Guidelines for predicting the dietary intake of pesticide residues*

JOINT FAO/WHO CONSULTATION

These guidelines have been developed to describe procedures for predicting the dietary intake of pesticide residues, and will assist national authorities in their considerations of the acceptability of the Codex maximum residue limits (MRLs). The relevant authorities are invited to consider the basic approaches described in these guidelines, which have been designed to provide reasonable assurance that such MRLs would not result in dietary intakes that exceed the acceptable daily intake (ADI) of a pesticide.

INTRODUCTION

Role of the Codex Committee on Pesticide Residues

The Codex Committee on Pesticide Residues (CCPR)\(^a\) is an intergovernmental body that advises the Codex Alimentarius Commission on all matters relating to pesticide residues.\(^b\) Its primary objective is to develop Codex maximum residue limits (MRLs), which are expressed in milligrams of the residue per kg of the commodity, in order to facilitate international trade, while protecting the health of the consumer. Public health considerations are taken into account by establishing the MRLs at levels not higher than those resulting from use of the pesticide in accordance with good agricultural practice (GAP).\(^c\)

From time to time the question has been raised at the CCPR of whether acceptance of Codex MRLs could result in a situation in which the acceptable daily intake (ADI)\(^d\) would be exceeded. A definitive

* This article is based on the guidelines (unpublished document WHO/EHE/FOS/88.2) that were developed by an FAO/WHO Consultation convened under the auspices of the Joint UNEP/FAO/WHO Food Contamination Monitoring Programme (or GEMS/Food) in collaboration with the Codex Committee on Pesticide Residues (CCPR), which met in Geneva on 5–8 October 1987, and on the report of this Consultation (unpublished document WHO/EHE/FOS/88.3). GEMS/Food forms part of the Global Environment Monitoring System established by the United Nations Environment Programme. Requests for reprints or for copies of the unpublished documents should be sent to Food Safety, Division of Environmental Health, World Health Organization, 1211 Geneva 27, Switzerland. A French translation of this article will appear in a later issue of the Bulletin.

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The CCPR, a subsidiary body established by the Codex Alimentarius Commission, has the responsibility for establishing maximum residue limits for pesticides in food and feed, to prepare priority lists of pesticides for evaluation by the Joint FAO/WHO Meeting on Pesticide Residues, to consider methods of sampling and analysis for the determination of pesticide residues in food and feed, and to consider other matters in relation to the safety of food and feed containing pesticide residues. Membership of the CCPR is open to all Member States and Associate Members of FAO and WHO. Representatives of international organizations that have formal relations with either FAO or WHO may attend meetings as observers. The CCPR is hosted by the Government of the Netherlands and has met 19 times since 1966.

Pesticide residue is any specified substances in food, agricultural commodities, or animal feed resulting from the use of a pesticide. The term includes any derivatives of a pesticide, such as conversion products, metabolites, reaction products, and impurities, considered to be of toxicological significance.

Good agricultural practice in the use of pesticides is the officially recommended or authorized use of pesticides, under practical conditions, at any stage of production, storage, transport, distribution or processing of food, agricultural commodities, or animal feed, bearing in mind the variations in requirements within and between regions. This takes into account the minimum quantities necessary to achieve adequate control, applied in such a manner that the amount of residue is the smallest amount practicable and which is toxicologically acceptable.

The acceptable daily intake (ADI) of a chemical is the daily intake which, during an entire lifetime, appears to be without appreciable risk, on the basis of all the facts known at the time. It is expressed in milligrams of the chemical per kilogram of body weight.
answer to this question can only be obtained by means of dietary intake studies (1). In many cases where the pesticide has not long been in use, it will be necessary to predict the pesticide residue intake. Thus, during its 18th session in 1986, the CCPR recommended that guidelines be developed to assist national authorities in the prediction of the pesticide residue intake that might result following the acceptance of Codex MRLs. The CCPR asked FAO and WHO to convene a special meeting of experts to prepare draft guidelines and to propose a mechanism for performing safety assessments of national MRLs and Codex-recommended MRLs. After further discussion, the 19th session of the CCPR, in 1987, recommended that the guidelines should be developed as soon as possible, taking into account the comments made by the CCPR participants.

Acceptable daily intake and maximum residue limits

The ADI is based on a complete review of the available data (biochemical, metabolic, pharmacological, toxicological, etc.) from a wide range of experimental animal studies and/or available relevant human data. The no-observed-adverse-effect level (NOAEL) for the most sensitive toxicological parameter, normally in the most sensitive species of experimental animal, is used as the basis for estimating the ADI. A safety factor that takes into consideration the type of effect, the severity or reversibility of the effect, and the problems of inter- and intra-species variability is applied to the NOAEL to determine the ADI for man. Pertinent human data may outweigh experimental animal data in the estimation of the ADI for man.

Maximum residue levels are estimated from globally generated pesticide residue data, obtained using appropriate good agricultural practice, and may change as the latter is modified. The MRLs recommended by the joint FAO/WHO Meeting on Pesticide Residues (JMPR), on which the Codex MRLs are usually based, are the considered decision of the experts present at the meeting after examination of all pertinent data. This is also true of the ADIs.

The ADI and the MRL are not permanently fixed values. Both are determined according to the best judgement of a group of internationally recognized experts on the data available to them at the time of the evaluation. Summaries of these data are published in the JMPR evaluations. However, as new data become available, the ADI or MRL may be revised.

From time to time, concern has been expressed over the possibility of adverse health effects arising from exposure to residues of more than one pesticide in food. This matter was considered by the 1981 JMPR (2) which concluded that, with the levels of pesticide residue intake found at that time, there was no need to alter the approach or the general principles for estimating ADIs. Consequently, the currently recommended approaches to the assessment of pesticide residue intake are also appropriate for the assessment of the concurrent intake of residues of more than one pesticide.

METHODOLOGY

General considerations for predicting the dietary intake of pesticide residues

The purpose of predicting the dietary intake of pesticide residues is to compare the prediction with the ADI, in order to reach a conclusion as to the acceptability of an MRL from a public health point of view. Such predictions require a knowledge of both the residue levels in food and the quantity of food consumed. The dietary intake of any particular pesticide residue is obtained by multiplying the residue level in the food by the amount of the food consumed. Ideally, total intake of the pesticide residue is then obtained by summing the intakes from all commodities containing the pesticide residue.

Residue level indices

Several indices can be used to represent the residue levels needed for predicting pesticide residue intake. The MRL is one such residue index and reflects the maximum residue level that is expected to occur in a commodity following the application of a pesticide according to good agricultural practice. Other factors should be taken into consideration when choosing an index of the levels to be used in pesticide residue intake predictions. These include estimates that take into account the residue levels actually found in practice, their distribution in the commodity, and the fate of residues in a variety of processes used in the preparation of food.

It is important to note that the use of the MRLs as an index of residue levels in the prediction of pesticide residue intake will lead to an overestimation of the true pesticide residue intake. The process of predicting the intake of a particular pesticide residue should include all commodities for which MRLs have been established unless the value has been estimated to be at, or about, the limit of determination.

Food consumption indices

There are several possible indices of food consumption. They are:

consumption, a commonly used index being the average daily consumption of a food or group of foods (expressed in kg of the item per person per day). Other indices include average portion sizes, percentile consumption values, and the average consumption by people who actually consume the commodity. The purpose of predicting pesticide residue intake is to allow comparison with the ADI, which, in turn, reflects an estimate of the acceptable lifetime intake. The predicted intake should therefore reflect long-term food consumption habits and not day-to-day variations in consumption. Thus, it is recommended that average daily food consumption values be used in predicting pesticide residue intake for comparison with the ADI.

It is also recognized that food consumption patterns vary considerably from one country to another and even within a country; therefore, to a large extent, individual countries will have to estimate their own food consumption. However, for the purpose of predicting pesticide residue intake at the international level, the use of average food consumption data given in the FAO food balance sheets (3) is recommended. Although the food consumption data derived from food balance sheets are subject to many uncertainties and limitations, they represent the best available data for international comparison. Thus, "it is believed that the food balance sheets so prepared, while often being far from satisfactory in the proper statistical sense, provide an approximate picture of the overall food situation in the countries which may be used for economic and nutritional studies" (3). This approximate picture of the overall food consumption patterns is adequate for predicting pesticide residue intakes, given the associated uncertainties in all the components involved in these predictions.

To carry out pesticide residue intake predictions at the international level, hypothetical diets should be developed for a limited number of dietary patterns, representative of various regions of the world ("cultural" diets). As a first approximation, a hypothetical global diet using the highest average food consumption value for each "cultural" diet may suffice. Selection of the highest average food consumption value for individual commodities from each "cultural" diet will result in an unrealistic total food consumption. To predict the pesticide residue intake, these values should be normalized to a 1.5 kg total daily consumption of solid food (i.e., excluding the liquid content of juices or milk). For more realistic predictions, the "cultural" diets should be used individually. This would make it possible to predict a range of potential intakes.

For pesticide residue intake predictions carried out at the national level, the best available food consumption data should be used. There should be caution in the use of food consumption values other than average values, if such use results in a hypothetical consumption that would not be attained. In carrying out pesticide residue intake predictions for identifiable subgroups (e.g., vegetarians), it would be appropriate to use relevant average food consumption data for that subgroup.

**Assessment of intake**

Prediction of pesticide residue intakes through the diet can be done with different degrees of realism. The more realistic predictions involve the consideration of many factors and may therefore be rather time-consuming. Comparison of the estimated pesticide residue intake with the ADI enables an assessment to be made of the potential risk to human health of pesticide residues.

The procedures described in the guidelines start with the most exaggerated intake predictions and proceed towards more and more realistic ones. Obviously, it would be desirable to make the best available prediction of intake first. However, by starting with the most exaggerated intake predictions, it is possible to eliminate at an early stage those pesticides, the intake of which is clearly unlikely to exceed the ADI. A more realistic prediction using refined data would make it possible to eliminate other pesticides from further consideration. This type of approach would facilitate acceptance of Codex MRLs and would allow the national authority concerned to direct its attention to the pesticides most likely to be of public health concern. Thus, a three-tier approach for predicting pesticide residue intakes is proposed, as outlined in Table 1.

**Theoretical maximum daily intake**

The theoretical maximum daily intake (TMDI) is an estimate of the dietary intake that is calculated by using the MRL and the average daily per capita food consumption of each food commodity for which an MRL has been established. Expressed in milligrams of residue per person, the TMDI is calculated by multiplying the MRL by the average food consumption for each commodity and then summing the product:

\[ TMDI = \sum_i F_i \times M_i \]

where: \( \sum_i \) indicates that the product \( F_i \) and \( M_i \) should be summed for all commodities for which there is an MRL;

\(^{\text{Risk is a statistical concept defined as the expected frequency of undesirable effects arising from exposure to a chemical. It may be expressed as absolute risk (i.e., excess risk due to exposure) or relative risk (the ratio between the risks in exposed and unexposed populations).}}\)
Table 1. Outline of proposed procedures for predicting pesticide residue intakes

<table>
<thead>
<tr>
<th>Residue level</th>
<th>Theoretical maximum daily intake (TMDI) (^a,b)</th>
<th>Estimated maximum daily intake (EMDI) (^a,b)</th>
<th>Estimated daily intake (EDI) (^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codex or national MRL</td>
<td>Codex or national MRL Corrections for:</td>
<td>Known residue level Corrections for:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(i) edible portion;</td>
<td>(i) edible portion;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(ii) losses on storage, processing, and cooking</td>
<td>(ii) losses on storage, processing, and cooking</td>
<td></td>
</tr>
<tr>
<td>Food consumption</td>
<td>Hypothetical global or national diet</td>
<td>“Cultural” or national diet</td>
<td>National diet</td>
</tr>
<tr>
<td>All commodities with a Codex or national MRL</td>
<td>All commodities with a Codex or national MRL</td>
<td>Known uses of pesticide, taking account of:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(i) range of commodities;</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(ii) proportion of crop treated;</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iii) home-grown/imported crops</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Estimated at the international level.
\(^b\) Estimated at the national level.

\(F_i\) = the food consumption value for the relevant commodity as derived from the hypothetical global or national diet in kg food per person per day;

\(M_i\) = the MRL for the relevant commodity given in mg pesticide/kg food.

While the TMDI is given in units of mg/person, the ADI is expressed in units of mg pesticide/kg body weight. In order to compare the TMDI with the ADI, the TMDI is divided by an assumed average body weight (60 kg). This calculation will result in gross overestimates of the true pesticide residue intake because:

(a) the percentage of a crop treated with a pesticide is usually far less than 100%;

(b) very few of the crops treated with a pesticide contain residues at the maximum residue level;

(c) residues normally dissipate during storage, transport, preparation, commercial processing, and cooking of the treated commodity;

(d) the MRL is set on the whole raw agricultural commodity, which frequently includes inedible portions. A large percentage of the residue may be discarded with the removal of the inedible portion.

For these reasons, it should not be concluded that the proposed Codex MRLs are not acceptable when the theoretical maximum daily intake exceeds the ADI. Instead, a TMDI calculation should be used only as a screening mechanism which may eliminate the need for further consideration of the intake of a pesticide residue.

If the TMDI does not exceed the ADI, further predictions of pesticide residue intake are not necessary. If good agricultural practices are followed, it is improbable that the ADI would be exceeded, provided the main uses of the pesticide are covered by the Codex MRL.

Estimated maximum daily intake

The estimated maximum daily intake (EMDI), which is also expressed in milligrams of the residue per person, is a more realistic estimate of the pesticide residue intake. It makes use of data on the edible portion of the commodity and takes into account the effects of the preparation, commercial processing, and cooking of the food. The formula for calculating the EMDI is:

\[
EMDI = \sum_i F_i \times R_i \times P_i \times C_i
\]

where: \(\Sigma\) indicates that the product of the four factors should be summed for all commodities for which there is an MRL;

\(F_i\) = food consumption value for the relevant commodity as derived from a specific hypothetical "cultural" or national diet in kg food per person per day;

\(R_i\) = the residue level in the edible portion of the commodity given in mg pesticide/kg food;

\(P_i\) = the correction factor that takes into account the reduction or increase in the residue on commercial processing, such as canning and milling;

\(C_i\) = the correction factor that takes into account the reduction or increase in the residue on preparation or cooking of the food.

To compare the estimated maximum daily intake with the ADI, the EMDI is divided by an assumed average body weight analogous to that used in the TMDI/ADI comparison.

The EMDI prediction is still an overestimate of the actual pesticide residue intake, because it does not take into account that:
— the percentage of a crop treated with a pesticide is usually far less than 100%; and
— very few of the crops treated contain residue levels as high as the MRL, the starting point of the calculation.

If the EMDI, which is an overestimation of the real intake, exceeds the ADI, a further refinement can be made in the prediction by introducing additional factors that bring the prediction closer to reality.

Estimated daily intake

Prediction of the estimated daily intake (EDI) of a pesticide residue takes into account the following factors:
— food consumption data, including that of subgroups of the population;
— known uses of the pesticide concerned;
— known residue levels;
— percentage of the commodity treated;
— quantity of contaminated home-grown/imported commodities;
— disappearance of the pesticide during storage, processing and cooking.

As this type of information is usually only available at the national level, these EDI predictions can only be done on a national basis and by those who have adequate information on food consumption, the potential use of the pesticide locally, and the nature and magnitude of food imports.

Table 2. Example of calculation of the theoretical maximum daily intake (TMDI) using maximum residue limits (MRL) and assuming an acceptable daily intake (ADI) of 0.02 mg/kg body weight

<table>
<thead>
<tr>
<th>Commodity</th>
<th>Food consumption (kg per person per day)</th>
<th>MRL (mg/kg)</th>
<th>TMDI (mg/person)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wheat</td>
<td>0.11</td>
<td>5</td>
<td>0.55</td>
</tr>
<tr>
<td>Rice</td>
<td>0.22</td>
<td>5</td>
<td>1.10</td>
</tr>
<tr>
<td>Apples</td>
<td>0.04</td>
<td>2</td>
<td>0.08</td>
</tr>
<tr>
<td>Bananas</td>
<td>0.08</td>
<td>1</td>
<td>0.08</td>
</tr>
<tr>
<td>Citrus fruits</td>
<td>0.03</td>
<td>5</td>
<td>0.15</td>
</tr>
<tr>
<td>Cabbage</td>
<td>0.10</td>
<td>0.5</td>
<td>0.05</td>
</tr>
<tr>
<td>Lettuce</td>
<td>0.02</td>
<td>0.5</td>
<td>0.01</td>
</tr>
<tr>
<td>Potatoes</td>
<td>0.40</td>
<td>0.2</td>
<td>0.08</td>
</tr>
<tr>
<td>Cattle meat</td>
<td>0.20</td>
<td>0.05*</td>
<td>—</td>
</tr>
<tr>
<td>Milk</td>
<td>0.30</td>
<td>0.01*</td>
<td>—</td>
</tr>
</tbody>
</table>

Total = 2.10 = 0.035 mg/kg body weight = 175% ADI

* At or about the limit of determination.

APPLICATION

As an illustration of the use of these guidelines, the TMDI (Table 2) and the EMDI (Table 3) values for a hypothetical pesticide have been calculated. For this

Table 3. Example of calculation of the estimated maximum daily intake (EMDI) assuming an acceptable daily intake (ADI) of 0.02 mg/kg body weight

<table>
<thead>
<tr>
<th>Commodity</th>
<th>Processed commodity</th>
<th>Food consumption (kg/person per day)</th>
<th>Residues level (mg/kg)</th>
<th>Processing factor</th>
<th>Cooking factor</th>
<th>EMDI (mg/person)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wheat</td>
<td>Bread</td>
<td>0.11</td>
<td>5</td>
<td>0.16</td>
<td>0.038</td>
<td>0.003</td>
</tr>
<tr>
<td>Rice</td>
<td>—</td>
<td>0.22</td>
<td>5</td>
<td>1</td>
<td>0.14</td>
<td>0.154</td>
</tr>
<tr>
<td>Apples</td>
<td>—</td>
<td>0.04</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0.080</td>
</tr>
<tr>
<td>Bananas</td>
<td>Edible flesh</td>
<td>0.08</td>
<td>0.05</td>
<td>1</td>
<td>1</td>
<td>0.004</td>
</tr>
<tr>
<td>Citrus fruits</td>
<td>Edible flesh</td>
<td>0.03</td>
<td>0.1</td>
<td>1</td>
<td>1</td>
<td>0.003</td>
</tr>
<tr>
<td>Cabbage</td>
<td>—</td>
<td>0.10</td>
<td>0.5</td>
<td>1</td>
<td>0.5</td>
<td>0.025</td>
</tr>
<tr>
<td>Lettuce</td>
<td>—</td>
<td>0.02</td>
<td>0.5</td>
<td>1</td>
<td>1</td>
<td>0.01</td>
</tr>
<tr>
<td>Potatoes</td>
<td>—</td>
<td>0.40</td>
<td>0.2</td>
<td>1</td>
<td>0.5</td>
<td>0.04</td>
</tr>
<tr>
<td>Cattle meat</td>
<td>—</td>
<td>0.20</td>
<td>0.05*</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Milk</td>
<td>—</td>
<td>0.30</td>
<td>0.01*</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

Total = 0.319

= 0.005 mg/kg body weight
= 25% ADI

* At or about the limit of determination.
example, an arbitrary diet was selected and the maximum residue limits applied to the listed commodities were those applicable to several pesticides in common use. It can be seen that, while the TMDI gives a figure greater than the fictional ADI (175%), the inclusion of more realistic information in the EMDI calculation brings this figure below the ADI (25%). In this case, an EDI calculation is unlikely to be required. However, noting the high proportion of the EMDI that is due to residues on rice, national authorities in areas where rice represents a greater proportion of the diet than in this example may wish to make the EDI estimation.

The correction factors for losses on processing or cooking have been derived from information given in various JMPR evaluations in which the results of appropriate studies were reported for several pesticides.

RECOMMENDATIONS

The Consultation recommended that:

1. The guidelines be used as a mechanism for the safety assessment of pesticide residue intake and for deciding on the acceptability of Codex MRLs.
2. FAO/WHO develop a hypothetical global diet to be used in TMDI calculations and several "cultural" diets suitable for EMDI calculations.
3. FAO/WHO use existing relevant data to validate the predictive models proposed.
4. FAO/WHO consider improving qualitative and quantitative definitions of regional and national diets, especially with regard to individual commodities, for use in dietary intake prediction. Special emphasis should be given to commodities of importance to developing countries.
5. TMDI and, where necessary, EMDI predictions be undertaken by FAO/WHO in collaboration with the JMPR and be published, preferably in the JMPR reports and evaluations.
6. The guidelines be used by national authorities for the prediction of dietary intake of pesticide residues.
7. FAO/WHO undertake to review the guidelines and their application when experience has been gained in their application, preferably within five years.

ACKNOWLEDGEMENT

The FAO/WHO Secretariat thanks Dr R. D. Schmitt, Office of Pesticide Programs, Environmental Protection Agency, Washington DC, USA, for his continued help through all phases in the preparation of these guidelines.

REFERENCES