by the chemical and physical properties of the pesticide, by its conditions of use and by its toxicological and biochemical actions, as they are discovered during the progress of the investigation.

16. The aims enumerated above have been satisfactorily achieved for pesticides now in use in those countries which exercise the most stringent control. This may not be the case for some pesticides in countries with less stringent control, and whenever possible such investigations should be undertaken or completed especially for new pesticides.

17. Observations upon man yield the soundest data for achieving the aims. Every effort should be made to collect and to evaluate data on human exposures and on the presence or absence of human response during production, handling and agricultural study of a pesticide. Even after the pesticide has been introduced into commerce, observations on the exposure and response of workers are useful, particularly because workers are exposed to much greater amounts of pesticide than is the general population.

18. Before adequate observations upon man become available, experiments on animals would allow sound judgment towards the realization of the primary aims. Programs which are sound guides to experienced investigators and which differ little among themselves are described in, for example, the Second¹ and Fifth² Reports of the Joint FAO/WHO Expert Committee on Food Additives. These programs are guides, but the conduct of the toxicological investigation remains the responsibility of the competent expert. This Meeting believes, however, that in the present state of toxicological knowledge, such programs should be followed when most new pesticides are being investigated. It is to be hoped that specific research, and accumulated experience with the investigation of pesticides,

¹ *FAO Nutr. Mtg. Rep. Ser.*, 1958, No. 17 ; *Wld Hlth Org. techn. Rep. Ser.*, 1958, 144.

² *FAO Nutr. Mtg. Rep. Ser.*, 1961, No. 29 ; *Wld Hlth Org. techn. Rep. Ser.*, 1961, 220.

will lead to new methods by which toxicological properties can be discovered more surely and perhaps more expeditiously than by following the mentioned programs.

19. It is important that the experimental studies be performed upon material which is chemically identical with the toxic products which the pesticide will leave in human or animal food. To assure this, the chemical changes which the pesticide undergoes from exposure to air, moisture, the enzymes of crops and food, and animals, as well as any reaction between the pesticide and nutrients by which food may be altered, must be known. It is necessary that investigations be made, both with the pesticide and with its specific formulations, under conditions of expected use. In the case of farm animals, it is of great importance to know the fate of a pesticide, and especially its rate of excretion in milk and its concentration in milk products, in eggs and in other animal products. This knowledge may lead to the prohibition of the use of a pesticide for treatment of farm animals or of their food and may require its replacement by a pesticide proved acceptable for this purpose.

20. An investigation designed to evaluate the safety of food treated with a pesticide should also provide information concerning the protection of the health of workers. Studies should therefore include, for example, skin penetration of the pesticide (particularly as it may be influenced by formulation), skin irritation and sensitization, possible corneal injury, and, with some pesticides, injury following inhalation. The results obtained should provide the basis for the preparation of instructions on the safe handling in manufacture, formulation, and application of that pesticide.

21. A difficulty in the independent evaluation of the safe use of pesticides is the fact that some of them have been put into use without full publication of the experimental work. It may be presumed that those pesticides have demonstrated their safety to the controlling authorities. The Meeting urges that FAO/WHO use every effort to persuade investigators to publish their past and future studies in adequate detail.

22. The first aim of the toxicological investigation was stated to be the assessment of the amount of a pesticide to which man can be exposed daily for a lifetime without injury. Of necessity, early views of this amount will be estimated and subject to revision as experience accumulates, particularly after the pesticide has been put into use. When the investigations are completed, it is possible, by the use of scientific judgment, to name an *acceptable daily intake*, as has been done for certain antimicrobials and antioxidants as stated in the Sixth Report of the Joint FAO/WHO Expert Committee on Food Additives.¹

¹ *FAO Nutr. Mtg. Rep. Ser.*, 1962, No. 31 ; *Wld Hlth Org. techn. Rep. Ser.*, 1962, 228.

23. Since, to be useful, pesticides must injure certain forms of life, it is generally presumed that they must be, in some degree, toxic to man. This is not necessarily true, as exemplified by the harmfulness of silica gel to certain insects. The Meeting urges that workers on crop protection should strive to find new compounds with a selective toxicity towards a particular pest, while being essentially non-toxic to man. Research should be encouraged on the differences between the metabolism of invertebrates, plants and warm-blooded animals as a basis for this desirable effort.

24. Different pesticides and other chemicals are often absorbed simultaneously during occupational use, or in food, by man or animals. It is important that more be learned about their combined toxic effects upon the body.

25. In 1958 the Food Protection Committee in the USA¹ discussed "insignificant or inconsequential intakes" of food additives, pointing out that regulatory action concerning the use of chemicals which result in insignificant intakes is neither helpful nor necessary. This point is obviously important to administrators of programs for the safe use of pesticides. The Meeting has not discussed this matter adequately, but recommends that further clarification of the principles and procedures for the estimation of insignificant levels should be assigned to a future FAO/WHO committee meeting on pesticides.

BASIC REQUIREMENTS FOR THE ESTABLISHMENT OF RESIDUE TOLERANCES

General principles

26. As already stated, the contamination of human and animal food should be restricted to the lowest possible level. At the same time, it has been recognized that pesticides are required during the production, processing, storage and distribution of food, even though sometimes their use results in unavoidable residues. In determining how much residue should be allowed in food, the main principle to be observed is that this amount should not be higher than that which results from "good agricultural practice", provided that the final amount of residue in the daily food is no greater than the amount accepted as safe for long-term consumption by man.

Information required

27. In the early stages of the development of a pesticide, frequent consultations should take place between the manufacturer and the agricultural

¹ U.S. Food Protection Committee (1958) *Food-Drug-Cosmetic Law Journal*, **13**, 477.

and health authorities to ensure that all the data which will eventually be required for its commercial introduction will be developed in an adequate and rational manner. Such consultations will also ensure that information related to the needs and conditions of use of a specific country, or region within a country, is made available for the issuance of adequate instructions on the effective and safe use of a pesticide locally.

28. It should be demonstrated by well-designed experiments that the pesticide will give effective and economical pest control in plant or animal production or in the processing, storage or distribution of food. Continuous search is being made for new compounds giving more economical pest control with a minimum of hazard to the user, consumer and wild life. The growing problem of resistance to insecticides by an increasing number of species of insects and mites of importance to agriculture and health is demanding new types of chemicals. Special attention is being given to the development of selective pesticide treatments leading to the maximum survival of the beneficial species of insects and mites. All these requirements vary from place to place. Therefore a wide variation in pest control recommendations and in the resulting residues is to be expected.

29. Experimental programs to decide amount, formulation, frequency and timing of the pesticide required should aim at providing an accurate forecast of the control obtained in commercial practice, the rate of pesticide disappearance and the residue likely to occur on that part of the food reaching the consumer. In the design of these experiments, provision should be made for factors such as differences in agricultural practice, soil type, husbandry practice, climatic conditions and severity of the pest control problems in different areas. The design should also allow for the occasions when larger amounts of pesticide and more frequent applications are needed to combat cases of unpredictably severe outbreaks of insects or plant diseases.

30. Several natural phenomena have an influence on pesticide performance and the rate of residue disappearance. Meteorological conditions prevailing during the experiment, the time of year of pesticide application, and the age and rate of growth of the plant surfaces involved are examples, while the maturity of plant surfaces and the activity of plant enzymes are important factors in the degradation of absorbed deposits or systemic compounds. Where soil applications are concerned, soil type and condition, temperature, moisture content and other factors must be taken into consideration. Wide variations in the residues in root crops are known to occur, due to these and other factors already mentioned. Information on all these aspects is required for intelligent interpretation of differences in residue data.

31. Frequently the raw agricultural product is not the final item that reaches the consumer. By-products obtained from processing raw agri-

cultural products into human food are often used as farm animal feed. Data on the effect of processing and on the initial and ultimate residues in such agricultural products are needed ; this information is of particular importance for staple foods such as cereals, dairy products and root crops. Adequate attention must be given to this aspect, otherwise uncertainty may lead to a restriction on the use of agricultural by-products, such as cannery wastes, sugar-beet pulp and molasses, and of certain oilseed meals, as animal feed.

32. The over-all approach to the evaluation of safety of a pesticide includes consideration of the operator during application, the worker handling the crop, the human consumer of the food product, the farm animal consuming treated plant material, and of wild life. In assessing safety to farm animals, distinction must be made between the effect of pesticides on those which are being raised for slaughter and the welfare and productivity of such animals as are used for breeding stock and draught and which remain on farms for longer periods of time.

33. All the listed variables may be involved in "good agricultural practice", and detailed information on these should therefore be made available.

Employment of residue data

34. From the residue data obtained, a calculation can be made of the total amount of residue likely to enter the diet with each food or group of foods. This is obtained by use of the *food factor*. A large additional measure of safety is contained in any such calculation, since the assumption is made that all the particular food in the national diet will contain the residue.

Following this calculation, it is necessary next to determine the *permissible level* using the *food factor*, the *acceptable daily intake* and the average weight of the consumer. If the figure derived from the residue data is less than the *permissible level*, the residue data can be used as a basis for setting a *tolerance*. Provided it does not exceed the *permissible level*, the *tolerance* is usually set a little above the upper limit of the residue level which occurred following the use of the pesticide according to good agricultural practice.

An example of the application of these principles is given in the Appendix. They are also described in the Sixth Report of the Joint FAO/WHO Expert Committee on Food Additives.¹

35. Regardless of whether or not *permissible levels* are used to establish *tolerances* for enforcement purposes, *permissible levels* and residue data are required in order to set the minimum interval that must occur between the last application of the pesticide and harvesting the crop, or between animal treatment and slaughter. *Permissible levels* and *tolerances* are of no help

¹ FAO Nutr. Mtg. Rep. Ser., 1962, No. 31 ; Wld Hlth Org. techn. Rep. Ser., 1962, 228.

to the farmer ; it is the schedule of application, and especially the minimum interval between last application and harvest, that is the practical guide to him.

36. The Meeting recognized that different *tolerances* for any one food may be established in different countries. However, as the *food factor*, *permissible level* and *acceptable daily intake* are the prime factors to be considered in establishing the safety of that food when it contains a residue, the existence of different *tolerances* does not necessarily impede the free movement of that food in international trade. When systems of inspection are sufficiently developed a country can solve problems on an individual basis, so that a particular shipment of a food containing a residue level higher than that accepted in the importing country will not, in fact, create a hazard to the consumer. (See Example 2 of the Appendix.)

Analytical procedures

37. Regardless of the method followed in the protection of the public health from potential injury by the ingestion of pesticide residues, adequate analytical procedures are required for a precise knowledge of the nature and the amount of the residues that are likely to be present in food.

38. The requirements for an analytical procedure depend on the scope of the investigation. Two distinct procedures have to be considered : (1) fundamental research that provides basic knowledge of the behaviour, metabolism and rate of degradation of the pesticide on or in crops and animal products ; and (2) the analytical methods for examination of market samples.

39. Knowledge of the behaviour, metabolism and rate of degradation of a pesticide residue is based on : (1) the nature and amount of the original deposit and its alteration products, in or on the plant or animal, from the moment of application until the lowest detectable level of residue is reached ; (2) the rate of penetration of the residue into the plant or animal and its distribution in different parts of the resulting food ; and (3) variations of (1) and (2) due to formulation used, environmental and climatic conditions, and exceptional conditions or scales of use, as in combating heavy outbreaks.

40. Fundamental research requires the availability of the most sensitive and specific procedures, which generally involve elaborate equipment and instrumentation. Data obtained in this manner are normally provided by highly specialized research centres, and it is obvious that no guidance needs to be provided for them.

41. Examination of residue levels in market samples consists mainly of the identification and measurement of residues that have a pharmacological

or toxicological significance. Analyses have to be performed on samples of known as well as unknown history and by many laboratories that share the responsibility for enforcing regulations. Therefore standardized procedures of identification and measurement that are reliable in the hands of a trained chemist are required. The Association of Official Agricultural Chemists (AOAC), in meeting this need, has promoted collaborative studies leading to the development and acceptance of official methods of analysis. Procedures have been adopted, either as official or as "first action" (tentative) methods, by the Association for a certain number of inorganic and organic pesticide residues. Similar work was started some years ago in the United Kingdom. Recently the European and Mediterranean Plant Protection Organization (EPPO) invited its member countries to submit for assessment those methods of residue analysis which they considered worthy of recognition on an international basis.

42. So far the main attention has been given to the development of methods for the measurement of pesticide residues in samples of known history. However, identification schemes to decide whether or not members of various groups of pesticides are present in a sample are equally important. The chemist who is required to deal with market samples must be able to identify and measure any pesticide residue in a possible mixture of several residues.

43. Therefore international attention is needed to promote collaborative studies on: (1) the development of identification schemes that facilitate the detection of any kind of pesticide residue in food; and (2) the development of acceptable quantitative and specific methods which, in the hands of workers in laboratories in different countries, uniformly yield the actual amount of the components of a residue. Each method will consist of a detailed, precise description of the extraction and clean-up procedures and of the technique employed for the final measurement.

44. An acceptable method of analysis of market samples must satisfy the following requirements:

(1) *Data obtained by fundamental research.* Information obtained with the methods used in fundamental research will determine the choice of an adequate analytical method for enforcement; the essential purpose of such a method is to measure the components which have pharmacological or toxicological significance.

(2) *Sensitivity.* The method must be sufficiently sensitive, in terms of micrograms which can be detected in the sample, to yield significant data relevant to the *tolerance*.

(3) *Reproducibility and efficiency of recovery.* The method must have an acceptable level of reproducibility and recovery of a given pesticide.

(4) "*Blank*" values. These, obtained from untreated plant or animal tissue, must be low and, in particular, reproducible. Reagent blanks, of course, should be low.

(5) *Specificity*. While specific or semispecific methods are always preferable, satisfactory results may often be obtained by the application of a non-specific method of measurement supplemented by a specific method of identification. For example, non-specific methods of measurement such as bioassay, cholinesterase inhibition, total organic chlorine or organic phosphorus determination may be employed for a quantitative determination provided they are accompanied by a suitable qualitative method such as paper or column chromatography. This is of particular value when specific methods of measurement do not exist.

PESTICIDE SCIENTIFIC AND REGULATORY INFORMATION SERVICE

45. Government offices in many countries receive information on the efficiency and safety of pesticides used in agriculture and food storage and on the persistence and analysis of their residues. This information, which remains unpublished, originates from both government and industrial sources. The information provided by industry is often supplied on a confidential basis and cannot receive wider circulation without the firm's consent.

46. Published scientific and regulatory information on pesticides appears in numerous journals and publications. It is seldom that any government office can keep abreast of these publications. Various journals devoted to providing abstract service cover only a portion of the publications related to pesticides. There is usually a considerable time lag between completion of research and publication of an original paper, and an even further delay before its appearance in the form of an abstract.

47. The Meeting considered that much of this unpublished information is worthy of a wider circulation. National and international groups and government offices responsible for evaluating the efficiency and safe use of pesticides would benefit from it.

48. The Meeting recognized that both FAO and WHO provide a service with the following publications: (1) FAO/WHO: *Current Food Additives Legislation* (monthly); (2) FAO/WHO: *Food Additive Control Series*; (3) FAO: *Plant Protection Bulletin* (bi-monthly); (4) FAO: *Food and Agriculture Legislation* (quarterly); (5) WHO: *Bibliography on Pesticide Toxicity and Accidental Poisoning* (twice a year); and (6) WHO: *Information Circular on the Toxicity of Pesticides to Man* (twice a year). It was,

however, of the opinion that the scientific aspect of this service should be made more comprehensive, both in coverage and in distribution. For example, the prompt, accurate and wide international exchange of scientific information on efficiency, persistence, residue analysis and toxicity of pesticides is essential for their rational use throughout the world.

49. The Meeting urged that both FAO and WHO give serious consideration to the establishment of a pesticide scientific and regulatory information service to collect, collate and disseminate published and unpublished information on all aspects of pesticides used in agriculture and food storage. This information should be made generally available to all research and regulatory agencies concerned with the evaluation of pesticides and the formulation of recommendations for their use.

RECOMMENDATIONS

50. The recommendations are divided as follows: (1) those on research needs for research workers generally, (2) those on matters requiring international attention and specific actions by FAO and WHO, and (3) those for the attention of governments.

51. Recommendations on research needs

(1) Research into the differences between the normal metabolism of invertebrates, plants and warm-blooded animals as it relates to the susceptibility of these organisms to possible poisons; this information would be of value in the development of new compounds having a selective toxicity to a particular pest while being essentially non-toxic to man, farm animals and wild life (paragraph 23).

(2) Research on the joint toxic action of pesticides and other chemicals on man and useful animals (paragraph 24).

(3) Research into the effects which pesticides may have upon the nutritive value of food (paragraph 19).

(4) Research into the chemical changes which may take place in the residue during food processing (paragraphs 19 and 31).

(5) Research to develop identification schemes for detecting the presence of any kind of pesticide residue alone or in admixture (paragraph 43).

52. Recommendations to the Directors-General of FAO and WHO

(1) Studies of the methods used to assess the toxicity of pesticides with the aim of improving the accuracy and speed of the assessment; examples of methods to be studied are those for determining percutaneous

toxicity, and the effects of long-term exposure, including carcinogenesis (paragraph 18).

(2) Studies to evaluate the evidence, including toxicological and other pertinent data, published and unpublished, on those pesticides known to leave residues in food when used according to good agricultural practice, and to issue the conclusions in the form of *acceptable daily intakes*, supported by explanations of the basis for each value (paragraph 22).

(3) Studies to define the principles and procedures for determining "insignificant or inconsequential intakes" of pesticides (paragraph 25).

(4) Collaborative studies leading to the production of internationally acceptable methods of measuring pesticide residues in food, for use by enforcement agencies (paragraph 43).

(5) The establishment of a pesticide scientific and regulatory information service to collect, collate and disseminate published and unpublished information on all aspects of pesticides used in agriculture and food storage (paragraphs 21 and 49).

53. Recommendation to governments

Governments are urged to extend their fullest co-operation in implementing the recommendations listed above.

APPENDIX

Example 1, illustrating the use of *food factor*, *acceptable daily intake* and *permissible level* to set a pesticide *tolerance*

1. A substance X, proposed as a pesticide on several crops or animals, left a residue level of 0 to 0.8, but not exceeding 1 ppm in food when first offered for consumption.
2. The foods in which it might occur and the amount of these foods that would be eaten daily on the basis of national food-consumption data were listed in order to determine the *food factor*. The total average consumption of treated food of an average man was found to be 500 g out of a total daily consumption of 2000 g, giving a *food factor* of 0.25. The daily intake of X was therefore estimated as 0.5 mg ($1 \text{ ppm (mg/kg)} \times 0.25 \times 2 \text{ kg} = 0.5 \text{ mg}$).
3. The body weight of an average man was 70 kg.
4. Therefore the proposed intake of X was 0.007 mg/kg body weight/day ($0.5 \text{ mg}/70 \text{ kg} = 0.007 \text{ mg/kg}$).
5. The *acceptable daily intake* (derived from the evaluation of toxicological data) for substance X is 0.1 mg/kg body weight/day or 7 mg/man/day ($0.1 \text{ mg/kg/day} \times 7 \text{ kg} = 7 \text{ mg/man/day}$).
6. Thus the *permissible level* in treated food (500 g) would be 14 ppm, corresponding to an acceptable daily intake of 7 mg/man/day ($7 \text{ mg}/0.5 \text{ kg} = 14 \text{ mg/kg} = 14 \text{ ppm}$).

7. But because such a level is not required under good agricultural practice, the *tolerance* would be set at 1 ppm.

More complicated examples illustrating the use of these principles in connection with multiple tolerances (that is, different tolerances of the same chemical for different foods consistent with good agricultural practice for each) are given by Lu (1961).¹

Example 2, illustrating the use of the *daily acceptable intake* to determine whether a country with a lower *tolerance* for a particular residue may import food from a country with a higher *tolerance* for the same residue

In this example, the assumption is made that imported and native rice will be marketed in country B. A further assumption is made that the average residue on the rice in each country is equal to the *tolerance* permitted in that country. As a matter of fact, as pointed out in Example 1, *tolerances* are usually set a little higher than the highest residue required under the range of conditions taken into account by good agricultural practice. The hypothetical data are as follows:

	Country A (exporting)	Country B (importing)
Average body weight of man	70 kg	50 kg
Acceptable daily intake of residue Y per kg	0.2 mg/kg/day	0.2 mg/kg/day
Acceptable daily intake of residue Y per man	$0.2 \times 70 =$ 14 mg/man/day	$0.2 \times 50 =$ 10 mg/man/day
Tolerance for residue Y on rice	15 ppm	10 ppm
Daily consumption of rice	100 g (0.1 kg)	400 g (0.4 kg)
Total residue of Y obtained from rice	$15 \text{ ppm (mg/kg)} \times$ $0.1 \text{ kg} = 1.5 \text{ mg/}$ man/day	$10 \text{ ppm (mg/kg)} \times$ $0.4 \text{ kg} = 4 \text{ mg/}$ man/day
Total residue of Y from other diet	10 mg/man/day	3 mg/man/day
Additional amount of residue Y which could be considered as acceptable	$14 - (10 + 1.5) =$ 2.5 mg/man/day	$10 - (3 + 4) =$ 3 mg/man/day

Calculation Related to Importation :

Total residue of Y on 200 g rice	$15 \text{ ppm (mg/kg)} \times$ $0.2 \text{ kg} = 3 \text{ mg}$	$10 \text{ ppm (mg/kg)} \times$ $0.2 \text{ kg} = 2 \text{ mg}$
Total residue of Y on 400 g imported rice (the normal intake of country B)	—	$15 \text{ ppm (mg/kg)} \times$ $0.4 \text{ kg} = 6 \text{ mg}$
Additional amount of residue Y which could be considered as acceptable if all rice is imported	—	$10 - (3 + 6) =$ 1 mg

Thus, although importation of rice will increase the total potential intake of residue Y in country B from 7 to 9 mg/man/day, the total potential intake will still be less than the *acceptable daily intake* (which is 10 mg/man/day). The importation will be scientifically justified despite the higher residue *tolerance* of Y on rice grown in country A.

¹ World Health Organization, unpublished working paper.

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