Pure & Appl. Chem., Vol. 59, No. 4, pp. 611–624, 1987.
Printed in Great Britain.

INTERNATIONAL UNION OF PURE AND APPLIED CHEMISTRY

APPLIED CHEMISTRY DIVISION
COMMISSION ON PESTICIDE CHEMISTRY*

IUPAC Reports on Pesticides (22)

RECOMMENDED APPROACH TO THE APPRAISAL OF RISKS TO CONSUMERS FROM PESTICIDE RESIDUES IN CROPS AND FOOD COMMODITIES

Prepared for publication by
J. A. R. BATES[1] and S. GORBACH[2]

[1]Pesticides Registration and Surveillance Department, Ministry of Agriculture, Fisheries and Food, Harpenden, UK
[2]Hoechst AG, Analytisches Laboratorium, Frankfurt/Main, FRG

*Membership of the Commission during the preparation of this report (1983–85) was as follows:

Chairman: J. A. R. Bates (UK); *Secretary*: R. Greenhalgh (Canada); *Titular Members*: N. Aharonson (Israel); A. Ambrus (Hungary); S. Gorbach (FRG); W. Klein (FRG); *Associate Members*: J. Desmoras (France); H. O. Esser (Switzerland); L. A. Golovleva (USSR); R. J. Hemingway (UK); R. Hollingworth (USA); N. Kurihara (Japan); W. B. Neely (USA); S. Otto (FRG); T. R. Roberts (UK); J. Seiber (USA); D. B. Sharp (USA); J. W. Vonk (Netherlands); *National Representatives*: A. M. P. D'Angelo (Argentina); W. Lara (Brazil); Zhengming Li (Chinese Chemical Society); J. Kovaçicova (Czechoslovakia); N. Drescher (FRG); F. Dutka (Hungary); S. K. Mukerjee (India); P. Bracha (Israel); J. Miyamoto (Japan); C. K. Heng (Malaysia); G. W. Mason (New Zealand); A. Kotarski (Poland); N. Bărbulescu (Romania); P. C. Kearney (USA).

Correspondence on the report should be addressed to the Secretary (1985–89) of the Commission: Dr T. R. Roberts, Shell Research Ltd., Sittingbourne Research Centre, Sittingbourne, Kent ME9 8AG, UK.

Recommended approach to the appraisal of risks to consumers from pesticide residues in crops and food commodities

Abstract - In order to assess potential health problems from pesticide residues in food the extent to which dietary intakes approach or exceed an estimated no-toxicological-effect level should be determined. Retrospective intake data may be obtained from dietary studies.

The 'best estimate' of prospective intake may be made from a knowledge of the use of a pesticide, its residues on a crop at harvest and the subsequent fate of those residues, including the effects of cooking and processing. A stepwise approach which contrasts the 'best estimate' of consumer dietary intake with an estimate of theoretical maximum dietary intake is recommended to Government agencies and to the pesticide industry.

CONTENTS

1. INTRODUCTION

The appraisal of risk to consumers from pesticide residues in crops and food commodities has been practised by national pesticide regulatory authorities for at least 30 years and since 1963 there has been international guidance from the FAO/WHO Joint Meeting On Pesticide Residues (JMPR) to supplement any national decisions on the registration of pesticides. Maximum residues limits for pesticides in food commodities have been recommended by the Codex Committee on Pesticide Residues (CCPR)[1]. However, the procedures involved in national and international appraisals of consumer risk from pesticides have not yet been adequately described in a publication.

At CCPR in April 1986 a discussion paper, CX/PR 86/12, considered by the *ad hoc* Working Group on Regulatory Principles, recommended that guidelines be developed for estimating possible dietary exposure to pesticide residues.

This report considers the requirements for a pragmatic prediction of human exposure to pesticide residues as an alternative to measuring dietary intake and recommends an approach, suitable for use by Government agencies and industry in making decisions on risks to consumers from pesticide residues in food.

2. DEFINITIONS

The following three definitions are in current use by the CCPR and the JMPR.

- a maximum residue limit (MRL) is the maximum (legal) concentration of a pesticide residue resulting from the use of a pesticide according to good agricultural practice. The concentration is expressed in mg of residues per kg of food.

- a no-observed-effect level (NOEL) is that quantity of a substance in mg/kg body weight which when administered daily to a group of experimental animals demonstrates the absence of effects observed or measured at higher levels of exposure and produces no significant differences between the test group of animals and an unexposed control group of animals maintained under identical conditions.

- the acceptable daily intake (ADI) is the daily exposure level of a pesticide residue in mg/kg body weight which during the entire lifetime appears to be without appreciable risks on the basis of all the facts known at the time of the evaluation. "Without appreciable risk" is taken to mean the practical certainty that injury will not result even after daily exposure during a lifetime. It is normally derived from the NOEL by applying a safety factor.

An additional term 'the no-effect residue level in a human diet, NERL', is used in this report. It is the level of pesticide in a total human diet, in mg/kg food, which, on the basis of extrapolating the experimental data used in estimating a NOEL, should have no observable effect in man. It is developed from the NOEL (see section 5).

3. GENERAL CONSIDERATIONS OF CONSUMER EXPOSURE

It is widely and mistakenly believed that consumers may be exposed continuously to one or more pesticides in a diet. This is not so and examination of the three levels of potential exposure to each of the three elements involved (Figure 1) shows that there are only four relevant scenarios to consider in the evaluation of the exposure of consumers to pesticide residues in food, namely

- some pesticides in some food for some of the time
- some pesticides in one food for some of the time
- one pesticide in some foods for some of the time
- one pesticide in one food for some of the time.

	all	some	one/once
pesticides	0	I	I
food	0	I	I
time	0	I	0

(0 = not relevant)

FIGURE 1. Scenarios in exposure of consumers to pesticide residues.

The real exposure of consumers is best measured by studies of pesticide residues in the total diet. Such dietary monitoring is realistic and results can best be regarded as confirmation of registration predictions of acceptable residues of individual pesticides. Special individual diets or diets of special populations can be studied in detail. However, with the complexity of many diets and varied sources of food commodities and unknown pesticide treatment there is no accurate way of comprehensively predicting exposure to some pesticides in some food for some of the time.

When a single food/commodity plays an important, even vital, part of the diet of a person or community then the monitoring of this specific item for all relevant pesticides over a period of time provides valuable information on the residues contributed to the total dietary intake. But, if the foodstuff comes from a variety of sources with wholly or partly unknown pesticide treatments then an accurate prediction of intake even from a single dietary item is difficult if not impossible. Monitoring of the commodity over a period of time will indicate trends which result from changes in good agricultural practices and accompanying registration status of one or more countries.

Although monitoring and analysis will provide important information on actual intakes of individual pesticides, it is also practical to consider estimating the intake of an individual pesticide from a knowledge of the use of the pesticide on a range of foods/commodities. It is important, as in dietary monitoring, to consider <u>all</u> sources, domestic, and imported.

Intake from one pesticide in one food can be measured or predicted reasonably at the time of registration, although its importance in the total estimated intake will vary with the importance of the food in a diet.

Clearly the most satisfactory way of determining exposure of consumers to pesticide residues is to measure the residues present by the analysis of total diets. This provides the public with practical reassurance of food safety. However such analysis refers retrospectively to pesticide use and cannot be used to make decisions at the time of registration on prospective use of pesticides. In this situation estimates of consumer intake are essential to provide reassurance of adequate safety margins if the pesticide leaves residues.

A first-choice alternative to measuring the dietary intake of a pesticide is the 'best estimate' of an intake, taking into account all available data on pesticide use and the occurrence, size and the fate of pesticide residues at harvest or after post-harvest treatment. Such an estimate is the most realistic achievable but does require a considerable amount of information which is not always available although now often required by agencies responsible for the registration of pesticides.

Alternative, less realistic estimates can be based on less information as shown in figure 2.

	1	Measured dietary intake
↑	2	"best estimate"
increasingly realistic estimates	3	Intermediate estimate based on average or most frequent residues, known uses and diet factors
	4	Maximum theoretical intake based on MRLs, all registered uses and diet factors

FIGURE 2. Estimate options as alternatives to measuring dietary intakes of pesticides

The least realistic estimate is the maximum theoretical intake based on the assumptions that a pesticide is always used for all registered uses and residues always occur at the maximum observed. Such 'worst case' estimates have been repeatedly shown to be gross overestimates and can only lead to unnecessary public alarm unless handled very carefully in decision making. However their use as a coarse screening device is valuable as a means of reducing the requirement for further assessment of those pesticides for which the maximum theoretical intake falls below the level of the estimated ADI.

Intermediate estimates based on some limited relevant data may be obtained if all the data required for a best estimate is not available.

4. MRLs AND ADIs

The acceptability of a maximum residue level on a crop or commodity forms the major part of the assessment of risk to the consumer during the registration of a pesticide by national authorities. Recognising that residues approaching the maximum will occasionally occur, even if good agricultural practice is observed, the maximum residue observed must be toxicologically acceptable for the agricultural practice to be acceptable.

Many countries convert the estimated maximum residues level into a legal limit (MRL) and the enforcement of such limits can be effective as an indication that good agricultural practice has been observed. MRLs themselves do not directly define health, safety or risk levels but sensibly applied, should contribute to ensuring a supply of safe food.

In estimating maximum residue levels some countries consider, or recognise, only a limited range of agricultural practices. In consequence, a number of countries have national MRLs for a pesticide/crop which conflict with each other, giving rise to problems in international trade. The primary objective of the Codex Committee on Pesticide Residues is to develop recommended maximum residues limits (Codex MRLs) for pesticides in food or feed commodities in order to facilitate international trade and to protect the health of consumers. Thus the acceptability of Codex MRLs by national governments is also governed by the requirement that this level of a pesticide in a commodity must be "toxicologically acceptable".

In proposing the suitability of an estimated maximum residues level as an MRL the FAO/WHO Joint Meeting on Pesticide Residues (JMPR) cannot consider the specific role that a particular commodity plays in a national or local diet. It must be the responsibility of national authorities to consider the relevance of local dietary patterns and scale of use of a pesticide in local agriculture and subsequent potential residues in food commodities.

Thus national authorities face essentially the same problem in two situations in considering -

1. the acceptability of a maximum residue level of a pesticide on a food commodity during the national registration of a pesticide; and

2. the acceptability of a Codex MRL in relation to residues of the pesticide resulting from uses on other food items.

A number of countries have developed procedures and positions on these related problems but as yet there is no recommended international approach to the use of residues data in the appraisal of risk to the consumer in these situations.

Some countries have indicated at meetings of the Codex Committee on Pesticide Residues that certain Codex MRLs are unacceptable because "the intake of the pesticide might exceed the ADI" (eg CCPR ALINORM 85/24, para 115). This brings sharply into focus the major difficulty in estimating maximum residues levels from a pesticide use data base and considering the health implications of a subsequent MRL out of context. MRLs and ADIs are developed from totally separate data bases and thus do not have a direct interdependence. However the acceptability of an MRL ultimately depends on the assurance that its use in regulating good agricultural practice will not result in a risk to consumers. It is necessary to provide a 'bridge' between the toxicological properties of a compound and maximum residues levels observed and an agreed scrutiny of relevant factors is required before an MRL is accepted nationally in registration procedures or recommended internationally by the Codex Alimentarius Commission.

Food commodities may contain pesticides residues following good agricultural practice which vary in identity and level depending on nature of commodity, country of origin, occurrence of pest/disease in that country, availability of the pesticide and many other factors. Since all the commodities on which the pesticide is registered will not necessarily be treated in any one season, the concept of 'additive' residues of a pesticide is not always valid, particularly since it also assumes that a single consumer could be exposed to all the treated commodities at the same time and for a long period of time (see Figure 1).

Clearly to reject an individual MRL because "the ADI may be exceeded" is scientifically unsound. Only direct determinations of residues levels at the point of consumption can be used to demonstrate that an ADI is being exceeded. Theoretical calculations of pesticide exposure estimates can be used to predict that residue intakes will <u>not</u> exceed the ADI, since such calculations usually result in considerable overestimates of actual consumer intakes. A nationally and internationally acceptable procedure is urgently required to extend the estimation process beyond the estimation of MRLs and NOELs (and ADIs) to include an appraisal of the potential risk based on estimated residues in diets.

Such a procedure should not be complex or too sophisticated bearing in mind that there are many undetermined factors in the overall estimation process. It is important that the real problem is brought clearly into focus and that it is recognised that there are so many variables involved that a definitive solution may not be possible. All that can be achieved with the present information is a 'best estimate' of consumer risk which incorporates substantial safety factors. Care should be taken to avoid an overcautious commitment to speculative 'worst case estimate' of risk, resulting in possible over-regulation and unnecessary public alarm.

Figure 3 summarizes the data inputs and the flow of information in assessing the risk to consumers. In the absence of the data necessary for a comparison of an <u>actual</u> dietary intake with a no-effect residue level in humans in the human diet it will be necessary to compare an <u>estimate</u> of residue level in the diet with an <u>estimate</u> of no-effect levels based on animal studies, NERL.

5. ESTIMATED NO-EFFECT RESIDUE LEVEL IN HUMAN DIET (NERL)

The end-point of many toxicological studies on experimental animals is the estimation of a no-observable-effect level (NOEL) of the toxicant in the daily diet and such a level is expressed in ppm in the diet of the animal. This does not usually discuss the significance (eg reversibility) of an effect but identifies, as effectively as the data base will allow, an intake of the pesticide that has no-observable-effect on the animal

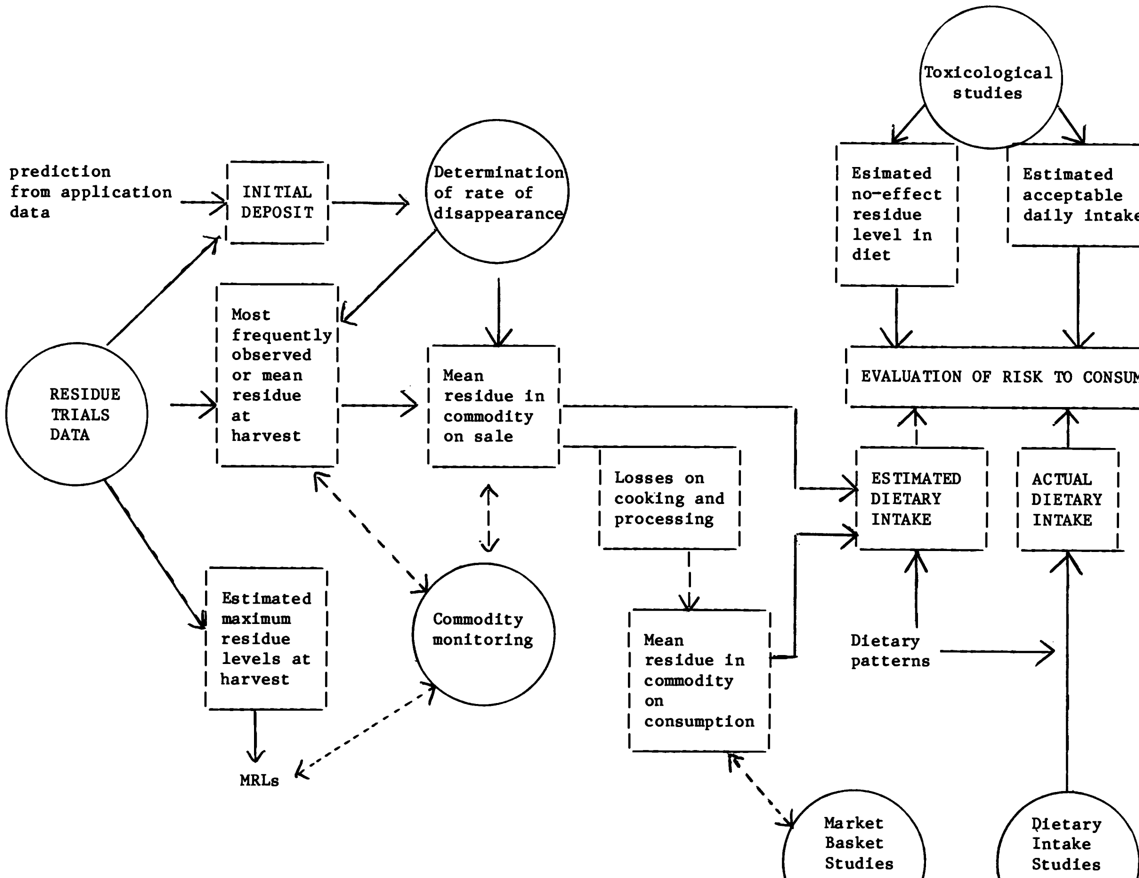

FIGURE 3. Pesticide residues - Data inputs and flow of information

tested. It may or may not include (hidden) safety factors depending on the design of the experiment, the amounts or levels of the toxicant in the diet and the interpretation of the results. Although often derived from life-span animal studies, NOELs are increasingly derived from special studies of shorter duration.

For a number of years it has been the practice of toxicologists to convert the NOEL into an acceptable daily intake (ADI) for man by the application of (arbitrary) safety factors said to allow for differences in sensitivity between animal species and human beings, the wide variations in sensitivity among humans and the small numbers of experimental animals in comparison with human populations that might be exposed to the pesticides.

'Acceptable' daily intake represents an unfortunate choice of words in the present day concern of unnecessary chemicals in human food. Many will argue that no daily dietary intake of a pesticide residue is "acceptable" but certain levels may be tolerated on certain food commodities on occasion or for a limited period of time. This is the situation with pesticide residues in food and it is quite different from the situation for food additives which are added to food in fixed and known quantities.

Unfortunately too, the 'ADI' has often been regarded as a definitive property of a pesticide and mis-used in mathematical calculations which have attempted to relate it, or fractions of it, to maximum residue levels in individual crops at harvest (MRLs). The vulnerability of the ADI when used as an quantified expression of the 'acceptability' of pesticide residues has been discussed by Paynter and Schmidt.[2]

Clearly the most satisfactory way of reassuring the consumer is to show that a level occurring occasionally in food, when compared with a level which has no-effect, demonstrates a substantial safety factor.

There are two alternative estimates of value in risk assessment starting from the experimentally determined NOEL (Figure 4). The first, via a no-effect daily intake in animals, concludes in the estimation of an ADI for man. The alternative concludes in an estimated no-effect residue level in a human diet (NERL). This is developed from the estimated experimental NOEL by assuming an average human body weight of 60 kg and an average food intake for that body weight of 1.5 kg per day. (This ratio of body weight/ food intake of 40 is maintained for a 20 kg child with a daily intake of 0.5 kg and a mature adult of 80 kg and a food intake of 2 kg/day).

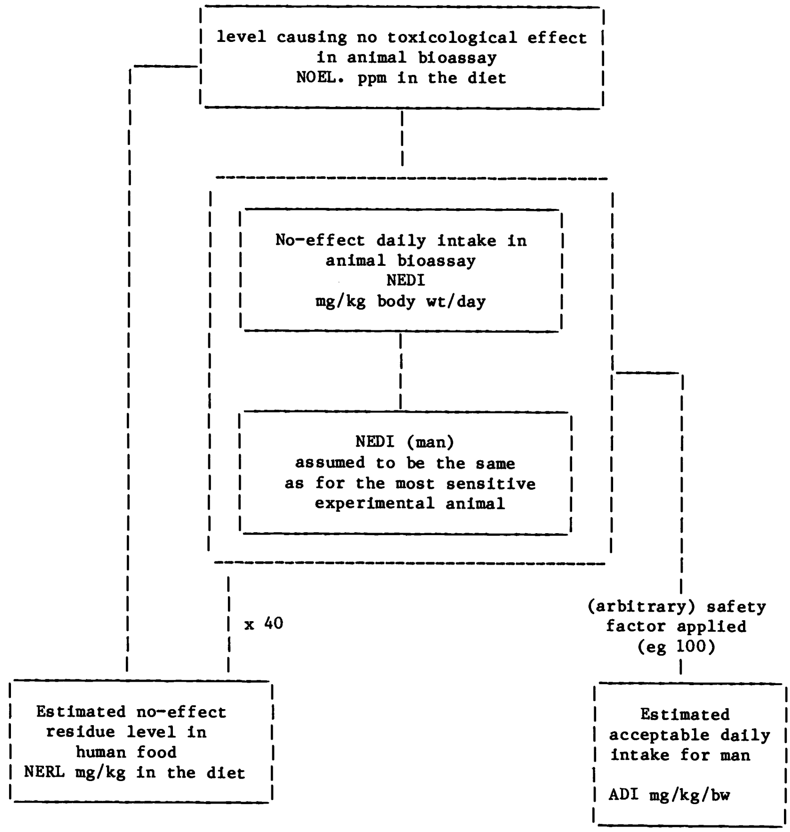

FIGURE 4. Alternative estimates from an experimental NOEL.

Thus the no-effect residue level in the human diet (NERL) is related to the no-effect daily intake from animal bioassay mg/kg body weight/day (NEDI) by the expression.

NERL = 40 x NEDI

No-effect exposure levels are often used in estimating risks to pesticide users and it is recommended that the NERL is used as a preliminary screen in judging the acceptability to consumers of the pesticide residues found in food following good agricultural practice. Table 1 lists the NERLs of over 120 widely used pesticides, based on no-effect daily intakes estimated by the FAO/WHO Joint Meeting on Pesticide Residues over a number of years. (Note: some NERLs are based on ADI x 100).

Since the no-effect residue level is derived directly from an estimated no-effect daily intake, it does not in itself, incorporate a "safety factor". Margins of safety become apparent when NERLs are compared with measured actual dietary levels of pesticides (or estimated dietary intakes).

The ADI and the NERL are both derived from the NOEL and therefore both equally depend on the quality of the NOEL. The use of the NERL to demonstrate margins of safety however enables a toxicologist to consider such margins in relation to the quality of the toxic effect used to estimate the NOEL.

6. ESTIMATION OF PESTICIDE INTAKE FROM RESIDUES IN CROPS

It is normally necessary, in the absence of information on actual dietary intake, to make an appraisal of potential risks to consumers from an estimation of dietary intake at the time of the registration of a proposed use of a pesticide. In such situations information is needed on:

1. known uses of the pesticide (not always the same as registered uses)

2. the contribution that the crop/commodity makes to the dietary pattern (diet factor)

3. the maximum residue that can be expected in the crop at harvest

4. the mean or most frequent residue in the crop at harvest

5. the distribution or partition of the residue in the crop and the fate of the residue on cooking or processing.

For the most realistic estimate of intake ('best estimate') information is required on all items above.

The estimation of the maximum theoretical intake requires least information, and is based on all registered uses and an estimate of the maximum residue level in the crop/commodity. Estimate of maximum residues levels by national registration authorities provide the best basis for estimating a maximum theoretical intake. Residues in imported commodities depend on good agricultural practice in the country of origin and a range of national MRLs or Codex MRLs is an appropriate guide to expected maximum residues if good agricultural practice is followed.

6.1 Food consumption (dietary) patterns—list of important crops

In order to estimate a dietary intake of a pesticide from residues on individual food commodities it is necessary to decide on a "diet factor" which will represent the contribution that commodity might make to the total food consumption. In view of the large variations in dietary patterns both between countries and within countries, preliminary consideration should be given to data on national average diets although the direct use of average consumption figures can be criticized for not allowing for above average food intakes. Excluding foods of animal origin (see para 6.2) and those contributing less than 0.5% to a diet, the majority of human diets are derived from no more than about 30 important agricultural crops and since the potential pesticide intake from the minor items of diet is minimal it is proposed that all estimates of intake should be based on the identifiable important food commodities only. Tables 2 and 3 list some examples of important and minor food commodities respectively. The lists are not necessarily definitive since in some countries what may be considered minor in many countries could form a significant part of a local or individual diet. Thus national authorities should compile their own definitive lists of important food commodities to be used in estimating pesticide intakes.

In view of the variability found in dietary patterns there is little significance in adopting mathematically derived averages which suggest a greater accuracy than is realistic. Thus "diet factors" could be based on numerical intervals 0.1, 0.2, 0.5, 1, 2, 5, 10 and 20%. (These numerical intervals have already been accepted as practical intervals in recommending Codex MRLs). The actual factors allocated to a particular food commodity will vary according to its importance in a national (local) diet. They should be based on average intakes from food consumption studies where these exist. In risk assessments it is important to consider sections of a population where food consumption patterns differ from the average both in total quantity and in consumption of specific items for example, infants and young children.

Experiments carried out on human energy requirements have indicated that total calorie intake of food and beverages is self limiting. Data show that the 95 percentile energy intake of an particular age-sex class never exceeds twice the average intake of the same class of people. Thus it is reasonable to apply a two-fold factor to the average total intake of food. Surveys have shown that the mean and the 95 percentile of the intake of individual foods are roughly in the ratio of 1 to 3[3].

It is proposed that the appropriate dietary factor used in estimating pesticide intakes can be derived by rounding up 2 x average food intake to the appropriate numerical intervals (that is, in effect at least 2 to 3 times the average consumption). Examples shown in Table 4 are based on average food consumption data from studies on West European and North American diets. If food consumption data are not available the dietary factors could be derived from data from other communities with recognised similar dietary patterns.

6.2 Foods of animal origin

Uptake of pesticides by animals leading to residues in human foods of animal origin can occur following either direct application of the pesticide to the animal or ingestion of feed containing residues of pesticides.

Foods of animal origin, namely, meat and meat products, eggs, milk and dairy products can contribute up to 40% of some human diets.

A study of the Codex MRLs for foods of animal origin shows that for pesticides occurring in such foods via the animal feed (resulting from agricultural uses) the maximum residues are often at or about the limit of determination. For a few pesticides, principally those used directly on animals, measurable residues do occur in foods of animal origin.

TABLE 1. Calculated no-effect residue levels (NERL) in total diet (mg/kg)

(From no-effect daily intakes estimated by JMPR assuming an average body weight of 60 kg and an average food intake of 1.5 kg/day) (Note: some NERLs are based on ADI x 100).

NERL (approximate)	
0.12	amitrole
0.4	aldrin/dieldrin, chlordimeform, endrin, phorate, triazophos
1.5	fensulfothion, methacrifos, methamidophos, vamidothion
2	acephate, carbophenothion, coumaphos, fenamiphos, heptachlor, isofenphos, monocrotophos, omethoate
4	ethion, dioxathion, fenthion, mecarbam, methiocarb, mevinphos, paraquat, phosphamidon, phoxim
8	azinphos-methyl, chlorfenvinphos, diazinon, disulfoton, dimethoate
15	amitraz, azocyclotin, bendiocarb, bromophos-ethyl, dichlorvos, diflubenzuron, edifenphos, etrimfos, fenitrothion, phenthoate, quinomethionate, thiometon
20	aldicarb, bitertanol, carbosulfan, chlorothalonil, fentin, methidathion, parathion, propineb, thiram
30	bromopropylate, cyhexatin, diquat, endosulfan, phosalone, quintozene
40	captafol, carbaryl, carbendazim, carbofuran, chlorpyrifos, chlorpyriphos-methyl, deltamethrin, dodine, fenchlorfos, imazalil, lindane, pirimiphos-methyl, prochloraz, tecnazene, triadimefon, trichlorfon
80	benomyl, chlorbenzilate, cyhalothrin, DDT, dicofol diphenylamine, fenvalerate, formothion, malathion, parathion-methyl, 2-phenylphenol, phosmet, pirimicarb, propamocarb, propoxur, triforine
130	bromophos, dichloran, fenbutatin, guazatine, metalaxyl, oxamyl, phenothrin, pyrethrins, 2,4,5-T
200	chlormequat, cypermethrin, mancozeb, maneb, permethrin, zineb
240	ethoxyquin, methoprene
320	thiophanate-methyl
400	captan, cartap, crufomate, folpet, ethiofencarb, sec-butylamine
600	propargite
800	phenothrin
20,000	maleic hydrazide

TABLE 2. Important food commodities (non-animal origin) in a number of human diets

Apples, bananas, beans, brassica leafy crops, Brussels sprouts, cabbage, carrots, cauliflower, celery, barley, maize, oats, rice, wheat, cherries, oranges, cucumbers, gooseberries, grapes, leeks, lettuce, mushrooms, onions, peaches, plums, pears, peas, potatoes, strawberries, tomatoes.

TABLE 3. Examples of food commodities which are minor ingredients in most human diets (less than 0.5% or approximately 3 kg/year)

Almonds, apricots, arichokes, asparagus, avocadoes, beetroot, blackberries, blueberries, loganberries, broccoli, melons, celeriac, chestnuts, chicory, cocoa beans, coffee beans, cranberries, currants (black, red, white), dates, dewberries, eggplants, endive, figs, garlic, gherkins, ginger, hops, horseradish, kiwifruit, kholrabi, mangoes, nectarines, olives, papaya, parsley, parsnips, pomegranates, passion fruit, pineapples, quinces, spinach, spices, raspberries, tea, watercress.

TABLE 4. Examples of diet factors allocated to important food commodities

Diet factors to be used in estimating intakes	Food commodities
20	potatoes, wheat, rice, maize
10	apples, beans, citrus fruit, tomatoes, leafy salads
5	bananas, carrots, cabbage, cucumbers, stone fruit, onions
2	Brussels sprouts, cauliflower, pears, small fruit, grapes
1	celery, cherries, mushrooms, strawberries
0.5	peaches, leeks, radishes
(0.5)	(others not mentioned above)

TABLE 5. Estimates of % crops treated in UK (selected high figures)

Crop	Year	Pesticide	Estimate of % crop treated
Brussels sprouts	1981	demeton-S-methyl	80
"	1981	carbofuran	38
Tomato (protected)	1981/82	dithiocarbamates	22
Lettuce (protected)	1981/82	pirimicarb	30
"	1981/82	vinclozolin	13
Strawberries	1980	dicofol	23
		dichlofluanid	61
		demeton-S-methyl	40

The report does not cover these situations directly although the principles used in the recommended approach can be applied equally to any items of any diet that are shown to contain pesticide residues and can be allocated a diet factor.

6.3 Maximum and mean residue levels

IUPAC Report No. 16(4) describes in some detail the quantity and quality of residues data needed for the registration of a pesticide and for estimating maximum residues levels. The procedures used in estimating maximum residues levels from data bases of variable quality are not fully described anywhere but it is clear that, as a broad thesis, an estimated maximum will include about 95% of all residue values observed in trials and sometimes as many as 98% of values. There is a very large volume of published and unpublished data on the distribution of residues on a crop/commodity either at harvest or in the food distribution chain. The data on many crops show that the mean or most frequently found residue generally does not exceed 20% of the estimated maximum residue level(6). For post-harvest treatments where deposits are less variable the mean or most frequently found residue can be up to 50% of the estimated maximum.

Although MRLs are based on estimated maximum residues levels at harvest (or equivalent) from controlled residues trials, monitoring is frequently carried out at both the farm gate following known pesticide uses and on the commodity on sale the analytical results are being compared with the MRL. Such widespread monitoring in many countries shows that the MRL for a given pesticide is exceeded in between 1-5% of the samples taken. This can be regarded as being generally supportive of the original estimate of the maximum residue on which the MRL was based. Residues much higher than on MRL can usually be considered to indicate that good agricultural practice has not been followed.

It is important to recognise that consumers are exposed only rarely and intermittently to the maximum permitted residues and, of course, residues will occur only in those crops treated. Although any generalisation will not be appropriate in all situations, with a few exceptions, it is estimated that less than 30% of any crop is treated in one year with a particular pesticide. Surveys of pesticide uses in the United Kingdom in recent years show that some widely used pesticides on certain crops exceed 30%. (Table 5). On the other hand, consumers in local situations could regularly take food commodities from a crop or supply wholly and regularly treated according to local practice.

In many situations pesticides are not used for all registered uses and it would be misleading to base a 'best estimate' of dietary intake on uses known not to occur.

6.4 Factors affecting disappearance or partitioning of any residues at harvest, including cooking and processing

Factors that often make a substantial contribution to reducing consumer intake usually apply to specific commodities and are not of general applicability. For this reason they should only be used in specific evaluations of the relevant commodities. Sometimes several factors apply to a commodity. Relevant data are not always readily available but are required for the 'best estimate' of consumer dietary intake.

1. the pesticide residue may occur in or be partitioned into a specific part or parts of a crop or commodity. MRLs apply to the whole commodity as it occurs in commerce yet residues are not always uniformly distributed, eg

   - in citrus, some pesticide residues are concentrated in the oily peel and are not transferred to the pulp or juice. In some situations the peel may be used separately for food or feed although the diet factors applicable to these 'secondary' uses will be normally much smaller.

   - in peas and some beans the normal edible part is protected by the pod which is discarded.

   - in fruiting vegetables and fruits with inedible peel such as melons, pumpkins, bananas and Kiwi fruit, the peel, which often contains most of the residue, is discarded.

2. Some crops are rarely if ever eaten raw, eg potatoes, Brussels sprouts and cereals, and information on the fate of any residue during preparation (incuding washing) and cooking is important in developing an estimate of the consumer intake of a pesticide in such a crop. Analytical data are needed on the effects of various cooking techniques, eg boiling, baking or frying, since each may have a different effect on the results.

3. Certain crops such as cereals, sugar beet and oilseeds are normally processed to produce "derived" food commodities such as flour, sugar and cottonseed oil. These processes normally lead to a reduction or even disappearance of pesticide residues. For some pesticides there can be concentration of residues in a derived food commodity and such situations require special consideration based on available data.

The emphasis in this report is on a technique to produce the 'best estimate' of pesticide intake, in the absence of data on actual dietary intake. The proposed approach makes allowances for food intakes which are higher than the average and provides for the identification of residues of concern by procedures which are feasible but not complex. In the absence of all the data necessary for a 'best estimate' intermediate estimates or even an estimate of the theoretical maximum intake can be of some value.

On rare occasions following the misuse of a pesticide, pesticide residues have occurred in amounts which have resulted in symptoms of acute toxicity being observed. These instances are exceptional and are not covered by the procedures described in this report for routine appraisal of consumer risks.

7. RECOMMENDED APPROACH FOR THE EVALUATION OF RISK TO CONSUMERS

It is proposed that the following approach will clearly identify those pesticide/commodity combinations that might cause concern in the overall examination of potential risks to consumers from agricultural commodities treated with pesticides and should be used during the registration of a pesticide. When a large safety margin is evident by estimating the theoretical maximum intake based on maximum residues from all registered uses then clearly risk to consumers is minimal. On the other hand small safety margins from the more realistic 'best estimates' taking all data into consideration could give cause for concern.

Step 1 Examine the registered/proposed uses of a pesticide. The initial marketing of a pesticide rarely indicates its full potential uses and a careful check should be maintained on the addition of further crops to an existing label. Use on imported commodities should also be considered and Codex MRLs used to indicate estimated maximum residues levels in such cases.

Step 2 Identify uses on commodities which make a significant contribution to a diet (say >0.5% or approximately 3 kg per year). Adjustments should be made for local or special diets if necessary (include imported foods). Allocate appropriate diet factor by rounding up 2 x average commodity intake to the next interval figure - 20, 10, 5, 2, or 1.

Step 3A Consider if the data are available to make a 'best estimate' of intake and contruct a best estimate intake table (figure 5).

Step 3B In absence of data for a best estimate construct a theoretical maximum dietary intake table (figure 5). If data permits, an intermediate estimate is more realistic.

Consider all registered/proposed uses of the pesticide (domestic and imported)

Construct a 'best estimate' of consumer dietary intake table using

1. Known uses
2. Diet factors
3. Mean (most frequent) residues
4. Distribution in crop and fate on cooking etc.

Construct a theoretical maximum dietary intake table using

1. all registered uses
2. Diet factors
3. MRLs

"Best Estimate" of consumer dietary intake level

Estimated theoretical maximum dietary intake level

Compare estimates with no-effect residue level

"Best estimate" margin small and unacceptable Examine all uses carefully. Review proposed agricultural practices. Reject uses if necessary.

Safety margins large (eg >100)

Theoretical maximum risk margin small. Require additional data necessary for best estimate.

ACCEPT uses of pesticide.

FIGURE 5. - Outline of the recommended approach for evaluation risk to consumers.

Step 4 Compare either (or both) estimated intakes from step 3 with the no-effect residue level (NERL). Consider safety margins in terms of the toxicological effects in the definitive toxicological study.

Step 5 DECISIONS

5.1 If (both) safety margins are reassuringly large (say >100, the uses of the pesticide are acceptable.

5.2 If the theoretical maximum safety margin is small, the data necessary for a 'best estimate' should be required.

5.3 If the 'best estimate' safety margin is unacceptably small (say less than 100) then a review of the proposed pesticide uses will be necessary. This could result in modification or even withdrawal of some uses.

Examples of estimated intake tables for thiophanate-methyl and fenitrothion based on Codex MRLs and registered uses are given in the Annex. Approximately 10% of the pesticides listed in Table 1 have estimated theoretical maximum dietary intake levels that result in safety margins less than 100. Only exceptionally is the safety margin less than 100 from the use of 'best estimates'. This is fully supported by dietary monitoring data.

REFERENCES

1. Guide to Codex Recommendations concerning pesticide residues CAC/Vol XIII Ed 1, 1983. FAO Rome.

2. O.E. Paynter and R. Schmidt. Pesticide Residues - A contribution to their interpretation, relevance and legislation. Ed H Frehse and H. Geissbühller, IUPAC 4th Int Cong of Pesticide Chemistry, Zurich 1978. p60-65

3. Guidelines for the Study of Dietary Intakes of Chemical Contaminants Joint FAO/WHO Food Contamination Monitoring Programme, WHO, Geneva, 1983.

4. IUPAC Report on Pesticides (16) 1982. Recommended Approaches to the Production and Evaluation of Data on Pesticide Residues in Food Pure & Appl. Chem. Vol 54, No. 7 p 1361-1450.

5. Pesticide Residues in Food - 1984. Report of the Joint Meeting on Pesticide Residues. FAO/WHO, Rome 1985, pages 4-8.

6. A Ambrus. Pesticide Residues - A contribution to their interpretation, relevance and legislation. Ed H Frehse and H. Geissbühler, IUPAC 4th Int Cong of Pesticide Chemistry, Zurich 1978. p1-18

7. J P Frawley and R E Duggan. Pesticide Residues - A contribution to their interpretation, relevance and legislation. Ed H Frehse and H. Geissbühler, IUPAC 4th Int Cong of Pesticide Chemistry, Zurich 1978. p82-86

References 2, 6, 7 are also published in Advances in Pesticide Science, Pergamon, 1979 part 3.

ANNEX

THEORETICAL MAXIMUM and 'BEST ESTIMATE" dietary intakes - THIOPHANATE-METHYL

Estimated no-effect residue level in the diet (NERL) = 320 mg/kg

Diet factor (average % in diet x 2 rounded up)	Important commodities in the diet	Maximum residue level in commodity (Codex MRL)	Estimated Level in the diet from commodity mg/kg Theoretical maximum	Best* estimate	Comments
20	wheat	0.1	0.02	0.02	
10	apples	5	0.5	0.1	mean residue
	beans	2	0.2	0.02	loss on cooking
	citrus	10	1	0.1	10% in pulp
	leafy salads	5	0.5	0.1	mean residue
	tomatoes	5	0.5	0.1	mean residue
5	Bananas	1	0.05	0.05	mean residue
	carrots	5	0.25	0.1	
	onions	0.1	0.005	0.005	
	stone fruit	10	0.5	0.1	mean residue
2	pears	5	0.1	0.05	
	small fruit	10	0.2	0.1	mean residue
1	celery	20	0.2	0.1	mean residue
	mushrooms	1	0.01	0.01	
	strawberries	5	0.05	0.05	
0.5	gooseberries	5	0.025	0.01	mean residue
Estimated dietary level mg/kg			4.1	1.0	

$$\text{Theoretical maximum intake safety margin} = \frac{\text{NERL}}{\text{Estimated theoretical maximum dietary level}} = \frac{320}{4.1} = 80$$

$$\text{'Best estimate' safety margin*} = \frac{\text{NERL}}{\text{Best estimate dietary level}} = \frac{320}{1.0} = 320$$

*This is an intermediate estimate since no account is taken of actual uses compared with registered uses for which Codex MRLs are available. Most commodities can be eaten fresh and no loss on cooking is assumed except for beans.

THEORETICAL MAXIMUM and 'BEST ESTIMATE" dietary intakes - FENITROTHION

Estimated no-effect residue level in the diet (NERL) = 15 mg/kg

Diet factor (average % in diet x 2 rounded up)	Important commodities in the diet	Maximum residue level in commodity (Codex MRL)	Estimated Level in the diet from commodity mg/kg Theoretical maximum	Best* estimate	Comments
20	potatoes	0.05*	0.01	0.01	
	rice	10)	2	0.2)	Based on residues
	wheat	10)		)	in wholemeal bread
				)	assuming 80% less
				)	on baking
10	apples	0.5	0.05	0.02	mean residue
	leafy salads	0.5	0.05	0.02	"
	oranges	0.2	0.02	0.01	"
	tomatoes	0.5	0.05	0.02	"
5	cabbage	0.5	0.03	0.01	"
	cucumbers	0.05*	0.003	0.003	
	onions	0.05*	0.003	0.003	
2	cauliflower	0.1	0.002	0.002	
	grapes	0.5	0.01	0.005	mean residue
1	cherries	0.5	0.005	0.005	
0.5	leeks	0.2	0.001	0.001	
	radishes	0.2	0.001	0.001	
<u>Estimated dietary level mg/kg</u>			2.3	0.32	

Theoretical maximum intake safety margin $= \dfrac{\text{NERL}}{\text{Estimated theoretical maximum dietary level}} = \dfrac{15}{2.3} = 6.5$

'Best estimate' safety margin* $= \dfrac{\text{NERL}}{\text{Best estimate dietary level}} = \dfrac{15}{0.32} = 50$

*This is an intermediate estimate since no account is taken of actual uses compared with registered uses for which Codex MRLs are available. Approximately 80% of the theoretical maximum intake is from supposed consumption of raw cereals for which the MRL is 10 mg/kg.