Notes *Benomyl* Residues arising from the use of benomyl are covered by the MRLs for carbendazim
Carbendazim MRLs cover carbendazim residues occurring as a metabolic product of benomyl or thiophanate-methyl, or from direct use of carbendazim
Thiophanate-methyl Residues arising from the use of thiophanate-methyl are covered by the MRLs for carbendazim

A major part of the residue of some pesticides is bound or conjugated, with the free residue disappearing very quickly The bound or conjugated residue is therefore a better indicator for monitoring compliance with GAP If the residue is defined as bound or conjugated there must be a clear instruction for the regulatory analyst as to how to measure it The instruction could be to extract samples with a particular solvent under specified conditions, or perhaps to begin with a hydrolysis step, etc

Example residue definition of bendiocarb

plant products unconjugated bendiocarb

animal products sum of conjugated/unconjugated bendiocarb, 2,2 dimethyl-1,3-benzodioxol-4-ol/N-hydroxymethyl-bendiocarb, expressed as bendiocarb

Fat-solubility is a property of the residue and is primarily assessed from the octanol-water partition coefficient and the partition of the residue between muscle and fat observed in metabolism and farm animal feeding studies The section in this chapter, "Physical and chemical properties" provides guidelines for deciding whether a pesticide is fat-soluble Sampling protocols for animal commodities depend on whether a residue is fat-soluble or not

The JMPR, for many years, included the qualification "fat-soluble" in the definition of the residues of fat-soluble pesticides, using the expression

"Definition of the residue [pesticide] (fat-soluble)"

The 1996 JMPR recommended that "fat-soluble" should no longer be included in the definition of the residue because "fat-soluble" is a qualification of sampling instructions and is not relevant to the dietary intake residue definition In order to avoid confusion while conveying the information that a residue is fat-soluble, the JMPR agreed that a separate sentence should indicate that the residue is fat-soluble

The definition of residues has not always been consistent with these principles, which were published in the 1995 JMPR Report Therefore, all residue definitions are re-examined during the periodic review of the compounds

An explanation of the residue definition for each compound is located in the monographs under the section, Residue Analysis

ESTIMATION OF MAXIMUM RESIDUE LEVELS

The JMPR examines the possibility of estimating maximum residue levels based on the submitted information and data, and subsequently proposes Maximum Residue Limits in commodities for pesticides used according to Good Agricultural Practice

Maximum residue levels are estimated for residues in or on the portion of the commodities to which Codex MRLs apply For dietary intake purposes the residue levels are estimated on the edible portion of the commodity See also Chapter 6, "Estimation of residue levels for calculation of dietary intake of pesticide residues "

In addition to primary and some processed food commodities, when the available information permits, the JMPR also recommends MRLs for animal feeds and food processing by-products (e g apple pomace, grape pomace) which can be used as animal feed Animal feeds are commodities of trade and therefore require Codex MRLs if pesticide uses result in detectable residues in the feed Residues in feed may also lead to detectable residues in animal tissues, milk and eggs, necessitating MRLs for animal commodities Some food commodities themselves (e g cereal grains) may be used as feedstuffs for food-producing animals

In estimating maximum residue levels, the FAO Panel takes into account all relevant information and especially the residues arising from supervised trials and the congruence of the trial conditions and the established GAP The procedure for estimating and recommending Codex MRLs may be somewhat different from that applicable at national level as Codex MRLs cover residues derived from authorized uses worldwide and therefore reflect a variety of agricultural practices and environmental conditions See also Chapter 6, "Definition of independent supervised residue trials and selection of one residue value from each trial"

An awareness of the expected variability of residues is necessary If the data truly reflect the range of conditions, application methods, seasons and cultural practices likely to be encountered commercially, then considerable variation in the resulting residue levels is expected Where copious data are available, consideration of the spread and variability of the residues helps to avoid misleading interpretations of small differences in estimates of the maximum level Where only limited data are available, the interpretation of fine differences is not valid It is not a criticism to say that the data are widely spread and variable If results have been obtained at a number of places over some years they are likely to be a better approximation to commercial practice and will be widely spread In addition to the variability of residues within a confined area which can be considered uniform regarding climate, agricultural practices, pest situation and use recommendations, there may be an even greater variation of residues among areas of widely differing conditions (e g countries in temperate, Mediterranean and tropical zones) The differences in use conditions can be so large that they result in different residue populations (see Chapter 6 section "Combining of populations of data for the calculation of STMRs")

Frequently the situation is complex even when copious data and information are available There are alternative interpretations, and judgement is required to arrive at an estimate that is realistic, practical and consistent

Although supervised residue trials are conducted according to the GAP prevailing at the time, GAP is often subsequently modified by changing the rate of application, type of formulation, method of application, number of applications and PHI Judgement is then required in order to determine whether the trial conditions are still close enough to GAP to be relevant (See also Chapter 6 section "Comparability of supervised trial conditions to GAP ")

Rate of application

The nominal rate of application in a trial would normally be considered still consistent with GAP when it is within approximately ± 30% of the GAP rate, which includes the probable variation in commercial practice When little or no residue is present, data from higher application rates may be important

Formulations

In many situations different formulations would cause no more variation than other factors, and data derived with different formulations would be considered comparable Experience from trials demonstrates that EC, WP and SC formulations (see Appendix III) lead to similar residues On the other hand, controlled-release formulations would be expected to lead to more persistent residues and would not be comparable to others

Application method and number

The method of application can be quite influential on residue levels For example, directed application is not comparable to cover spray, and aerial application may not be comparable to ground application

For a non-persistent pesticide the number of applications is unlikely to influence residue levels For a persistent pesticide the number of applications would be expected to influence residue levels The nature of the crop should also be considered Where the interval between the flower and the harvest of the resulting fruit is only a few days, e g summer squash, residues of a non-systemic pesticide applied before flowering would be expected to be low and the number of applications should have little influence on the residue level

Pre-harvest interval

The pre-harvest interval usually, but not always, influences residue levels (See Chapter 6 section "Comparability of supervised trial conditions to GAP")

Non-detectable residues

Some pesticide uses, such as seed treatments and pre-emergence herbicide treatments, usually lead to non-detectable residues in the final harvested crop, but when many results are provided residues may be detected in occasional samples While residues resulting from use according to GAP are most likely to be undetectable, the occasional detectable residues should not be ignored when a maximum residue level is estimated Phorate on potatoes and residues arising from the pre-planting application of glyphosate are two examples

Climate

Greater certainty that the climatic conditions are properly reflected in the supervised trials is afforded when the trials are carried out in a country with established GAP Trials conducted in other countries with similar climatic conditions may be acceptable on a case-by-case basis An assessment of those conditions is difficult, and a critical evaluation is needed as only some difference in conditions, such as temperature or intensity of sunlight, may be of great importance for the persistence of many pesticides and consequently for the residue level

Crop description

The trials should be carried out with the same crops as those specified in the national GAPs The proper description of the crops used in the supervised trials is important for deciding if crops referred to in GAP information are in accordance with those for which trials have been carried out Codex Classifications should be used for describing harvested commodities A crop description such as "beans" is difficult to interpret because of the wide variety of beans grown A more specific description is needed Foliar application to head lettuce and leaf lettuce may produce different residue levels, so it may not be possible to use trials for a crop described as "lettuce"

Crop groups such as leafy vegetables, cole crops and grain legumes on national labels may not have precisely the same meaning as the Codex commodity groups It is necessary to check the crops included in a national label crop grouping

Commodity of trade and edible portion

Codex establishes MRLs on commodities as they move in trade to enable the control of compliance with and enforcement of GAP Consequently, the maximum residue levels are estimated on a whole commodity basis (see Appendix VI) as far as practical

In addition to residues in or on the whole commodity, the JMPR is also interested in residues in the edible part of the crop Residues of systemic pesticides may be expected to be present in all parts of the crop, while residues of non-systemic pesticides are not always present or may be present in minor quantities in the edible part of a crop For each pesticide, information on the distribution between edible and non-edible parts should be available to the JMPR from supervised trials or special experiments, e g measurement of weights and residue levels for edible portion and peel for fruits such as melons and citrus This information is also essential for deciding on the toxicological acceptability of the dietary intake of residues on or in food commodities For example, MRLs are established for whole bananas including the inedible peel Some MRLs may appear to be unacceptably high based on residues on the whole commodity However, information that residues on edible portion are practically non-detectable often alleviates that concern Another example is oranges where usually most residues are present in the peel, especially for non-systemic pesticides

Residue data populations

When estimating maximum residue levels, the FAO Panel examines all residue data arising from supervised trials supporting or reflecting the reported GAPs Firstly the uniformity or continuity of residue population reflecting GAPs is considered When there is a large gap in residue values, inferred either from the coefficient of variation of residues in composite samples or other appropriate statistical methods, the presence of different populations may be suspected (see also Chapter 6 section "Combining of populations of data for the calculation of STMRs") The residue data and trial conditions need more stringent analysis before the maximum residue level can be estimated The maximum residue level estimation is based either on all approved uses or on only those which lead to the highest residues In each case, a sufficient number of trials (residue data) reflecting a particular use should be available to enable the estimation of a maximum residue level It follows that, in the case of suspected multiple residue populations, a few data indicating the high population may not be sufficient to estimate a maximum residue level reflecting that population (and use pattern), and the FAO Panel may estimate a maximum residue level reflecting only those uses for which sufficient residue data are available On the other hand, it is not possible to reconsider and reduce a

previous estimate based on a few new trial data, unless the GAP on which the old recommendation was based has been changed in the meantime or the original trials on which the MRL were estimated are now considered inadequate

The maximum residue levels are usually estimated taking into account the spread of residues within the selected set of trials Although the JMPR may use statistical tools, it has not routinely adopted standard statistical methods There are several reasons for this One is the lack of internationally accepted standards for such an approach A more operational reason is the nature and quality of the data usually available (The number of trials is generally too low to apply statistical methods to render a given probability and confidence level to the estimated limits) The form in which the residue data are provided often does not lend itself to statistical analysis, while treatments which involve more subjective judgements, such as taking into account data from similar crops or the consideration of historical data, are difficult to fit into a statistical approach Whenever the data package is suitable, the FAO Panel may also take into account statistical considerations (e g in the 1996 Evaluations, aldicarb residues in potato and in the 2000 Evaluations, EMRL recommendations for DDT residues in meat)

Specific considerations in estimating maximum residue levels

Fruits and vegetables

All the previously described general considerations apply for estimating maximum residue levels in fruits and vegetables Applications on fruit and vegetables may take place at any stage of the developments of the plants and in the soil before and after sowing, and the residue levels are highly dependent on the treatment

The pre-harvest interval (PHI) is usually an important component of GAP that has a strong influence on the resulting residues It is especially important for fruit and vegetables for foliar application close to harvest See Chapter 6 section "Comparability of supervised trial conditions to GAP" for the latitude of acceptable intervals around the PHI

The whole fruit residue level may sometimes be derived from residue data obtained separately for peel and pulp if the weights of peel and pulp are available

Grains and seeds

The MRL for seeds or grains applies to the whole commodity It is important for the JMPR to be able to distinguish between the forms in which the commodities are present and to describe the raw and processed commodities according to the Codex Commodity Classification, as some grains and seeds are still in the husks and others are without husk The residue levels are usually considerably different for those sorts of commodities Sometimes residues are reported in polished rice The estimation of the maximum residue levels should be based on residues in commodities which may move in international trade

The milling of grains and seeds produces processed commodities such as polished rice, bran and flour

Animal products

The results of farm animal feeding studies and residues in animal feed and processing by-products of food serve as a primary source of information for estimating maximum residue levels (See also Chapter 3 section "Information and data from farm animal feeding and

external animal treatment studies" and Chapter 6 section "Estimation of maximum residue levels and STMR values for commodities of animal origin) In addition, animal metabolism studies may give useful information

Uptake of pesticides by animals can lead to residues in animal products following either direct application of the pesticide to the animal or its housing, or ingestion of feed containing pesticide residues

Animal feeds with residues of pesticides may derive from

- crops produced mainly for animal feed (e g pasture, straw, forage),
- crops produced mainly for human food which are fed to animals (e g cereal grains),
- waste from crops grown primarily for human food (e g skins, pulp, stems, stubble, trash),
- animal feeds that have not themselves been treated, but in which environmental contaminants occur, for example, from crops or pastures grown in DDT contaminated soil

When the animals are fed, the potential for dilution of feed residues is considerable Not all producers of the primary crop are likely to have used the same pesticide simultaneously, and the pesticides used are not always used at their highest permitted use rates or at the nearest time to harvest Consequently, the calculations based on maximum intake and MRL values give an unrealistic overestimate of residue levels in animal products

When residues arise from direct application to animals the resulting MRLs should relate to the species stated on the registered label and the animal studies provided, i e if the label use applies to sheep only, the MRLs should apply to sheep commodities (meat, offal) only

When residues in animal products arise from residues in feeds, the options are to recommend MRLs for cattle commodities only, assuming cattle feeding studies are available, or to extrapolate to group MRLs The group could be mammals other than marine mammals, or cattle, goats, horses, pigs and sheep, or cattle, pigs and sheep

The information from the animal metabolism and feeding studies and the likely levels of residues should support the decision to extrapolate Extrapolation is encouraged to the group when there is no reason to expect higher residues in other animals than in cattle

The same type of argument applies to the other farm animal products in extrapolating from studies on chickens to poultry

Meat

For pesticides which are not fat-soluble, maximum residue levels are estimated for muscle tissue and recommended for use as MRLs for meat

For fat-soluble pesticides, maximum residue levels are estimated on residues in trimmable fat expressed on the lipid content For those commodities (e g rabbit meat) where the adhering fat is insufficient to provide a suitable sample, the whole meat commodity (without bone) is analysed and the maximum residue level is estimated on the whole commodity basis

Edible offals

The maximum residue levels are estimated on a whole commodity basis

Milk and milk products

For milk it is known that the fat content varies widely among different breeds of dairy cattle In addition, there are a large number of milk products with varying fat content and it would be difficult to propose separate MRLs for each of them It was therefore originally decided to estimate MRLs for fat-soluble compounds for milk and milk products on a fat basis, i e the residue levels expressed as if wholly contained in the extracted fat

Currently the JMPR follows the CCPR convention of expressing the MRL for fat-soluble compounds in milk on a calculated whole product basis, assuming all milks to contain 4% fat (The residue is calculated for the whole product based on the residue measured in the fat) For compounds which are not fat-soluble, the analytical portion for enforcement purposes is whole milk and MRLs are expressed on a whole milk basis

Details of expressing residues in milk and milk products are given in this chapter section "Expression of maximum residue limits "

Eggs

For eggs, the maximum residue level is estimated on the whole commodity after removal of the shell

Estimation of group maximum residue levels

The establishment of commodity group MRLs as opposed to MRLs for individual commodities has long been considered an acceptable procedure at both the national and international levels The use of the approach is recognition that economics may not justify residue trials on all of the individual crops in a group It also follows naturally in national registration systems where the registered use is on a crop group such as citrus In principle the approach recognizes that adequate data for the major crops of a group may be sufficient to estimate maximum residue levels for the whole group

Some pesticides behave differently in different circumstances Consequently, it is not possible to define precisely those commodities on which trials will always provide data that can lead to a group MRL If the "highest residue" situation can be identified, however, the relevant data can be extrapolated to other crops with confidence An acceptable example is extrapolation of residue data from gherkins to cucumber, however, the converse is not possible due to the higher residues that can be expected in gherkins as a consequence of their slower growth rate and the difference in weight/surface ratio Extrapolation requires a detailed knowledge of agricultural practices and growth patterns In view of the large differences in texture, shape, growth habits, rate of growth and seasonal cultivation and the significant role played by the surface/weight ratio, the JMPR has emphasized that decisions to extrapolate should be made on a case-by-case basis when adequate relevant information is available

The JMPR approaches the issue of group or individual MRLs on a case-by-case basis Many factors can affect a decision on whether or not to propose a group MRL and, in addition, there is the lack of international consensus on criteria These considerations have prevented the

JMPR from developing specific guidance for estimating group MRLs that might be applied at the international level in all situations

Although such specific guidance is not available, the following general principles and observations reflect the current views of the JMPR on estimating group MRLs

(a) The JMPR continues to rely on the Codex Classification of Foods and Feeds as the primary basis for recommending MRLs for individual or grouped commodities

(b) Generally the JMPR now refrains from estimating maximum residue levels for large Codex 'classes' of foods or feeds such as fruits, vegetables, grasses, nuts and seeds, herbs and spices, or mammalian products Residue data and approved uses are usually more likely to refer to smaller Codex "groups" such as pome fruits, citrus fruits, root and tuber vegetables, pulses, cereal grains, cucurbit fruiting vegetables, milks, meat of cattle, pigs and sheep, etc As well as being more likely to be justified by the available data on residues and information on GAP, this is judged to be more in line with national approaches and affords more accurate estimates of dietary intake

(c) When adequate residue data are available for only a few primary commodities in a food group, separate MRLs should generally be recommended for each commodity on which the data are considered adequate

(d) In some cases the JMPR may, in the absence of sufficient data for one commodity, use data from a similar crop for which GAP is similar to support estimates of maximum residue levels (e g pears and apples or broccoli and cauliflower)

(e) If other considerations permit, data on residues in all or most of the major commodities with the potential for high residues within a group may allow estimates of maximum residue levels to be extrapolated to minor crops in the group However if the variability of the residue levels is too great, even though data on the major crops within the group are available, a group limit cannot be established

(f) When residue levels in a number of commodities in a group vary widely, separate recommendations should be made for each commodity A limit for a group "except one or more commodities" which are known to deviate from the norm may be justified (e g citrus fruits, except mandarins), in such cases separate MRLs should be estimated for the exceptional commodities

(g) In order for a group limit to be proposed, not only must residue levels in the major commodities in the group not be too different, but the physical nature and other characteristics of the crops that might influence residue levels, as well as cultural practices and GAP for the individual commodities, must also be taken into account

(h) Generally, residue data for a crop growing quickly in summer cannot be extrapolated to the same or related crops growing slowly under less favourable conditions (e g from summer to winter squash)

(i) In establishing group MRLs, detailed knowledge of the metabolism or mechanism of disappearance of a pesticide in one or more crops must be taken into account

(j) Group MRLs recommended by the JMPR that generally appear to be acceptable include those for cereal grains (based on data for maize, wheat, barley, oats and rice without specific data on millet, rye or sorghum), pome fruit, based on apples and pears, extrapolated to quinces, stone fruits, poultry meat, milks; meat from mammals other than marine mammals, and oilseed

(k) A group MRL is generally preferred in the case of citrus fruits, but care must be used in estimating a maximum level for the group Large variations in fruit size and in the ratio of peel to pulp need to be considered, together with the propensity for residues of many pesticides to concentrate in the peel Data on major members of the group are especially important

More Codex limits have been established for citrus fruits as a group (41 pesticides) than for individual citrus fruits (12 pesticides) lemons (2 pesticides), lemons and limes (1), mandarins (5), sweet and sour oranges (10), sweet oranges (1), shaddocks or pomelos (1), and grapefruit (2)

(l) All else being equal, data may sometimes be extrapolated from a crop picked when immature but which grows quickly to maturity, to a closely related species with a lower surface area/weight ratio Thus, because of dilution by crop growth, estimated maximum residue levels can be extrapolated from gherkins to cucumbers, but not vice versa

(m) Individual MRLs can be extrapolated more readily to groups when there is no expectation that terminal residues will occur and when this is supported by studies of metabolism Examples are early treatments, seed treatments and herbicide treatments in orchard crops

While the JMPR generally adheres to these principles on a case-by-case basis, it recognizes certain difficulties or limitations in the acceptance of group limits at the international level A primary weakness is the lack of formal criteria or an agreed mechanism to determine the members of a group for which data are needed before a group MRL can be established One approach that is sometimes used effectively at the national level is to identify commodities of a group (often botanical) that represent both major crops within the group and those most likely to contain the highest residues The factors used to determine whether a crop is a major or representative member of the group include its dietary significance as a food or feed

The premise of this approach is that if data are available for representative crops, and if GAP and cultural practices among the individual members are similar, the residue levels will not vary widely and a maximum residue level can be estimated that will suffice for other members of the group for which no data are available As noted earlier, this approach constitutes the use of common sense and is more or less dictated by the economics of data generation and evaluation

While the JMPR recognizes real advantages in this approach, there is unfortunately no consensus at the international level on the selection of representative commodities for estimating maximum residue levels for groups Similarly, while the JMPR bases its recommendations on the Codex Classification of Foods and Feeds, this classification has not been fully adopted at the national level in most countries

Until there is more international agreement in this area, the JMPR will continue to make judgements on a case-by-case basis, using the general policy summarized above or as it may

be subsequently amended The recommendations of a workshop[7] are currently being considered and elaborated under the auspices of the OECD Pesticide Working Group

Extrapolation of residue data to minor crops

Decisions to extrapolate are on a case-by-case basis when adequate relevant information is available Adequate information includes information on GAP for the relevant crops, a reference to the residue data used to support the original MRL, and an explanation of the logic for the extrapolation

The previous section, "Estimation of group maximum residue levels," explains the estimation of group maximum residue levels and gives examples and limitations Adequate data for the major crops of a group may be sufficient to estimate maximum residue levels for the whole group, including the minor crops of that group

Extrapolation from a major to a minor crop is possible if

- the use pattern on the minor crop matches the use pattern on the major crop, and
- the growth habits and the cultural practices of the minor and major crops are similar

See also Chapter 3 section, "Data required for extrapolation to minor crops"

ESTIMATION OF EXTRANEOUS MAXIMUM RESIDUE LEVELS

Chemicals for which EMRLs (extraneous maximum residue limits) are most likely to be needed are those which have been widely used as pesticides, are persistent in the environment for a relatively long period after uses have been discontinued and are expected to occur in foods or feeds at levels of sufficient concern to warrant monitoring

Predictions of persistence in the environment (and the potential for uptake by food or feed crops) can often be based on a combination of data sources normally available for chemicals previously approved as pesticides These may include information on their physical and chemical properties, metabolism studies, data on supervised field trials, data on environmental fate, rotational crop data, the known persistence of similar chemicals, and especially from monitoring data

All relevant and geographically representative monitoring data (including nil-residue results) are required to make reasonable estimates to cover international trade Better extraneous maximum residue level estimates, taking into account trade concerns, can be made when more extensive data are available However, typically data are available from only three or four (usually developed) countries at the most By the nature of national monitoring, data are usually received primarily on those commodities in which residues have been found at the national level and which have the potential to create trade difficulties

The JMPR attempts to take into account a number of factors in estimating an extraneous maximum residue level These include the amount of data, the relative importance of the

[7] Harris, C and Pim, J 1999 Minimum data requirements for establishing maximum residue limits (MRLs) including import tolerances Recommendations from the Scientific Workshop held at the Pesticides Safety Directorate, York, UK on 6-8 September 1999 European Commission Document 2734/SANCO/99

commodity in international trade, the potential for trade difficulties or accounts thereof, the frequency of positive results, a knowledge of the propensity of a particular crop to take up residues (e g the uptake of DDT by carrots), historical monitoring data (e g previous monographs), and the level and frequency of residues in similar crops, especially those in the same crop group In some cases the estimate has turned out to be the highest level reported, especially if a relatively good database is available and the spread of results is reasonably narrow

In recent years there have been cases where the extraneous maximum residue level was estimated below the highest residue found, especially if the higher values occur infrequently For example, the 1993 JMPR recommended an EMRL of 0 2 mg/kg for DDT in carrots, although 2 of 4 imported samples reported from one country were 0 4 and 0 5 mg/kg The JMPR took into account that only 2 of over 800 imported samples exceeded 0 2 mg/kg This limit covers > 99% of the residue population with 99% confidence A similar approach was taken for DDT in the fat of meat by the 1996 JMPR This approach also recognizes that residues gradually decline and that monitoring data are often somewhat out-of-date by the time they reach the JMPR It is more likely to be used when the higher residues occur infrequently

In the context of EMRLs, the JMPR does not consider extreme values to be outliers in a statistical sense, because high residue levels are usually not true statistical outliers but values on one tail of a large distribution The challenge is to decide when it is reasonable to discard those values in order to reflect the expected gradual decline in the levels of chemicals that are typically subject to EMRL recommendations, while not creating unnecessary barriers to trade

Generally, the JMPR considers that the databases needed for estimating extraneous maximum residue levels should be substantial because the EMRL data are very far from a normal distribution (Note that it is difficult to compare the database required for EMRLs and MRLs because the nature of the data is quite different – supervised trials are used for estimating MRLs whereas monitoring data are used for estimating EMRLs) For example, samples from 598 randomly selected animals are needed to ensure that the estimated EMRLs cover 99 5% of a population, allowing a 0 5% violation rate with 95% confidence (Codex Alimentarius, Vol II, 2nd Ed , p 372) On the other hand, if a country had only 100 random samples analysed with a 10% violation rate this is quite significant, despite the small number of samples

As EMRL databases are derived from the random monitoring of different populations, the JMPR does not normally consider a 'world" population of data, but gives independent consideration to different populations, e g of different geographical regions or of different animals, before deciding which data populations might be combined Therefore, all relevant monitoring data should be submitted regardless of the number of samples analysed

The JMPR compares data distribution in terms of the likely percentages of violations that might occur if a given EMRL is proposed Since there is no internationally agreed level of acceptable violation rate, the JMPR recommends EMRLs based on the available data The 2000 JMPR, in the evaluation of DDT in meat, estimated the residue levels in fat that related to violation rates of 0 1, 0 2 and 0 5% The compromise among an acceptable violation rate, recommended EMRL and the potential for trade disruption are not scientific matters to be decided by JMPR

It is to be expected that there will be a gradual reduction or elimination of residues of the chemicals for which EMRLs have been proposed The rate will depend on a number of factors, including the nature of the chemical, the crop, the location and environmental conditions

The JMPR intends to continue lowering the EMRLs as the results of monitoring permit The aim of lowering EMRLs is to discourage unauthorized uses which higher levels might accommodate, and it is hoped to encourage those who might not otherwise submit data to do so

Because residues gradually decrease, the JMPR recommends reassessment of EMRLs about every 5 years Eventually, the data may indicate that there is no longer a need to monitor the chemical This view would be based on the conclusion that there is no longer a potential for significant disruption of trade and that the incidence or level of residues is no longer a significant health concern

Although the JMPR does not use targeted monitoring data for estimating extraneous maximum residue levels, it agrees that follow-up studies are important when high residues are found in random monitoring to give a clearer view of the significance of the high levels If properly conducted, such studies may indicate whether or not the higher residues resulted from intentional unauthorized uses and may allow the identification of areas in which production should be limited or where residue reduction strategies should be implemented

EXPRESSION OF MAXIMUM RESIDUE LIMITS (MRLs)

The estimated maximum residue levels and recommended residue limits are expressed in mg residue (as defined)/kg commodity The portion of commodity to which Codex MRLs apply is given in Codex Alimentarius Vol 2 (extracted in Appendix VI)

The residues are expressed on fresh-weight basis or as they enter international trade (as received by the laboratory) in most commodities, with the exception of animal feeds Because of the great variation of their moisture content, MRLs for animal feeds are recommended on a dry-weight basis This implies that the commodity is analysed for pesticide residues as received, that the moisture content of the sample is determined (preferably) by a standard method recommended for use on that commodity, and that the residue content is then calculated as if it were wholly contained in the dry matter

If it is not clear in animal feed residue data submissions whether residues are expressed on dry weight, or the moisture content of the feed is not reported, the data may not be suitable for estimating maximum residue levels Alternatively, if residues are expressed on fresh weight, default percentage dry matter values may be used to change the residue values to expression on dry weight (Appendix IX)

For animal products there are certain special cases which need to be mentioned

For meat and fat-soluble pesticides (see also this Chapter section, "Physical and chemical properties" and Chapter 3 section, "Nature of fat samples in studies on fat-soluble compounds") the residue limits for meat are expressed on the fat (the residue content in trimmable fat or fat tissue expressed on the lipid content) which is indicated in brackets (fat) after the residue value For those commodities where the adhering fat is insufficient to provide

a suitable sample, the whole meat commodity (without bone) is analysed and the MRL applies to the whole commodity

For all other pesticides the MRLs apply to the whole commodity as it moves in trade

The MRLs and EMRLs for fat-soluble pesticide residues in milk and milk products are expressed on a calculated whole product basis assuming all milks to contain 4% fat Milk products with a fat content of 2% or more are expressed on a fat basis The MRL would be 25 times the MRL for milk, i e the same value as if expressed on the fat of milk The MRL for milk products with a fat content lower than 2% are considered to be half the value for milk and are expressed on a whole product basis

Milk MRLs for fat-soluble pesticides are indicated by the letter "F"

Examples for recommended MRLs (mg/kg) for diazinon –

MO 0098	Kidney of cattle, pigs and sheep	0 03
MM 0097	Meat of cattle, pigs and sheep	2 (fat)
ML 0106	Milks	0 02 F

For compounds that are not fat-soluble, MRLs are expressed on the whole milk

MRLs based on direct animal treatment are footnoted "the MRL accommodates external animal treatment"

MRLs reflecting special uses or conditions are also distinguished by letters after the limit Currently the following cases are distinguished by the letters indicated below

E The MRL is based on extraneous residues
Po The MRL accommodates post-harvest treatment of the commodity
PoP The MRL for the processed commodity accommodates post-harvest treatment of the primary commodity
T The MRL or EMRL is temporary, irrespective of the status of the ADI, until required information has been provided and evaluated

For the numerical expression of the limits, the following scale was adopted in 2001 0 01, 0 02, 0 03, 0 05, 0 07, 0 1, 0 2, 0 3, 0 5, 0 7, 1, 2, 3, 5, 7, 10, 15, 20, 25, 30, 40, and 50 mg/kg Other values may be used as necessary

In general, it has been shown that the expected minimum coefficient of variation of residue results of supervised trials is around 30-40%[8] Therefore, MRLs below 10 mg/kg should be expressed to only one significant figure to reflect the inevitable variation of analytical results, incorporating the uncertainty of sampling, sample preparation and analysis

Expression of MRLs at or about the LOQ

The LOQ is the lowest concentration of a compound that can be determined in a commodity with an acceptable degree of certainty (See Appendix II "Glossary of terms")

[8] Ambrus, A 1996a Estimation of Uncertainty of Sampling for Analysis of Pesticide Residues J Environ Sci Health B31 435-442

The JMPR recognizes the difficulties that may arise in regulatory laboratories analysing low levels of residues in samples of unknown origin, and so usually estimates an LOQ which is achievable under those conditions It is this figure that is proposed as a maximum residue limit "at or about the LOQ" These limits are indicated with an asterisk (*) after the numerical value (e g 0 02*) This limit is often referred to as a "practical LOQ" to distinguish it from the LOQs reported in supervised trials

An MRL so identified does not always necessarily imply that residues of the pesticides do not occur in that commodity The application of a more sensitive or specific method may reveal detectable residues in some commodities as shown, e g in Tables 14 and 26 of the 1995 monograph on quintozene

In many instances the use of a pesticide according to GAP results in a residue level in crops or commodities that is too low to be measurable by available analytical methods Setting and enforcing MRLs for residues occurring at or about the LOQ of analytical procedures may require different approaches depending on the composition and definition of the residues It is emphasized that all available relevant information should be carefully considered to ensure that an MRL established at a level equivalent to a practical LOQ of the individual residue components will fully accommodate the levels of these components which could occur in commodities following treatment according to GAP

As in cases of detectable residues, the definition of residues at or about the LOQ may also include a single residue component (e g fenpropimorph in sugar beet) or several residues components (e g aldicarb, its sulphoxide and its sulphone expressed as aldicarb in peanut oil, bentazone, 6-hydroxy bentazone and 8-hydroxy bentazone expressed as bentazone in soya bean, and fenthion, its oxygen analogue and their sulphoxides and sulphones expressed as fenthion in potato)

In cases where several metabolites are included in the definition of the residue two basic situations can be distinguished

(1) The residue components are or may be converted to a single compound or analyte by the analytical method (e g fenthion) The total residue is measured as a single compound and expressed as the parent compound (i e fenthion oxygen analogue sulphone is measured and expressed as fenthion) The MRL is set and enforced on the basis of the total measured residue After the conversion of all the residue components a single compound is determined, the MRL can be simply enforced either at or above the LOQ This situation is similar to other cases where the residue is defined as a single compound

(2) The residue components are determined separately by the method The concentrations of measurable residues are adjusted for molecular weight and summed, and their sum is used for estimating the maximum residue level

The problem is best illustrated with an example The residues of bentazone in plant commodities are defined as the sum of bentazone, 6-hydroxybentazone and 8-hydroxybentazone, expressed as bentazone The LOQs reported in supervised trials for each of the three components were generally 0 02 mg/kg, but the practical LOQs were regarded as 0 05 mg/kg for regulatory purposes If an MRL for bentazone was set as the sum of the practical LOQs of the three components of the residue, it would have to be established at 0 2 mg/kg (3 times the practical limit of determination to incorporate all three residue

components) In this case, any one of the residue components could be present at 0 2 mg/kg, or all of the three at 0 06 mg/kg, without exceeding the MRL Consequently, individual residue components could be respectively 10 and 3 times those which should arise from the recommended use of the compound but would be within the MRL Similarly, if the sum of the LOQs achieved in the supervised trials was considered, an MRL of 0 1 mg/kg would be needed, which would still allow 5 times the residue that would arise from treatments complying with GAP

The 1995 JMPR concluded that when residues are undetectable in a commodity an MRL based on the sum of the LOQs of the individual residue components is not appropriate for enforcement purposes

The JMPR considered some of the situations which occur under practical conditions and used the examples to explore the possible actions in order to facilitate the elaboration of an internationally acceptable procedure

From the regulatory laboratory perspective the best option is to choose a simple enforcement residue definition, i e a single component if possible Standards of the single component should be readily available and not excessively expensive

RECOMMENDATIONS FOR MAXIMUM RESIDUE LIMITS

The JMPR recommends to the CCPR that the estimated maximum residue levels be used as MRLs if the risk assessment process demonstrates that consumption of the relevant foods does not result in dietary intakes of residues exceeding the ADI or acute RfD (see Chapter 7, "Estimating dietary intake of pesticide residues")

In those cases where a full ADI could not be estimated or the previously estimated ADI has to be withdrawn, the JMPR does not recommend MRLs If an ADI is withdrawn, existing MRLs may be converted to Temporary MRLs pending review

Recommendation of temporary MRLs

A temporary maximum residue limit is a maximum residue limit for a specified limited period, which is clearly related to required information

As a general policy, TMRLs will not be introduced for a new compound, a compound in the periodic review programme or when there is no established GAP

Temporary MRLs may be recommended when some information, which is still lacking, is unlikely to affect the validity of the estimated maximum residue level and there is a clear commitment that the information will be available by a specified date

The JMPR may recommend a TMRL in some special circumstances on a case-by-case basis, for example

- The JMPR is informed that experiments are in progress and data from residue or processing trials will be available for a specified meeting in the future
- Immediate withdrawal of an MRL may be too disruptive if insufficient opportunity has been given for comment and data submission

The JMPR may also recommend conversion of an MRL to a TMRL when there is a significant change in GAP which would affect residue levels The JMPR would require complete information to be supplied by a specified date

TMRLs for specific commodities may be used to replace group commodity MRLs or "fruit" and "vegetable" MRLs where residue trials on those specific commodities are known to be in progress Such a situation has arisen when a group MRL has been scheduled for review and residue data are being developed for some commodities in the group It would not be correct to withdraw the group MRL without introducing some recognition of the continued validity of maximum residue levels estimated for those commodities while the work is in progress In the absence of other information, the TMRLs would be recommended at the same level as the group MRL to be withdrawn

Each recommended TMRL will be directly related to an item of required information Each such item will have a due date specified The information is to be available for review at the Joint Meeting in the year specified If the required information is not supplied by the due date, the TMRL will be withdrawn

The FAO Panel applies the same principles for estimation of maximum residue levels for TMRLs as those followed for estimating maximum residue levels for recommending MRLs

Guideline Levels

A Guideline Level is the maximum concentration of a pesticide residue occurring after use of the pesticide according to Good Agricultural Practice, but for which no Acceptable Daily Intake has been established or it has been withdrawn by the JMPR There may still be a need to inform regulatory authorities about the residue levels to be expected in food items when these pesticides are used in accordance with Good Agricultural Practice

Over a number of years the Codex Committee established a list of Guideline Levels for pesticides These Guideline Levels had not been submitted to the Commission for adoption, but were used for the internal reference of the Committee In 1993 the Codex Alimentarius Commission decided that Guideline Levels would no longer be established The existing Guideline Levels had been submitted to a review programme in order to delete compounds from the list Currently, Guideline Levels exist for methyl bromide and guazatine

CHAPTER 6

ESTIMATION OF RESIDUE LEVELS FOR CALCULATION OF DIETARY INTAKE OF PESTICIDE RESIDUES

CONTENTS

INTRODUCTION

The JMPR evaluates the possible risks to consumers from pesticide residues in foods by assessing available residue data and then using this information to estimate the short-term and long-term dietary intakes of residues This chapter deals with the residue data assessment and the following chapter will deal with estimating dietary intakes This chapter should be read in the context of the "Estimation of maximum residue levels" section in Chapter 5 The same principles apply to selection of supervised trials data for maximum residue levels, supervised trials median residue levels and highest residue levels

The following guidelines are provided for selecting data that support supervised trials median residue (STMR) levels The same data are used for estimating the HR (highest residue in edible portion of composite sample)

It is not necessary to estimate HR values for compounds where the JMPR has concluded that an acute RfD is unnecessary

COMPARABILITY OF SUPERVISED TRIAL CONDITIONS TO GAP

Residues data are evaluated against the GAP in the country of the trials or a neighbouring country with similar climate and cultural practices

In identifying the STMR and HR values, the trials values selected should be comparable with the maximum registered use (i e maximum application rate, maximum number of treatments, minimum pre-harvest interval (PHI)) on which the MRL is based

The application rates in the trials should generally deviate no more than ±30% of the maximum application rate Deviations from this should be explained in the appraisal

The latitude of acceptable intervals around the PHI depends on the rate of decline of residues of the compound under evaluation The allowable latitude should relate to a ±30% change in residue level and may be estimated from residue decline studies If the decline is assumed to be first order it may be shown that the acceptable intervals are PHI + 0 51 × $t_{1/2}$ (half-life) and PHI - 0 38 × $t_{1/2}$ When the PHI is more than a few days, the estimation of half-life should exclude the data from day 0 (day of application) because the initial decline of residues is generally much faster than the later decline

Consideration of whether the number of treatments reported in trials is comparable to the registered maximum number of treatments will depend on the persistence of the compound and the interval between applications Nevertheless, when a large number of treatments are made in the trials (more than 5 or 6), the residue level should be considered very little influenced by further treatments unless the compound is persistent or the treatments are made with unusually short intervals Residue data are sometimes provided from just prior to the final treatment as well as after it, which is direct evidence of residue contributions from previous applications to the final residue Also, treatments from more than about 3 half-lives (obtained from residue decline trials) prior to the final treatment should not make a significant contribution to the final residue

In establishing comparability of residue trials data in which more than one parameter (i e application rate, number of treatments or PHI) deviate from the maximum registered use, consideration should be given to the combination effect on the residue value which may lead to an underestimation or overestimation of the STMR For example, a trial result should not normally be selected for the estimation of the STMR if both the application rate is lower (perhaps 0 75 kg/ha in the trial, 1 kg ai/ha GAP) than the maximum rate registered and the PHI is longer (perhaps 18 days in the trial, 14 days GAP) than the minimum registered PHI, since these parameters would combine to underestimate the residue When results are selected for the estimation of STMRs and HR values, despite combination effects, the reasons should be explained in the appraisal

If a residue value is lower than another residue value from the same trial which is within GAP, then the higher residue value should be selected in identifying the STMR and HR values For example, if the GAP specified a minimum PHI of 21 days and the residue levels in a trial reflecting GAP were 0 7, 0 6 and 0 9 mg/kg at 21, 28 and 35 days respectively, then the residue value of 0 9 mg/kg would be selected

Interpretation tables for supervised trials data

When residue data are available from several countries the results may be tabulated to show the comparison of trial conditions with GAP to assist with interpretation In the example in Table XI 1 (Appendix XI) residue data on tomatoes from 6 countries are compared with GAP Note that some countries specify application rate (kg ai/ha) while others specify spray concentration (kg ai/hl) in their GAP Italian trials may be evaluated against the conditions of Spanish GAP

The interpretation table provides the set of residues that match maximum GAP from the various countries The next step is to decide if the residues constitute a single population or different populations

DEFINITION OF INDEPENDENT SUPERVISED RESIDUE TRIALS AND SELECTION OF ONE RESIDUE VALUE FROM EACH TRIAL

The estimation of STMR and HR values relies on the selection of residue data from trials within GAP One data point for each value is selected from each trial A sufficient number of trials are needed to represent field and cultural practice variability

Judgements are needed on whether trials should be considered sufficiently independent to be treated separately

The following trial conditions are usually recorded and are taken into consideration

- geographical location and site – trials at different geographic locations are considered independent
- dates of planting (annual crops) and treatments
- crop varieties – some varieties may be sufficiently different to influence the residue
- formulations – trials with different formulations are generally counted as separate trials
- application rates and spray concentrations – trials at significantly different application rates and spray concentrations are counted as separate trials
- types of treatment, e g foliar, seed treatment, directed application – different types of treatment on different plots at the same site are considered as separate trials
- treatment operations – trials at the same site treated in the same spray operation are not counted as separate trials
- application equipment – trials at the same site treated by different equipment, other things being equal, are not counted as separate trials
- addition of surfactants – a trial with the addition of surfactant may constitute sufficient difference to be treated as independent

The set of trials should be examined for its overall suitability in representing the variability which may occur in farming practice For example, two trials with different commercial formulations (otherwise essentially the same use) at the one site may be considered sufficiently independent to be useful, but a series of three or more trials at the same site with different formulations is adding little further information

For trials at the same location there should be convincing evidence that additional trials are providing further independent information on the influence of the range of farming practices on residue levels

Various situations may apply when several residue values are described as "replicates", i e

- replicate laboratory samples taken from a field sample
- replicate field samples (each sample is taken randomly through a whole sprayed plot)
- samples from replicate plots or sub or split-plots (the whole trial is subject to the same spraying operation, but it is divided into 2 or more areas that are sampled separately)
- samples from replicate trials (trials from the same site that are not independent may be considered as replicate trials)