REPORT

JECFA/JMPR INFORMAL HARMONIZATION MEETING

1-2 February 1999, Rome, Italy

WORLD HEALTH ORGANIZATION

and

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

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Summary of the Informal JECFA/JMPR Harmonization Meeting

The Codex Committee on Residue of Veterinary Drugs in Foods (CCRVDF) at its 11th Session recommended a Harmonization Meeting on residue definitions and other issues relating to the use of chemicals both as veterinary drugs and as pesticides because of the differences in the evaluation processes by Joint FAO/WHO Expert Committee on Food Additives (JECFA) and Joint Meeting on Pesticide Residues (JMPR) leading to different MRLs for the same chemical.

The Meeting was held in Rome, Italy from 1-2 February 1999. Mr. Denis Hamilton, Pricipal Scientific Officer, Animal and Plant Health Service Department of Primary Industries, Brisbane, Australia, was appointed chairman of JECFA/JMPR Harmonization Meeting and Dr. Jacques Boisseau, Director National Agency for Veterinary Medicine, Fougeres, France served as the vice-chairman. Dr. Richard Ellis, Director, Scientific Research and Oversight, Office of Public Health and Science, USDA, Washington D. C. and Dr. Stephen Funk, Health Effects Division US-EPA Washington D. C. were the rapporteurs.

The main task of the meeting was to have informal exchange of information related to the same chemical which is of interest to both parties, to come up with only one recommendation on definitions of terms and MRL, used both as pesticide and as veterinary drug, among others. Papers prepared by Dr. Richard Ellis, Mr. Denis Hamilton, and Dr. Alan Hill were the bases of the deliberations.

It was recommended that JMPR/JECFA should continue to hold ad hoc meetings to address issues of mutual interest and should consider the exchange of one panel member to facilitate the harmonization of MRLs and risk assessment for substances used as veterinary drugs and pesticides. The JMPR Secretary should attend part of the JECFA meeting and the JECFA Secretary to attend the JMPR meeting. Ad hoc meetings to deal with specific issues prior to JECFA or JMPR meeting should be conducted, if necessary.

The recommendations of the JECFA/JMPR Harmonization Meeting will be brought up to the JECFA (Feb. 1999) and JMPR (Sept. 1999).

Report of the Informal JECFA/JMPR Harmonization Meeting
FAO Headquarters, Rome, 1-2 February 1999

1. Introduction

Some chemicals are registered for use both as a pesticide and as a veterinary drug. Pesticide residues may arise in animal commodities (meat, milk, and eggs) from the application of the compound to animal feed items or from direct dermal treatment. Veterinary drug residues may arise in animal commodities from the administration of the same compound to livestock. Because of differences in the evaluation processes used by JECFA and JMPR, divergent MRLs have sometimes resulted for the same chemical. The Codex Committee on Pesticide Residues (CCPR) at its 30th Session (1998) recommended that the JMPR and JECFA work to harmonize the residue definitions, and the 11th Session (1998) of the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF) recognized the harmonization problem and recommended that the secretaries of JMPR and JECFA convene an informal meeting of experts to address the issues (ALINORM 99/31).

Mr. Hamilton and Dr. Boisseau served as chair and co-chair, respectively. Drs. Ellis and Funk served as rapporteurs. The participants of the JECFA/JMPR Harmonization Meeting are given in Appendix II.

The Meeting based its deliberations on the following papers given in Appendix I:

1. *Definition of Food Commodity Muscle and Meat*, Richard Ellis.
2. *Recommending MRL's for Lipid Soluble Residues in Milk and Muscle Tissue Based on Fat Content*, Richard Ellis.
3. *JMPR Estimation of Pesticide Residue Dietary Intake*, Denis Hamilton.
4. *Sampling and Fat*, Alan Hill.

2. Discussion

2.1 Meat /Muscle/Fat

The commodity definitions and portions of commodities to which the Codex MRLs apply were considered by the Meeting. Veterinary drug MRLs are established for "muscle" whereas pesticide MRLs are established for "meat." Meat is generally considered to be muscle plus connective tissue and variable amounts of trimmable fat, but monitoring laboratories and some national governments equate muscle to meat. The presence or absence of the trimmable fat in the sample to be analyzed is particularly important when dealing with fat-soluble pesticides. It was decided that the tissue "muscle" as defined by JECFA could be made equivalent to "meat" as defined by JMPR if the sample preparation instructions for meat be specified 'removal of the trimmable fat'. This step eliminates any need to change definitions and only requires instructions on sample preparation for analysis (portion of the commodity to which the MRL applies and which is analyzed) both for studies on which MRLs are based and for monitoring and enforcement work. For fat-soluble pesticides and veterinary drug residues the trimmable fat would be analyzed on a lipid basis. This fat would be that referenced by the "JECFA fat MRL" and the "JMPR meat (fat) MRL". For non-fat soluble pesticides and veterinary drugs residues,

the muscle or the trimmed meat would be analyzed as referenced by the 'JECFA muscle MRL' and the 'JMPR meat MRL'.

It was noted that the 'JMPR fat MRL' refers to the fat commodity in international trade (Volume 2, *Codex Alimentarius*). CCPR does not establish fat MRLs for fat-soluble pesticides. The difference between JECFA fat (trimmable fat) and JMPR fat was viewed as a confusing situation for those outside the process. For transparency, JECFA/CCRVDF ought to establish a definition for fat (there is none in Volume 3 of *Codex Alimentarius*). Likewise, for sampling purposes, CCPR should revise the term "fatty tissue" to "fat tissue." Fatty tissue could contain appreciable water or other components.

This approach has one fault i.e. there is no mechanism for handling processed commodities, such as sausage, where fat content may be quite significant because fat analyses are limited to trimmable fat (not extractable fat) in fresh or raw product,

Generally, pesticides do not present significant residues in meat per se. Veterinary drugs can have substantial residues in muscle. For the non-fat soluble compounds, it was resolved that meat with trimmable fat removed should be analyzed. This brings the 'meat' in line with the 'muscle'. Again, commodity / tissue definitions need not be modified. The portion of the commodity / tissue to which the MRL applies and which is analyzed needs to be specified.

The inclusiveness of muscle tissue was also discussed. Certain non-skeletal muscle tissues may be included with offal. It was decided that muscle would not be limited to skeletal muscle tissue, and that the MRLs for muscle would be inclusive, unless data for non-skeletal tissues show the need for higher MRLs for the latter.

Where residue definitions agree but MRL magnitudes vary on a given commodity for use as a pesticide versus use as a veterinary drug, the Meeting decided that the MRL of greater magnitude should be recommended for both categories.

2.2 Milk

Currently, JECFA procedures designate the commodity to be analyzed as whole milk. Processed milk products are not included under the JECFA guidelines. JMPR guidelines specify the commodity to be analyzed as milk fat for fat-soluble pesticides and as whole milk for non-fat soluble pesticides. Results are reported on a whole milk basis assuming a fat content of 4%. This is the procedure both for establishing the MRL and for enforcement analyses.

The issue of introducing a variable fat content into the procedure (by JMPR) was discussed. Milk fat content may vary from 3 to 6%, and in some regions herds of high milk fat producing cows are maintained. As most fresh, liquid milks are blended, the 4% is a viable estimate for the vast majority of situations. The Meeting decided to recommend analysis of the milk fat for fat-soluble pesticides in milk and the use of 4% milk fat content to calculate the residue result on a whole milk basis.

Concern was expressed that whole milk with a fat-soluble residue in excess of the MRL could be processed into a low fat product (yogurt) that would not be in excess of the MRL if the nominal 4% is used. However, for enforcement or monitoring actions for milks or processed milk products with fat contents significantly different from 4%, the MRL value can be adjusted to accommodate the different measured fat contents. The measurement for the milk fat residue in the yogurt would be adjusted to a whole product on the basis of the measured 0.5% milk fat, not the nominal 4%.

In recommending MRLs for milk, JECFA uses ug/l, whereas JMPR uses mg/kg. For consistency, it was agreed to convert the unit of all MRLs to mass basis (mg/kg). However, the use of ug is preferred by JECFA and any change will be at JECFA's discretion. The use of ug does not imply additional precision, provided the number of significant figures are maintained, e.g. 0.1 mg/kg has the same precision connotation as 100 ug/kg.

2.3 Eggs

The Meeting considered the current definition of the JECFA for egg commodity to be analyzed as ambiguous: egg (in shell) of domesticated chickens (hens). This could be interpreted to mean that the shell plus contents are to be analyzed. The shell conceivably could have residues of environmental contaminants, and normally only the edible commodity is analyzed. While the commodity to be sampled is egg in shell, the commodity to which the MRL applies and which is to be analyzed is the contents of the shell.

Commodity definitions (Volume 2 and Volume 3 of *Codex Alimentarius*) were reviewed. For CCRVDF, the egg commodity has been restricted to chickens (hens) only. The commodity should be expanded to avian eggs. For CCPR, various commodity types are described (6 whole chicken eggs, 24 whole quail eggs), but some types (e.g., ostrich) are missing, and a minimum sample size (500 g) might better serve the commodity type description. CCRVDF commodity descriptions exist for various processed meats (Class E, type 16 – 19), but MRLs are not established for veterinary drugs in processed meats.

2.4 Residue Definitions

In defining the MRL marker residue (JECFA) or residue (JMPR), consideration is given to the ability to analyze for the targeted residue components. Residue components amenable to multi-residue methods are preferable to components that require specialized single analyte methods. Also, exotic metabolites with no available reference standards are avoided.

The marker residue for the veterinary drug abamectin has been defined as abamectin B1a. The residue definition for the pesticide abamectin has been defined as the sum of avermectin B_{1a}, avermectin B_{1b}, and two photodegradation isomers. The generally used HPLC residue control methods do not separate B_{1a} and a photoisomer, although it was reported that methods are

available to separate the isomer from B_{1a}. Avermectin B_{1b} is a minor component of the residue,

and its elimination from the residue definition will be considered during the upcoming JMPR

periodic review. JECFA was requested to consider the addition of the photoisomers in the marker residue definition, although photodegradation is not an issue for the veterinary drug.There is no toxicology problem; both avermectinB_{1a} and avermectin B_{1b} are covered.

JECFA has recommended MRLs for cypermethrin and for alpha-cypermethrin. JMPR has recommended MRLs for cypermethrin (sum of isomers). JECFA wishes to retain the separate MRLs, although this violates the general principle of having only one definition for a compound. Maintaining the isomer-specific MRL is an incentive to the registrant for producing a purified drug product. Alpha-cypermethrin provides a distinct chromatography peak, whereas the cypermethrin mixture yield several peaks, one of which co-elutes with alpha-cypermethrin. When use as a veterinary drug, alpha-cypermethrin residues will yield a much larger chromatographic response than the minor isomers from possible incorporation of cypemethrin pesticide residues in the same commodity. Multiple chromatographic signal responses (peaks) would be treated as cypermethrin. It was noted that alpha-cypermethrin and cypermethrin have different ADI's.

CCRVDF has recommended MRLs for both muscle and fat. This may be inappropriate, as alpha-cypermethrin and cypermethrin are fat-soluble. Typically, MRLs would be recommended only for fat. Under the present situation, laboratories could analyze both trimmable fat and muscle (for National residue control or for international trade).

Residue definition differences are complex and unique to the particular pesticide/veterinary drug. Harmonization must be considered on a case-by-case basis.

2.5 Dietary Intake Estimation and Risk Assessment

Dietary intake estimation and risk assessment procedures are quite different in JECFA and JMPR. JECFA establishes MRLs based on clinical trials, with withdrawal periods established to yield residues within acceptable limits relative to the ADI. The diet is extremely conservative, with large portions of animal products, e.g., 300g meat per day and 1.5 liter (1.5kg) milk per day. JECFA may have data available for typical residues in commodities, as opposed to upper bound residues, and will supply the data to JMPR, as needed.

JMPR establishes MRLs based on field trials conducted under good agricultural practice. Dietary chronic intake calculations are not made with the MRLs, however, they are based on the STMRs (supervised field trial median residues). Additionally, diets are based on regional compilations of actual food consumption and include the entire range of foods.

The extreme differences in dietary intake calculation methodologies may make data transfer between JECFA and JMPR very difficult. The differences could result in conflicting conclusions

on the safety of the pesticide/veterinary drug, based on the percent ADI consumed by the different uses.

The process used by JMPR in arriving at MRLs and STMRs was explained in some detail, and an example calculation spreadsheet for dietary exposure was reviewed. The transparency of the process, implemented by the 1998 JMPR, was appreciated. Prior to 1998, the JMPR simply reported that a pesticide use did or did not exceed the ADI.

The *FAO Manual on the Submission and Evaluation of Pesticide Residues Data for the Estimation of Maximum Residue Levels in Food and Feed* (1997) will be provided to the JECFA. JECFA guidelines are in the draft stage, and copies of the finalized document will be presented to JMPR. This will promote a better understanding of expert committee procedures.

For compounds that are used as veterinary drugs and pesticides, a mechanism is needed for sharing risk assessment information between JECFA and JMPR. Although the estimation methods are quite different and inconsistencies abound, the exchange of information will at least provide JECFA and JMPR with information on the percent of ADI consumed by the pesticide residue or veterinary drug residue, respectively. Several mechanisms were suggested.

The JMPR Secretary should attend a portion of the JECFA meeting, and the JECFA Secretary should attend part of the JMPR meeting. They will have the responsibility of providing relevant data and information to their respective expert panels.

It was also suggested that JMPR and JECFA could exchange one panel member each to facilitate information exchange and harmonization. Work load and monetary constraints were mentioned as negative factors for this proposal.

Finally, ad hoc meetings of the JECFA/JMPR Harmonization Work Group were suggested to deal with specific issues. A suggested topic was the common mode of action for dietary intake concerns. The meeting would be held immediately prior to a JECFA or JMPR meeting.

3. Recommendations

The Meeting addressed five topic areas: muscle versus meat; fat soluble residues; definition of residues of pesticides with isomers like cypermethrin, abamectin, cyfluthrin, and others used for agricultural and veterinary purposes; standardization of sampling procedures for animal and agricultural products; harmonization of approaches for risk assessment. The recommendations derived from those discussions are summarized below in four topic areas.

The recommendations are directed to CCRVDF/CCPR or JECFA/JMPR, as appropriate.

3.1 Tissue

1. For sampling purposes, CCPR should revise the term “fatty tissue” to “fat tissue” in the definition of meat and fat in the Codex Classification of Food and Feed.

2. Clarification of the definition of muscle tissue (Volume 3 of Codex Alimentarius) is needed to establish the portion of the commodity to which the MRL applies. Muscle tissue (JECFA/CCRVDF) shall include interstitial fat and exclude trimmable fat. It is recognized that other minor components, e.g., connective tissue, may be present in muscle tissue. Muscle tissue includes skeletal muscle tissue and all other edible muscle tissues. For muscle tissues other than skeletal muscle, the MRLs for skeletal muscle tissue shall apply, unless studies show greater residues in the other types of tissue. Sponsors may submit data for consideration for other muscle tissues, such as tongue, etc.

3. For the determination of fat-soluble pesticide/veterinary drug residues in meat/muscle for enforcement or monitoring purposes, laboratories are advised to collect and to analyze trimmable fat and to report the residue on a lipid basis, i.e., meat (fat) for JMPR and fat for JECFA. For meat without trimmable fat, the entire commodity should be analyzed as meat/muscle, but only where the MRL has been set on meat/muscle basis.

4. For the determination of non-fat soluble pesticides/veterinary drugs residues in meat/ muscle, laboratories are advised to analyze meat/muscle with trimmable fat removed, as far as is practical.

5. Where JECFA and JMPR have recommended MRLs for the same chemical with the same residue/marker residue definitions on the same commodity, the higher MRL shall prevail.

6. CCRVDF should consider describing fat as the trimmable lipid-based tissue (eg., subcutaneous, perirenal, etc) from food producing animals.

3.2 Milk

7. For the determination of fat-soluble pesticide/veterinary drug residues in milk, the milk fat portion of fresh milk should be analyzed, and the results should be expressed on a whole milk basis using 4% as the nominal fat content.

8. For the determination of non-fat soluble pesticide/veterinary drug residues in milk, laboratories should analyze the whole milk and should report residues on a whole milk basis.

9. JECFA should consider expressing MRLs for milk on a weight (kg) basis rather than the current volume (l) basis.

3.3 Eggs

10. JECFA should specify that the portion of the raw commodity “egg” (in shell) to be analyzed is the whole egg white and yolk combined after removal of the shell. The present description suggests that shell is included in the commodity analyzed.

11. The description of eggs should not be limited to chicken, and sampling size should be a minimum of 500 grams. CCRVDF and CCPR are invited to modify the appropriate sections of Volumes 2 and 3 on sampling, accordingly.

12. CCRVDF stablishes MRLs on raw meat and poultry products only. CCRVDF should consider deletion of the sampling guidelines for the processed products for Class E (types 16 - 19).

3.4 Harmonization

13. The working group noted disparate residue definitions by CCPR and CCRVDF for abamectin and recommended that CCRVDF/JECFA consider expansion of its residue definition to include other isomers, such as the photodegradation isomer of B1a. CCPR/JMPR should consider its need to include the various isomers as part of the periodic review of abamectin.

14. Cypermethin and alpha-cypermethrin should remain as the marker residue definitions for their use as veterinary drugs for cypermethrin and alpha-cypermethrin, respectively, and cypermethrin (sum of isomers) should remain as the residue definition for the pesticide cypermethrin. Guidance should be supplied to laboratories on the designation of the measured residue as cypermethrin or alpha-cypermethrin based on the chromatography of the test substance.

15. Harmonization efforts should be undertaken on a case-by-case basis where marker residue definition/residue definition differences occur between JECFA and JMPR.

16. JECFA should review the apparent anomaly of MRLs for both fat and muscle for the fat-soluble drugs alpha-cypermethrin and cypermethrin. JECFA should consider which sample tissues are to be analyzed by the enforcement laboratory.

17. CCPR should amend the note explaining the “V” designation for MRLs. The present description, “the MRL accommodates veterinary uses,” is confusing and should be amended to “the MRL accommodates external animal treatments.”

18. For compounds that are common to both, JMPR and JECFA should use the more specific animal commodity descriptions to enhance harmonization. For example, separate MRLs for cattle muscle, goat muscle, horse muscle, pig muscle, and sheep muscle are preferable to meat of cattle, horses, pigs and sheep.

19. Each expert panel needs a better understanding of the other’s procedures for food safety assessments for estimating MRLs and dietary exposure, for example. JECFA will provide JMPR its guidance document describing the JECFA evaluation procedures when the draft

version is finalized. The JMPR FAO Manual (1997) will be distributed to the JECFA members at the February 1999 meeting.

20. The JECFA/JMPR Group acknowledged the very different approaches used for dietary

exposure determinations. JMPR will provide JECFA with detailed reports of its assessments, dietary intake calculations and % ADI determinations for compounds of interest to JECFA. When the data are available, JECFA will provide JMPR with median and upper limit animal commodity residue values and dietary intake calculations/% ADI determinations for compounds of interest to JMPR.

21. JECFA and JMPR should consider the exchange of one panel member each for a portion of the expert panel meetings to facilitate the harmonization of MRLs and risk assessment for substances used as veterinary drugs and pesticides.

22. The Joint Secretary for JMPR will attend the JECFA meeting, and the Joint Secretary for JECFA will attend the JMPR meeting, particularly when MRLs and risk assessments of substances used as veterinary drugs and as pesticides are being considered.

23. Joint meetings of JMPR and JECFA should be held on an *ad hoc* basis to address issues of a mutual interest, for example, how to address MRL and ADI issues for classes of compounds with common modes of action, e.g., organophosphorus compounds.

24. For compounds of mutual interest, JMPR and JECFA should have each other's recommendations/reports available when conducting evaluations. The Joint Secretaries will have responsibility for obtaining and distributing the documents and information, as appropriate.

APPENDIX I

DEFINITION OF FOOD COMMODITY MUSCLE AND MEAT

Richard Ellis

Traditionally, JMPR has recommended MRLs in meat and meat by-products when pesticide residues in agricultural crops may result in residues in food animals. JECFA has recommended MRLs in muscle, liver, kidney and fat individually and in milk and eggs, as appropriate, in food producing animals where the substance has been used as a veterinary drug. Differences in approaches used in recommending MRLs in muscle and meat have presented some complications on a limited number of substances for the two expert committees (based upon the approaches used by the respective expert committee) as well as CCPR and CCRVDF.

Codex definitions provide little guidance on muscle versus meat. For example, in Codex Alimentarius, Volume 3 (1995), meat is defined as "the edible part of any mammal". The definition for muscle is "muscle tissue only". One may imply that muscle is a portion of meat in a food producing animal. This reference citation did not contain a definition for fat. Using the United States Code of Federal Regulations (CFR 9,ə 301), meat is defined as "the part of the muscle of any cattle, sheep, swine, or goats, which is skeletal or which is found in the tongue, in the diaphragm, in the heart, or in the esophagus, with or without the accompanying and overlying fat, and the portions of bone, skin, sinew, nerve, and blood vessels which normally accompany the muscle tissue and which are not separated from it in the process of dressing. It does not include the muscle found in the lips, snout, or ears. This term as applied to products of equines, shall have a meaning comparable to that provided in this paragraph with respect to cattle, sheep, swine, and goats."

Definitions for fat are not included in Codex Alimentarius, Volume 3. Similarly, there is no definition for fat included in the United States Code of Federal Regulations, Title 9, ə 301 et seq. The only definition in the CFR is found in CFR 21, ə 101, in the U.S. Food and Drug Administration regulations on food labeling. That definition states that fat (total), is "A statement of the number of grams of total fat in a serving defined as total lipid fatty acids and expressed as triglycerides". Lipid fatty acids identified in the definition include lauric, palmitic, and stearic acids. However, in AOAC International, several analytical methods for fat are included in the AOAC International *Official Methods of Analysis.* Some of the methods rely on heat rendering of trimmed fat or fatty tissue, some rely on solvent extraction using organic solvents and some rely on use of supercritical fluid carbon dioxide. Thus, there are at least three basic methods used for providing a fat sample for residue analysis (as well as compositional analysis). Fortunately, the differences in fat yields typically differ by less than 5 percent from each other. However, it would be most appropriate to have an agreed upon definition of fat for purposes of Codex and its accompanying expert committees.

The following table is provided for information to indicate the distribution of residues in tissues for those substances used as a veterinary drug.

JECFA Residue Data on Compounds as Veterinary Drugs and Pesticide (µg/kg)
(Residues expressed as percent of residue marker in tissue)

Substance	Treament	Withraw Time	Musce	Liver	Kidny	Fat
Abamectin (cattle)	0.3 mg/kg S.C.	20 days	3 (4.2)	30 (41.7)	9 (12.5)	30 (41.7)
Cyfluthrin (cattle)	ca. 2 mg/kg Dermal	14 days	<10 (4.8)	<10 (4.8)	<10 (4.8)	90 (85.7)
	5 @ 0.9 mg/kg Dermal	2 days (5^{th} dose)	10 (2.5)	13 (6.5)	17 (7.5)	165 (82.5)
Cyper-methrin (cattle)	ca. 0.4 mg/kg Dermal	14 days	<10 (1.3) (5.3)	<10 (1.3) (5.3)	40 (10.5) (21)	330[a] 140[b] (86.8)[a] (73.7)[b]
(laying hen)	ca. 6 mg/kg Spray	14 days	18 (15)	5 (4.2)	12 (10)	85[c] (70.8)
∀-Cyper-methrin (cattle)	ca. 0.1 mg/kg Dermal	14 days	<10 (4.6) (16.7)	<10 (4.6) (16.7)	10 (9.3) (33.3)	90[a] 10[b] (81.8)[a] (33.3)[b]

Footnotes: a) peritoneal fat; b) subcutaneous fat; c) skin residues 170-1300µg/kg.

Note that residue data for cypermethrin in sheep using dip or pour-on formulations were summarized for omental, perirenal and subcutaneous fat only. Residues in muscle, liver and kidney were not included in the FAO monograph (FNP No. 41/9), however, were indicated to be less than the limit of quantification of the analytical methods in the studies using the dip formulations.

RECOMMENDING MRL's FOR LIPID SOLUBLE RESIDUES IN MILK AND MUSCLE TISSUE BASED ON FAT CONTENT

Richard Ellis

I have chosen to start by making some assumptions and posing (for guidance) a list of questions.

Starting point assumptions:

1. The issue seems to be more one of compliance (e.g., member state national residue control programmes). The principle Codex mission objectives are to establish standards to protect public health and promote international trade of agricultural commodities. See discussion.
2. There should only be one MRL for the same commodity/substance pair regardless of agricultural/animal health use (i.e., pesticide or veterinary drug). Extending that same premise, there should only be one MRL for each matrix (i.e., fat) regardless of source.
3. Selection of the test sample may contribute to the issue. In particular, the Codex definition for meat (Meat is the muscular tissue, including intramuscular fat and adhering fatty tissues such as intermuscular and subcutaneous fat).
4. As a first approximation, residues are distributed equitably amongst differing fat depots in animals.
5. JECFA, to the extent of available residue data, recommends MRLs on individual tissues based on the distribution of residues in muscle, liver, kidney and fat based upon sponsor recommended dosing and withdrawal period.

My assumptions and questions influence my comments noted below.

Some questions:

1. If we consider MRL's for meat and milk on a fat basis, should we consider residues for these substances in liver and kidney on the same basis?
2. Should there be a more comprehensive definition of fat (e.g., is fat described as free fatty acid equivalents, heat rendered material from an aliquot of omental (or other) fat deposit or fatty tissue, solvent extracted material, etc.)?
3. Should the Committee more clearly define meat and/or muscle tissue (e.g., does meat equate to muscle tissue only or to muscle tissue with interstitial fat, or does it equate to muscle tissue with interstitial and some adhering fat or some other entity?
4. If one designates an MRL for muscle as muscle MRL (fat basis), what or how would JECFA set an MRL in the muscle tissue (on the protein, moisture and ash portion)?

Comments on the issue.

In the development of its procedures for recommending MRLs for substances used as veterinary drugs in food producing animals, JECFA has indicated that MRLs in at least two tissues are necessary – one for national residue control programmes and one for the commodities most often

employed in international trade. Regarding the latter, it is meat that is most often used in trade and for this reason, at least one MRL should be recommended in muscle or fat. For national residue control programmes, the marker residue in the target tissue ought to be used. In most
instances the target tissue will be either liver or kidney, with the exception being the lipid soluble substances used as either a veterinary drug or agricultural chemical (i.e., as a pesticide).

Regarding my first assumption, I include a quote from a 1994 CAC document (CX/PR 94/12). "The fat solubility of many pesticides has given rise to problems in setting and enforcing MRL's and, therefore, to specific solutions in the regulation of their residues. The general problem is that the residues are not evenly distributed in the animal tissues, but accumulate in the fat, so that variations in the fat content of the animal as such, and of derived animal products, have a large effect on the pesticide concentration in the product. When these effects are not accounted for in the regulation of the residues, it may give rise to unjustified actions against products". In fairness, I note that the paper also states that "the solution was found in the CCPR, and that was internationally accepted, was the expression of the residue on a fat basis, both for meat and for milk". This seems to address needs more for laboratory residue analysis for national authorities. JECFA notes that MRLs in animal tissue at or below the recommended value provide assurance that the ADI, the public health endpoint, will not be exceeded. JECFA, as noted above, does not limit its assessment to an individual MRL in a single tissue.

If we desire to have a consistent approach of one MRL for the same commodity/substance pair, we should consider having only one MRL for the matrix – in this case fat, regardless of its source - whether it is adipose tissue or fat associated with muscle tissue. The argument might be extended to liver and kidney also as they contain small amounts of fat as well as to milk. To do so, we may be creating a pseudo *default approach* to MRL's for lipid soluble analytes. Potentially, this may require reassessment of a number of substances for consistent application of a universal approach within Codex. In the assessment of substances used as pesticides and veterinary drugs, JECFA has identified several examples of lipid soluble compounds under consideration that distribute differently among the edible tissues – muscle, fat, liver and kidney (references include FAO Food and Nutrition Papers 41/5, 41/8, 41/9 and 41/10).

Reviewing the USDA Agriculture Handbook No. 8 database, I was able to gather some useful information to address the amount of fat in a muscle sample as well as liver and kidney percent fat in poultry, pigs and cattle. Before addressing these data, it would be helpful to comment on the third assumption on the selection of the test sample. I have reviewed sample receipt and residue analysis procedures with our laboratory personnel and may be able to provide photographs of what a muscle sample collected by USDA inspector's looks like.

In general, the muscle-fat samples received by USDA laboratories from imported product contain subcutaneous fat (from the adipose layer between the hide and carcass meat), whereas samples from domestic product is typically perirenal fat – others may comment on the samples collected in their national residue control programme. For perspective, a "fat" sample for poultry is adipose tissue collected from the abdominal cavity.

The implications for preparing a sample for residue analysis are influenced by the composition of the muscle and fat test samples. In USDA procedures, adipose fat samples are placed in a vessel
over a bed of anhydrous sodium sulfate that allows liquid fat to drain from the sample as it is processed. Typically, processing involves placing the test sample in a convection oven set at 80^{o}C overnight. The residue analysis is performed from an aliquot of the rendered liquid fat sample. Pesticide residues are reported on a fat basis. For a muscle tissue or "low fat" sample consisting of less than approximately 10% fat, solvent extraction is used and the fat is determined by gravimetric methods. However, solvent composition may, to a limited extent, influence the extracted "fat" (in quotes because the solvent choice can influence whether or not phospholipids, for example, are extracted as fat or equivalents of free fatty acids). This typically, however, makes a small (<5%) difference in the yield of fat. This also indicates that extraction of low fat meat samples is more labor intensive and an additional processing step that must be carried out prior to performing the residue analysis. A realistic consequence is that fewer analyses are possible given a fixed number of available analysts and other resources. This provides some of the rationale on sample instructions to an inspector in an abattoir.

If one were to address the issue from a consumption of some fixed quantity of residue, then the discussion that follows should be considered.

To address the composition of muscle tissue, data from the USDA Agriculture Handbook No. 8 was searched. The search examined species commonly addressed by the Committee and was sorted as" lean muscle" and "muscle and fat" for a variety of different meat portions. (The data were available for review at the 50th JECFA). What it shows, is that the average fat (lipid content) in lean muscle (equated to interstitial fat) for horse is 4.60%; for lamb, 5.16%; chicken, 2.91%; pig, 6.07%; and for cattle, 6.08%. The grand average for all species is 4.97%. Thus, there is not a big difference in the fat content of lean muscle across animal species (poultry may be an exception). For the arguments below, I have used a value of 6.0% for interstitial fat in muscle tissue. Though not provided, the average fat content used for milk is approximately 4 %.

For fat (lipid) composition in kidney and liver, data from the USDA Agriculture Handbook No. 8
indicates the following composition. For kidney, values for cattle, pigs and poultry are 3.1%, 3.3% and 4.2% (poultry giblets – kidney is not listed separately), respectively. For liver, values for cattle, pigs and poultry are 3.9%, 3.7% and 4.0%, respectively.

If JECFA, JMPR or Codex in general, were to apply a constant value (as Φg or mg of residue, for example) for all tissues, one can calculate a default ratio between MRL's in muscle and milk compared to the MRL in adipose tissue. Using the JECFA daily food intake for residues of veterinary drugs in food, the ratios reported below take into account the food composition factors, 300g muscle, 50g fat, and 1500ml milk. For fat/muscle the ratio is, 2.78; for fat/milk, 0.83; and for muscle/milk, 0.30. One can do the same calculations by food animal species. Poultry would give noticeably different values. I do not support taking this approach. You may draw your own conclusions – pro or con.

As the issue seems to be one more of addressing compliance by national authorities, then a

different approach ought to be considered. Though it is not an easy one, a refinement of the

definition of meat may be warranted. Second, it might be considered whether or not providing guidance for collection of "fat" and "muscle" tissues for residue analysis would be constructive. The difficulty of course, is not in revising a definition or providing the sample collection guidance. The difficulty will be on getting the revised definition and guidance (a new paradigm) accepted by the necessary Codex Committees, in particular CCPR, CCRVDF and probably CCMAS. Practical issues of adoption by national residue control authorities remain. I recognize the implications will apply to a number of Codex commodities and standards as well. Thus, this does not seem to be a fruitful exercise to pursue.

As to the original issue of reporting residues of lipid soluble material on a fat basis in muscle and milk, this document in the eyes of most may not provide enough constructive guidance. I agree, and do not have a "best" solution to recommend that pleases me. Rather, my expectation is that this paper will stimulate a thorough discussion upon which Codex expert committees might draft a document that reflects a consensus approach on recommending MRLs for lipid soluble residues in muscle and milk for those substances that are used as a pesticide in agricultural practice and a veterinary drug for animal health purposes.

We must keep in mind our responsibility to provide the best expert guidance for public health purposes and facilitating international trade – the primary Codex mission.

JMPR ESTIMATION OF PESTICIDE RESIDUE DIETARY INTAKE

Denis Hamilton

Introduction

Reconciling dietary intakes of residue likely to occur in practice and acceptable intakes derived from toxicology studies is known as the risk assessment process. Dietary intake estimation of pesticide residues has progressed rapidly in recent years.

WHO, in 1989, issued a publication[1], "*Guidelines for predicting dietary intake of pesticide residues"* based on the recommendations of an expert consultation in 1987. These guidelines relied heavily on the TMDI (Theoretical Maximum Daily Intake), with calculations based on MRLs and subsequent stepwise refinements. The guidelines were useful in many cases, but their limitations also became apparent.

WHO issued revised guidelines[2] in 1997 based on the recommendations of an expert consultation[3] in 1995. The guidelines were further developed into practical procedures for evaluating pesticide residues data and were included as Chapter 6, "Estimation of residue levels for calculation of dietary intake of pesticide residues" of the FAO Manual[4].

The revised guidelines emphasise the best use of available data. The guidelines focus mainly on pre-registration data, but recognise that, where available, total diet studies or other measured estimates of pesticide residue intake are more accurate records of dietary intake than calculated intakes, but are expensive and results are available only for some pesticides in some countries.

Data requirements

The FAO Panel of the JMPR has outlined its data requirements in Chapter 3 of the FAO Manual[4]. Briefly, the data requirements for a new compound or a periodic review compound (an old compound being revised to modern standards) are as follows. The data requirements are quite different for pesticides which are no longer used but have become environmental contaminants, which will not be discussed further in this paper.

Identity

- names, formulae.

Physical and chemical properties

- properties of pure active ingredient and technical material

Formulations

- commercially available formulations

Metabolism and environmental fate

- farm animal metabolism
- plant metabolism
- environmental fate in soil and in water/sediment systems (metabolism in soil, mobility, hydrolysis, photolysis, residues in rotational crops.)

Methods of residue analysis

- methods used in supervised trials and environmental fate studies
- enforcement methods
- freezer storage stability studies

Use pattern

- complete and current registered uses (GAP, Good Agricultural Practices).

Residues resulting from supervised trials

- residue trials for crops, feeds and post-harvest commodity treatments
- external animal treatments
- farm animal feeding studies

Fate of residues in storage and processing

- changes in the nature of the residue during processing and levels occurring in processed commodities

Residues in food in commerce and consumption

- monitoring data, market basket studies.

National maximum residue limits

Residue definition

The residue definition established for MRL enforcement purposes may not necessarily be the ideal definition for dietary intake assessment.

For dietary intake purposes it is desirable to include metabolites which have similar toxicity properties to the parent.

For enforcement purposes (testing of food consignments for compliance with MRLs) it is not desirable to include metabolites if they are present as only a minor part of the residue, or if present in a relatively constant ratio to the parent. Monitoring for additional compounds only adds to the cost of analysis and standards for metabolites are not always readily available.

The JMPR considers many factors before proposing residue definitions (Chapter 5.3 of FAO Manual[4]).

- composition of the residues in animal and plant metabolism studies
- toxicological properties of metabolites and degradation products
- nature of the residues in the supervised residue trials
- fat solubility
- practicality of regulatory analytical methods
- whether metabolites or analytes are common to other pesticides
- whether a metabolite of one pesticide is registered for use as another pesticide.

We should note that the dietary intake residue definition is not necessarily the same as the residue definition suitable for monitoring compliance with GAP.

JMPR, in the residue definition section of the residue monographs, explains the basis for residue definitions and includes an explicit statement of residue definitions in the recommendations for each compound.

Examples of residue definition from 1998 JMPR.

Disulfoton.Definition of the residue
for compliance with the MRL and for estimation of the dietary intake: *sum of disulfoton, demeton-S and their sulfoxides and sulfones expressed as disulfoton.*

Quintozene. Definition of the residue
for compliance with the MRL for plant commodities: *quintozene.*
for compliance with the MRL for animal commodities: *sum of quintozene,*

pentachloroaniline and methyl pentachlorophenyl sulfide, expressed as quintozene.

for estimation of the dietary intake for plant and animal commodities: *sum of quintozene, pentachloroaniline and methyl pentachlorophenyl sulfide, expressed a quintozene.*

Supervised residue trials and estimation of STMRs

Supervised residue trials are defined as scientific studies in which pesticides are applied to crops or animals according to specified conditions intended to reflect commercial practice after which harvested crops or tissues of slaughtered animals are analysed for pesticide residues. Usually specified conditions are those which approximate existing or proposed GAP[4].

The JMPR estimates MRLs on commodities from supervised residue trials where conditions match GAP. The MRLs are usually expressed on the whole commodity of trade, but the precise description of commodity and the portion to be analysed are described in the Codex Classification of Foods and Animal Feeds[5].
If the whole commodity corresponds with the edible portion and the residue definitions for MRL enforcement and dietary intake are identical the same set of residue data can be used to estimate the STMR.

The supervised trials median residue[4] is the expected residue level in the edible portion of a food commodity when a pesticide has been used according to maximum GAP conditions. The STMR is estimated as the median of the residue values (one from each trial) from supervised trials conducted according to maximum GAP conditions.
Additional data are needed from the trials if the dietary intake definition or the edible portion of commodity do not match those relevant to the MRL.
An example of an evaluation for abamectin is given in Annex 1.

Primary feed commodities and animal commodities

MRLs and STMRs for primary feed commodities are established in the same way as for food commodities except that they are expressed on a dry weight basis.
The 1997 JMPR[6] explained the current procedures for estimating MRLs and STMRs for animal commodities from the farm animal feeding studies and the expected residues in primary feed commodities. The procedures were summarised in a table.

	Residue reaches plateau rapidly		**Residue reaches plateau slowly**	
	Max residue level	**STMR**	**Max residue level**	**STMR**
Feed item residue level	MRL	STMR	STMR	STMR
Feed incorporation rates	maximum	maximum	maximum	maximum
Feeding study residue level 1/	highest	mean	highest	mean

1/ highest residue level in the tissue of an individual animal or mean residue level in the specific tissue of animals in the relevant dosing group.

Fate of residues in food processing

Processing studies provide information on the nature and levels of residues in processed food which may result from residues in primary food commodities. In typical cases the studies provide

a processing factor (residue level in processed commodity ÷ residue level in primary commodity).

JMPR then calculates an STMR-P (STMR for a processed food) by multiplying the STMR by the processing factor.

Diets used in chronic intake assessment

JMPR uses the Food Balance Sheet data compiled by FAO and recently published by WHO[7]. Data are available for most primary food commodities and some processed commodities for 5 regional diets – Middle Eastern, Far Eastern, African, Latin American and European.

Acute intake

JMPR has established, for a number of pesticides, acute reference doses suitable for checking short term exposure of residues.

Beginning in 1999 JMPR will estimate residue levels suitable for acute dietary exposure estimation. These levels will be equivalent to the highest residue in the edible portion for most commodities, or the highest residue multiplied by a variability factor (10) for commodities such as apples or carrots typically consumed as a single unit rather than as the average of a commodity consignment or lot.

Large portion size and 97.5th percentile diet information are being compiled by WHO and will be combined with the residue levels described above to calculate acute intake for comparison with the acute reference dose.

Conclusions

The 1998 JMPR introduced a new section into the report for each compound, *Dietary Risk Assessment*, which included a clear statement on the estimated intake for the 5 regional diets. Estimated intakes (and MRLs) are derived through a transparent procedure and are traceable in JMPR Evaluations through processing and supervised trials data summaries back to GAP. The time and effort now required for JMPR evaluation of chronic intake of residues have increased considerably but generally the assessments are more realistic and convincing.

Concern with acute intakes has arisen recently but the methodology for assessing acute intake is still in the development phase. JMPR will make the first formal assessment of acute intakes in 1999.

References

1. WHO. 1989. Guidelines for Predicting Dietary Intake of Pesticide Residues.

2. WHO. 1997. Guidelines for Predicting Dietary Intake of Pesticide Residues (revised), WHO/FSF/FOS/97.7.

3. WHO. 1995. *Recommendations for the revision of the guidelines for predicting dietary intake of pesticide residues*. Report of a FAO/WHO Consultation. WHO/FNU/FOS/95.11.

4. FAO. 1997. FAO manual on the submission and evaluation of pesticide residues data for the estimation of maximum residue levels in food and feed. D/W5998E/1/9.97/500.

5. FAO, WHO. 1993. Codex Alimentarius. Pesticide Residues in Food. Second Edition.

6. JMPR Report. 1997. *The estimation of maximum residue and STMR levels for products of animal origin when residues are transferred from feed items.* FAO Plant Production and Protection paper 145. Chapter 2.4.

7. WHO. 1998. GEMS/Food Regional Diets. WHO/FSF/FOS/98.3

Example: Evaluation of abamectin residues on apples (1997 JMPR)

Residue definition (for MRL enforcement and dietary intake)

Sum of avermectin B_{1a}, avermectin B_{1b}, 8,9-Z avermectin B_{1a} and 8,9-Z avermectin B_{1b}.

Method of adding residue components

The B_{1b} component, when its residues were measurable, was consistently around 10% or less of the total residue. For the purposes of evaluation, when B_{1a} was positively detected in a trial and B_{1b} was not detectable the total residue is calculated taking the not detectable residue as zero.

When both components in a trial were not detectable (ND) the total residue is taken as <limit of detection. A residue reported as NQ (not quantitated, detected but <LOQ) is treated as equal to the LOQ when it is to be added to a measurable residue.

The method of calculating the total residue for various situations is illustrated by example:

B_{1a}	**B_{1b}**	**Total residue**
0.013	NQ (>0.001 but <0.002)	0.015
0.006	ND (<0.001)	0.006
NQ	ND	<0.002
ND	ND	<0.001

Evaluation of supervised trials (Registered uses in Table 1, trial summaries in Table 2 and interpretations in Table 3)

Abamectin is registered for a single application on apples in Australia at 0.014 kg ai/ha with harvest after an interval of 14 days. In 3 trials corresponding to this use pattern the abamectin residues were <0.002, 0.003 and 0.005 mg/kg.

Abamectin is permitted for use on pome fruit in New Zealand with 1 application at 0.027 kg ai/ha and a PHI of 14 days. Abamectin residue levels on apples were 0.004 and 0.007 mg/kg in 2 New Zealand trials where GAP was followed except 2 applications were made instead of 1.

Abamectin is registered in the USA for 2 applications on apples at a rate of 0.026 kg ai/ha and harvest 28 days after the final application. In 14 US trials corresponding to these conditions abamectin residues in rank order (median underlined) were: <0.001 (2), <0.002 (3), 0.002, <u>0.003</u> (4), 0.004, 0.006, 0.007 and 0.012 mg/kg.

The residue data from Australia, New Zealand and USA appear to be one population and can therefore be combined. Residues of abamectin for apples in rank order in the 19 trials (median underlined) are: <0.001 (2), <0.002 (4), 0.002, <u>0.003</u> (5), 0.004 (2), 0.005, 0.006, 0.007 (2) and 0.012 mg/kg.

The JMPR estimated a <u>maximum residue level</u> of 0.02 mg/kg and an <u>STMR level</u> of 0.003 mg/kg for abamectin in apples.

A similar process was followed for other commodities reviewed in 1997. No STMRs were available for commodities reviewed at previous meetings (1992 and 1994) so the MRLs were used instead. A compilation of the intake calculations is shown in Table 4.

Table 1. Registered or approved uses of abamectin on apples.

Crop	Country	Form	Application				PHI, days
			Method	Rate, kg ai/ha	Spray conc., kg ai/hl	Number	
Apple	Australia	EC	foliar	0.014	0.0014	1	14
Apple	USA	EC	foliar	0.013-0.026	0.00035-0.00070	2 or 4	28
Pome fruit	New Zealand	EC	foliar HV	0.027	0.00068	1	14

Table 2. Abamectin residues in apples resulting from foliar application in supervised trials in Australia, New Zealand and USA. Residues from replicate sub-plots are recorded individually. Double-underlined residues are from treatments according to GAP and are valid data for MRL and STMR estimation.

APPLE, country, year (variety)	Application				PHI, days	Residues, mg/kg <u>1</u>/		Ref
	Form	kg ai/ha	kg ai/hl	no.		B_{1a} + 8,9-*Z* B_{1a}	B_{1b} + 8,9-*Z* B_{1b}	
Australia (NSW), 1995 (Granny Smith)	EC	0.014 + oil	0.0008	1	0	0.015 0.015	ND ND	114-95-0001R
					14	<u><u>0.003</u></u> 0.002	ND ND	
					21	NQ NQ	ND ND	

APPLE, country, year (variety)	Application				PHI, days	Residues, mg/kg 1/		Ref
	Form	kg ai/ha	kg ai/hl	no.		B_{1a} + 8,9-*Z* B_{1a}	B_{1b} + 8,9-*Z* B_{1b}	
Australia (Tas), 1995 (Red Delicious)	EC	0.014 + oil	0.0007	1	0 14 21	0.013 0.012 0.005 0.002 0.002 0.004	NQ NQ ND ND ND ND	114-95-0003R
Australia (Vic), 1995 (Fuji)	EC	0.014 + oil	0.0007	1	0 14 21	0.009 0.007 ND NQ ND ND	ND ND ND ND ND ND	114-95-0002R
New Zealand, 1994 (Braeburn)	EC	0.027 +oil	0.0014	2	0 7 14 21 28 35	0.014 0.018 0.012 0.005 0.003 0.004 0.002 ND 0.003 ND NQ 0.002	ND NQ ND ND ND ND ND ND ND ND ND ND	115-94-0005R
New Zealand, 1994 (Gala)	EC	0.027 +oil?	0.0014	2	0 7 14 21 28 35	0.018 0.019? 0.006 0.006 0.007 0.003 0.003 ND c 0.005 0.003 0.004 NQ 0.003	0.002 0.002 ND ND ND ND ND ND c ND ND ND ND ND	115-94-0004R
USA (CA), 1991 (Golden Delicious)	EC	0.027 +oil	0.0038	2	0 28	0.019 0.020 0.010 0.008	0.003 0.003 NQ ND	001-91-6016R 618-936-AP
USA (CA), 1991 (Granny Smith)	EC	0.027 +oil	0.0010	2	0 28	0.009 0.010 ND ND	ND NQ ND ND	001-91-6024R 618-936-AP
USA (GA), 1992 (Red Delicious)	EC	0.027 +oil	0.0072	2	0 28	0.047 0.045 ND NQ	0.006 0.005 ND ND	001-92-0027R 618-936-AP
USA (MI), 1990 (Golden Delicious)	EC	0.028 +oil	0.0010	2	0 3 7 14 28 45	0.011 0.042 0.026 0.091 0.010 0.010 0.008 0.006 0.009 0.010 0.010 0.006 0.005 0.005 0.010 0.005 0.004 0.006 0.003 0.003 0.004 0.006 0.006 0.005	ND 0.005 0.004 ND NQ (4) NQ NQ NQ ND ND ND NQ NQ ND ND NQ ND ND (4)	001-90-5018R 618-936-AP
USA (MI), 1990 (Golden Delicious)	EC	0.056 +oil	0.0020	2	0 3 7 14 28 45	0.049 0.031 0.040 0.033 0.020 0.011 0.018 0.012 0.011 0.009 0.021 0.016 0.013 0.006 0.008 0.006 0.005 0.009 0.004 0.004 0.004 0.004 0.004 0.004	0.008 0.006 0.006 0.007 0.003 NQ 0.003 NQ NQ NQ 0.003 NQ NQ ND ND ND ND (4) ND (4)	001-90-5018R 618-936-AP

APPLE, country, year (variety)	Application				PHI, days	Residues, mg/kg 1/		Ref
	Form	kg ai/ha	kg ai/hl	no.		B_{1a} + 8,9-*Z* B_{1a}	B_{1b} + 8,9-*Z* B_{1b}	
USA (MI), 1991 (Jonathan)	EC	0.027 +oil	0.0036	2	1 7 14 28	0.008 0.008 0.002 0.003 NQ NQ NQ 0.002	ND ND ND ND ND ND ND ND	001-91-1024R 618-936-AP
USA (NC), 1992 (Red Delicious)	EC	0.026 +oil	0.0071	2	0 28	0.031 0.027 0.003 NQ	0.003 0.003 ND ND	001-92-0026R 618-936-AP
USA (NY), 1990 (Twenty Ounce)	EC	0.028 +oil	0.0007	2	0 3 7 14 28	0.011 0.012 0.030 0.018 NQ 0.004 0.011 0.012 0.002 0.003 0.004 0.005 0.002 NQ 0.003 0.002 ND NQ 0.003 NQ	0.002 0.002 0.004 0.003 ND ND NQ NQ ND (4) ND (4) ND (4)	001-90-5016R 618-936-AP
USA (NY), 1990 (Twenty Ounce)	EC	0.056 +oil	0.0015	2	0 3 7 14 28	0.033 0.028 0.028 0.035 0.062 0.011 0.016 0.009 0.015 0.007 0.003 0.008 0.003 0.002 0.003 0.004 0.002 NQ 0.003 0.003	0.004 0.004 0.004 0.005 0.009 NQ NQ NQ 0.003 NQ ND NQ ND (4) ND (4)	001-90-5016R 618-936-AP
USA (NY), 1991 (Red Delicious)	EC	0.027 +oil	0.0038	2	0 7 14 28	0.040 0.037 0.008 0.008 0.011 0.011 0.007 0.007	0.004 0.004 ND NQ NQ NQ ND ND	001-91-3000R 618-936-AP
USA (NY), 1992 (Rome Beauty)	EC	0.027 +oil	0.0072	2	0 28	0.020 0.020 NQ 0.004	0.002 0.003 ND ND	001-92-3020R 618-936-AP
USA (OR), 1992 (Golden Delicious)	EC	0.027 +oil	0.0008	2	0 28	0.022 0.017 0.003 ND	0.003 NQ ND ND	001-92-6012R 618-936-AP
USA (OR), 1992 (Red Delicious)	EC	0.027 +oil	0.0081	2	0 28	0.009 0.016 ND ND	ND NQ ND ND	001-92-1014R 618-936-AP
USA (WA), 1991 (Red Delicious)	EC	0.027 +oil	0.0011	2	0 28	0.012 0.010 ND NQ	NQ NQ ND ND	001-91-1021R 618-936-AP
USA (WA), 1991 (Red Delicious)	EC	0.026 +oil	0.0037	2	0 7 14 28	0.021 0.027 0.008 0.005 0.007 0.004 0.002 0.003	NQ 0.003 ND ND ND ND ND ND	001-91-1023R 618-936-AP

APPLE, country, year (variety)	Application				PHI, days	Residues, mg/kg 1/		Ref
	Form	kg ai/ha	kg ai/hl	no.		B_{1a} + 8,9-*Z* B_{1a}	B_{1b} + 8,9-*Z* B_{1b}	
USA (WA), 1992 (Red Delicious)	EC	0.027 +oil	0.0072	2	0 28	0.018 0.019 NQ ND	0.002 NQ ND ND	001-92-1018R 618-936-AP

1/ NQ: not quantitated; detected but <0.002 mg/kg.
ND: not detected, <0.001 mg/kg.

Table 3. Interpretation table for abamectin residues on apples from trials in Table 2. GAP and trial conditions are compared for treatments considered valid for MRL and STMR estimation.

APPLE	Use pattern				Trials	Residues, mg/kg abamectin
	kg ai/ha	kg ai/hl	No of applics	PHI days		
Australia GAP	0.014	0.0014	1	14		
Australia trial	0.014	0.0007	1	14	114-95-0003R	0.005
Australia trial	0.014	0.0007	1	14	114-95-0002R	<0.002
Australia trial	0.014	0.0008	1	14	114-95-0001R	0.003
NZ GAP	0.027	0.00068	1	14		
NZ trial	0.027	0.0014	2	14	115-94-0005R	0.004
NZ trial	0.027	0.0014	2	14	115-94-0004R	0.007
USA GAP	0.026	0.0007	2	28		
USA trial	0.028	0.0007	2	28	001-90-5016R	0.003
USA trial	0.027	0.0008	2	28	001-92-6012R	0.003
USA trial	0.027	0.0010	2	28	001-91-6024R	<0.001
USA trial	0.028	0.0010	2	28	001-90-5018R	0.006
USA trial	0.027	0.0011	2	28	001-91-1021R	<0.002
USA trial	0.027	0.0036	2	28	001-91-1024R	0.002
USA trial	0.027	0.0037	2	28	001-91-1023R	0.003
USA trial	0.027	0.0038	2	28	001-91-6016R	0.012
USA trial	0.027	0.0038	2	28	001-91-3000R	0.007
USA trial	0.026	0.0071	2	28	001-92-0026R	0.003
USA trial	0.027	0.0072	2	28	001-92-0027R	<0.002
USA trial	0.027	0.0072	2	28	001-92-3020R	0.004
USA trial	0.027	0.0072	2	28	001-92-1018R	<0.002
USA trial	0.027	0.0081	2	28	001-92-1014R	<0.001

Table 4. Abamectin estimated dietary intake. STMRs (supervised trials median residues) are available for 12 commodities, with the MRLs being used for the remaining 12. Total intake (µg/day) = sum of calculated intakes for each commodity. %ADI = total intake expressed as % of 60 □ ADI. Standard body weight is taken as 60 kg.

	Commodity	mg/kg			Diet, g/day					estimated dietary intake, µg/day				
		MRL	STMR	STMR (or MRL)	ME	FE	Afr	Lat Am	Eur	ME	FE	Afr	Lat Am	
				e	f	g	h	i	j	= e □ f	= e □ g	= e □ h	= e □ i	= e
660	Almonds	0.01*	0	0	0.5	0	0	0.1	1.8	0	0	0	0	
26	Apple	0.02	0.003	0.003	7.5	4.7	0.3	5.5	40	0.023	0.014	0.001	0.017	0.1
312	Cattle fat	0.01 V		0.01	0.3	0.3	0.3	1.5	0	0.003	0.003	0.003	0.015	
280	Cattle kidney	0.05 V		0.05	0.1	0	0.1	0.2	0.2	0.005	0	0.005	0.010	0.0
281	Cattle liver	0.1 V		0.1	0.2	0	0.1	0.3	0.4	0.020	0	0.010	0.030	0.0
9812	Cattle meat	0.01*		0.01	18.5	3.5	10.4	30	63.3	0.185	0.035	0.104	0.300	0.6
312	Cattle milk	0.005		0.005	79.5	23.2	35.8	159.3	287.0	0.398	0.116	0.179	0.797	1.4
001	Citrus fruits	0.01*		0.01	54.3	6.3	5.1	54.8	49	0.543	0.063	0.051	0.548	0.4
591	Cotton seed	0.01*		0.01	0	0	0	0	0	0	0	0	0	
424	Cucumber	0.01	0.005	0.005	4.8	4.5	0	8.3	9	0.024	0.023	0	0.042	0.0
9814	Goat meat	0.01*		0.01	2	0.7	2.3	0.8	0.3	0.02	0.007	0.023	0.008	0.0
314	Goat milk	0.005*		0.005	14	0.7	3.6	0.8	2.3	0.070	0.004	0.018	0.004	0.0
814	Goat, Edible offal of	0.1		0.1	0.3	0	0.4	0	0	0.030	0	0.040	0	
100	Hops, Dry	0.1	0.016	0.016	0	0	0	0	0	0	0	0	0	
483	Lettuce, Leaf	0.05	0.02	0.02	2.3	0	0	5.8	22.5	0.046	0	0	0.116	0.4
046	Melons, except watermelon	0.01*	0.002	0.002	16	2	0	2.8	18.3	0.032	0.004	0	0.006	0.0
30	Pear	0.02	0.005	0.005	3.3	2.8	0	1	11.3	0.017	0.014	0	0.005	0.0
445	Peppers, Sweet	0.02		0.02	3.3	2	5.3	2.3	10.3	0.066	0.040	0.106	0.046	0.2
589	Potato	0.01*	0	0	59	19.2	20.6	40.8	240.8	0	0	0	0	
431	Squash, Summer	0.01*	0.002	0.002	10.5	2.2	0	14	3.5	0.021	0.004	0	0.028	0.0
275	Strawberry	0.02		0.02	0	0	0	0	5.3	0	0	0	0	0.1
448	Tomato	0.02	0.0085	0.0085	81.5	7	16.5	25.5	66	0.693	0.060	0.140	0.217	0.5
678	Walnuts	0.01*	0	0	0	0	0	0	0.5	0	0	0	0	
432	Watermelon	0.01*	0.002	0.002	49.3	9.5	0	5.5	7.8	0.099	0.019	0	0.011	0.0
									Total (µg/day) =	**2.29**	**0.41**	**0.68**	**2.20**	**4.**
	ADI = 0.002 mg/kg bw or 0.12 mg/person									**2% ADI**	**0% ADI**	**1% ADI**	**2% ADI**	

ME: Middle Eastern diet. FE: Far Eastern diet. Afr: African diet. Lat Am; Latin American diet.
Eur: European diet
* MRL set at or about analytical limit of determination
V: MRL is based on a direct animal treatment.

SAMPLING AND FAT

Alan Hill

In principle, sampling of animal tissues should be relatively straightforward because the various organs or parts should be easily defined. However, uneven distribution of fat within an animal creates problems, especially for fat-soluble residues. Measurement of these residues on a fat basis provides one solution to the sampling dilemma but doesn't resolve all problems involved in controlling residues in traded food. So, provision of unambiguous instructions for sampling is actually rather difficult.

Following sampling, where the sample preparation (removal of bones, skin, etc.) and processing ("homogenisation") procedures, used in the development of an MRL, differ from the procedures adopted for monitoring and enforcement, the results are not likely to be comparable. Thus, as in the case of sampling, these procedures must also be described clearly.

Present recommendations for sampling animal products, and those proposed by CCPR, are summarised in Tables 1 and 2. Existing CCPR and CCRVDF recommendations are virtually identical and most of the recommendations proposed by CCPR are unlikely to affect measured residues, significantly.

The problems of fat are common to all sampling recommendations: fat is not well defined; it is often heterogeneously distributed within a commodity; and slightly illogical assumptions may be made in calculating residue levels from a fat basis. At its 30th session[1] CCPR proposed that MRLs for fat soluble pesticides in meat should apply to the "lipid portion" of the fat from any part of the animal.

Data provided by Australia in 1998 showed that residue distributions within different fatty tissues cut from a single animal could be expected to vary by a factor of 2 or so (an extreme case produced a factor of 5). The range of variation may have been larger or smaller if residue concentrations had been based on whole fatty tissues, because of "dilution" with non-lipid material. Fatty tissues are not 100% lipid material and the proportion of lipid may vary considerably. Up to 50% water and other fat insolubles may be present, especially as it may not be possible to obtain a sample of "pure" fatty tissue. In residues monitoring, lipid extraction may be by rendering or using solvents but determination of the "true" fat content requires a separate and potentially costly analysis. But MRLs for "fat" and for fat-soluble pesticides apply to the whole of the fatty tissue sample, not just the extracted lipid.

Actually, data evaluated by JMPR are rarely given in sufficient detail to distinguish the exact basis for expression of the results (comment from D J Hamilton, 1998), so there is clearly potential for monitoring and enforcement to be conducted on a different basis to that used to develop the MRL.

What if fatty tissues are not available for analysis? Where this is taken into account in deriving the MRL (e.g. rabbit), and there is no likelihood of a different approach for monitoring, there is no problem. However, in response to increasing consumer demand for leaner meat products, there is an increasing trend for much fat to be removed at some point in the trade. In this case,

the monitoring laboratory has no option but to extract the fat. Converting results for such products to a "whole fat" basis is impossible and an assumption is generally made that interstitial and adhering fats contain similar residue levels. There does not appear to be much evidence to support or refute this assumption.

Present Codex recommendations for low fat products produce some anomalies in the calculation of residue levels, if the original MRLs were not derived on the same basis.

> Group 31 fat of small animals (CCPR and CCRVDF, see Table 2). "Where adhering fat is insufficient to provide a suitable sample, the whole commodity, without bone, is analysed and the MRL applies to the whole commodity". This is most likely to apply to meat or carcasses bearing less than 10% fat but, if the MRL has the same basis, there is no problem. However, if the sample is analysed on the "opposite basis" to that used to derive the MRL, an error of more than a factor of 10 could be made. Fortunately, this situation should be rare.
>
> Group 30 mammalian meats (CCPR, see Table 1). "Where adhering fat is insufficient to provide a suitable sample, the whole commodity, without bone, is analysed and the MRL applies to the whole commodity (e.g. rabbit meat)". Now that leaner meats are frequently traded, this clause *appears* to include them, but the MRLs will have been derived on a fat basis and so products could appear to comply with MRLs, when in fact they do not.
>
> Groups 90 and 92 milk products (CCPR[2]). "Where the fat content is less than 2%, the MRL should be half that specified for milk but the MRL for those with a fat content of 2% or more should be 25 times the MRL specified for milk, on a fat basis. This assumes that milk contains 4% fat. A product containing less than 2% fat (say 1%) but made from "non-compliant" milk may thus comply with the MRL. Where an MRL is set on milk containing more or less than 4% fat (or alternatively where a product is made from such a milk), compliance/non-compliance may be determined incorrectly because the conversion factor is large.

In the UK, monitoring of fat soluble residues in animal products at slaughter is based on analysis of perirenal fat and the results are expressed on a whole product basis. Monitoring of fat soluble pesticide residues in imported and home-produced animal products at the retail and wholesale level is based on solvent-extracted fat. In this case, results are expressed an extracted fat basis for products with ≥10% fat, or on a whole product basis for products of <10% fat.

Apart from fat, there are other anomalies in the Codex recommendations for sampling of animal products.

The most important of these is the distinction made by JECFA/CCRVDF between meat[(a)] and muscle[(b)]. Neither definition is very explicit. In contrast, the JMPR/CCPR definition of meat[(c)] is

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(a) Meat: the edible part of any mammal.

(b) Muscle: muscle tissue only.

(c) Meat: muscular tissues, including adhering fatty tissues such as intramuscular and subcutaneous fat from animal cacasses or cut of these as prepared for wholesale or retail distribution in a "fresh" (including frozen or thawed) state. Cuts may include bones, connective tissues, tendons, nerves and lymph nodes).

much more explicit but could be interpreted as different from the product defined as meat by JECFA/CCRVDF. It would be helpful if the definitions were harmonised.

A difference of lesser importance but nonetheless anomalous is the description of whole eggs[(d)] . Perhaps the JECFA/CCRVDF definition just requires clarification, as it seems unlikely that measured residues would be affected significantly by the analysis of the shells.

Where do we go from here?

I have no easy solutions. Inadequate knowledge and the cost of developing MRLs for fat soluble pesticides on a new basis present major obstacles to resolving the "fat problems".

We need data on the relative levels of residues in adhering and interstitial fats. As significant differences occur in residue levels in the adhering fats of a single animal, it does not seem safe to assume that the levels in interstitial fat will be similar.

A central requirement is to ensure that a common definition of fat is used by all. JECFA and JMPR definitions appear simple but they create problems in some cases where fatty tissues cannot be removed as a sample. If the data used to develop the MRLs were not based on "whole" fatty tissue but an extracted fat basis, a change in the definition of the product to which the MRL applies would be of benefit to some enforcement agencies. A change to expression of MRLs (and residues) on a "whole product" basis would probably appear more logical to consumers, and would be simpler for analysts employing solvent extraction, but the MRLs would have to have been derived from similar data. Such data may not exist.

Harmonisation of definitions of "meat" and "eggs" between JECFA/CCRVDF and JMPR/CCPR should involve little risk of changing the basis for enforcement of MRLs.

CCPR has rationalised its recommendations for sampling[1]. Hitherto, these were similar to those of CCRVDF, although the respective definitions of the product to be analysed differed in some cases. Any harmonisation of JECFA and JMPR approaches to sampling that emerge from this meeting should be reflected in the new CCPR sampling recommendations.

References

1. Report of the 30th Session of the Codex Committee on Pesticide Residues, 1998. ALINORM 99/24, Appendix III.

2. Codex Alimentarius, volume 2, 2nd edition (1993). Pesticide Residues in Food, Section 1, p4.

3. Codex Alimentarius, volume 2, 2nd edition (1993). Pesticide Residues in Food, Sections 2 and 3.

(d) JMPR/CCPR: fresh edible portion of the body produced by female birds. JECFA/CCRVDF: egg (in shell) of domesticated chickens (hens).

4. Codex Alimentarius, volume 3, 2nd edition (1993). Residues of Veterinary Drugs in Foods, Sections 3 and 4.

Table1.Definitions of the portions of products to which MRLs apply and to be analysed

Commodity		**CCPR 1993**[3]	**CCRVDF 1993**[4]
Class B, type 6, mammalian products, group 30, meat	Definition	Muscular tissues, including adhering fatty tissues such as intramuscular and subcutaneous fat from animal cacasses or cut of these as prepared for wholesale or retail distribution in a "fresh" (including frozen or thawed) state. Cuts may include bones, connective tissues, tendons, nerves and lymph nodes	**Meat: the edible part of any mammal** **Muscle: muscle tissue only**
	Portion of commodity to which MRL applies	Whole commodity (without bones). For fat soluble pesticides a portion of adhering fat is analysed and MRLs apply to the fat. For those commodities where the adhering fat is insufficient to provide a suitable sample, the whole commodity (without bone) is analysed and the MRL applies to the whole commodity (e.g. rabbit meat).	Not defined
Class B, type 6, mammalian products, group 31, fat	Definition	Derived from the fatty tissues of animals (not processed). Excludes milk fats.	Not defined
	Portion of commodity to which MRL applies	Whole commodity	Not defined
Class B, type 6, mammalian products, group 32, offal	Definition	Edible tissue and organs other than muscles (=meat) and animal fat. Example: liver, kidney, tongue, heart, stomach, sweetbread (thymus gland), brain, etc.	Not defined
	Portion of commodity to which MRL applies	Whole commodity	Not defined

Class B, type 6, mammalian products, group 33, milk	Definition	The normal mammary excretion of lactating herbivorous ruminants, obtained from one or more milkings, without either addition thereto or extraction therefrom. The term also defines "milk" which may have been treated without affecting its composition, or milk of which the fat content has been standardised.	The normal mammary excretion of lactating herbivorous ruminants, obtained from one or more milkings, without either addition thereto or extraction therefrom. The term also defines "milk" which may have been treated without affecting its composition, or milk of which the fat content has been standardised. The term may be used in association with a word or words to designate the type, grade, origin and or intended use, or to describe the physical treatment **or the modification of composition to which it has been subjected, provided that the modification is restricted to an addition and/or withdrawal of natural milk constituents.**
	Portion of commodity to which MRL applies	Whole commodity	Not defined
Class B, type 7, poultry products, group 36, meat	Definition	Muscular tissues including adhering fat **and skin** from poultry carcasses as prepared for wholesale or retail distribution	Not defined
	Portion of commodity to which MRL applies	Whole commodity (without bones). For fat soluble pesticides a portion of adhering fat is analysed and MRLs apply to poultry fat **[Note: no indication of application to low fat products]**	Not defined
Class B, type 7, poultry products, group 37, fat	Definition	Derived from the fatty tissues of poultry	Not defined
	Portion of commodity to which MRL applies	Whole commodity	Not defined
Class B, type 7, poultry products, group 38, offal	Definition	Edible offal, other than meat and fat. Examples: liver, gizzard, heart, **skin**, etc.	Not defined
	Portion of commodity to which MRL applies	Whole commodity	Not defined

Class B, type 7, poultry products, group 39, eggs	Definition	Fresh edible portion of the body produced by female birds	Egg **(in shell)** of **domesticated chickens** (hens)
	Portion of commodity to which MRL applies	Whole egg whites and yolks combined after removal of shell	Not defined
Class E, processed foods of animal origin, type 16 secondary food commodities of animal origin, group 80, dried meat and fish products	Definition	Naturally or artificially dried meat and fish products, including other marine animals such as crustaceans	Not defined
	Portion of commodity to which MRL applies	Whole commodity as prepared for wholesale or retail distribution	Not defined
Class E, processed foods of animal origin, type 16 secondary food commodities of animal origin, group 82, Secondary milk products	Definition	Milk products which have undergone simple processing such as removal of certain ingredients e.g. water, milk fat etc. The group and the commodities therein will only be used for pesticides which are not partitioned exclusively or nearly exclusively into the milk fat. For example, milk powder, evaporated milk, skimmed milk.	Not defined
	Portion of commodity to which MRL applies	Whole commodity	Not defined
Class E, processed foods of animal origin, type 17 derived edible products of animal origin, group 85, processed animal fats	Definition	Processed animal fats, including rendered or extracted (possibly refined and/or clarified) fats from land and aquatic animals and poultry, and fats and oils derived from fish	Not defined
	Portion of commodity to which MRL applies	Whole commodity	Not defined

Class E, processed foods of animal origin, type 17 derived edible products of animal origin, group 86, milk fats	Definition	Fatty ingredients derived from the milk of various mammals	Not defined
	Portion of commodity to which MRL applies	Whole commodity	Not defined
Class E, processed foods of animal origin, type 17 derived edible products of animal origin, group 87	Definition	Food or edible substances isolated from milks, using physical, biological or chemical processes. The group and the commodities therein will only be used for pesticides which are not partitioned exclusively or nearly exclusively into the milk fat. For example, butter, butter oil, whey, cream powders, edible caseinates, etc.	Not defined
	Portion of commodity to which MRL applies	Whole commodity	Not defined
Class E, manufactured foods (single ingredient) of animal origin, type 18, group 90	Definition	Processed food consisting of one identifiable food ingredient, with or without minor ingredients. The group and the commodities therein will only be used for pesticides which are not partitioned exclusively or nearly exclusively into the milk fat. For example, cheese, yoghurt, etc.	Not defined
	Portion of commodity to which MRL applies	Whole commodity as prepared for wholesale or retail distribution.	Not defined
Class E, manufactured foods (multi-ingredient) of animal origin, type 19, group 92	Definition	Processed food consisting of more than one major food ingredient, in which animal ingredients are predominant. The group and the commodities therein will only be used for pesticides which are not partitioned exclusively or nearly exclusively into the milk fat. For example, processed cheese, flavoured yoghurt, sweetened condensed milk, etc.	Not defined
	Portion of commodity to which MRL applies	Whole commodity	Not defined

Group 030, mammalian meats, large mammal carcass	500g diaphragm muscle supplemented with cervical muscle if necessary	500g diaphragm muscle supplemented with cervical muscle if necessary	500g diaphragm muscle supplemented with cervical muscle if necessary
Group 030, mammalian meats, small mammal carcass	500g after removal of skin and bone hind quarters or whole carcass	500g after removal of skin and bone hind quarters or whole carcass	500g after removal of skin and bone hind quarters or whole carcass
Group 030, mammalian meats, fresh/chilled parts, unit weight >500g excluding bone	500g Muscle portion from one unit	500g Portion from one unit	500g Muscle portion from one unit
Group 030, mammalian meats, fresh/chilled parts, unit weight <500g	500g after removal of bone Units collected from 1 container	500g after removal of bone	500g after removal of bone Units collected from 1 container
Group 030, mammalian meats, bulk frozen parts	500g Cross-section from 1 container, or muscle from 1 large part	500g after removal of bone Cross-section from 1 container, or the whole (or portions) of individual meat parts	500g Cross-section from 1 container, or muscle from 1 large part
Group 030, mammalian meats, retail packaged	500g after removal of skin and bone A number of units from 1 container	500g after removal of bone	500g after removal of skin and bone A number of units from 1 container
Group 031, mammalian fats including carcass fat	500g Abdominal and subcutaneous fat from one or more animals MRL applies to sole (sic) commodity without bone where adhering fat is insufficient to provide a suitable sample	500g Abdominal or subcutaneous fat from one or more animals	500g Abdominal and subcutaneous fat from one or more animals MRL applies to whole commodity without bone where adhering fat is insufficient to provide a suitable sample
Group 031, mammalian bulk fat tissue	500g equal size portions from 3 locations	500g portions from at least 3 locations	500g equal size portions from 3 locations
Group 032, mammalian edible offal - liver Group 032, mammalian edible offal - kidney	400-500g Whole liver or portion 250-500g One or both kidneys from one or more animals Do not collect from more than 1 animal if the sample meets the low range for the laboratory sample size requirement	400g Whole liver or portion 200g One or both kidneys from one or more animals	400-500g Whole liver or portion 250-500g One or both kidneys from one or more animals Do not collect from more than 1 animal if the sample meets the low range for the laboratory sample size requirement

Group 032, mammalian edible offal - heart	400-500g Whole heart or ventricle portion to meet requirement for laboratory sample	400g Whole heart or ventricle portion to meet requirement for laboratory sample	400-500g Whole heart or ventricle portion to meet requirement for laboratory sample
Group 032, mammalian edible offal - other fresh, chilled or frozen	500g Portion derived from one animal unless product from more than 1 animal is required for laboratory sample. A cross-section from bulk frozen product	500g Portion derived from one or more animals. A cross-section from bulk frozen product	500g Portion derived from one animal unless product from more than 1 animal is required for laboratory sample. A cross-section from bulk frozen product
Group 033, mammalian milk	500g	500g	500g
Group 036, poultry meats, >2kg carcass	500g after removal of skin and bone Thighs, legs and other dark meat from one bird	500g after removal of skin and bone Thighs, legs and other dark meat	500g after removal of skin and bone Thighs, legs and other dark meat from one bird
Group 036, poultry meats, 500g - 2kg carcass	500g after removal of skin and bone Thighs, legs and other dark meat from 3-6 birds	500g after removal of skin and bone Thighs, legs and other dark meat from at least 3 birds	500g after removal of skin and bone Thighs, legs and other dark meat from 3-6 birds
Group 036, poultry meats, <500g carcass	250-500g muscle tissue from at least 6 carcasses	200g muscle tissue from at least 6 carcasses	250-500g muscle tissue from at least 6 carcasses
Group 036, poultry meats, parts, fresh, chilled, frozen	500g after removal of skin and bone 1 interior large unit, or units from 1 layer, from a wholesale container; or units from one retail container	500g after removal of skin and bone packaged or individual units	500g after removal of skin and bone 1 interior large unit, or units from 1 layer, from a wholesale container; or units from one retail container
Group 037, poultry fats, carcasses at slaughter	Sufficient for 50-100g fat Abdominal fat from 3-6 birds	500g Abdominal fat from at least 3 birds	Sufficient for 50-100g fat Abdominal fat from 3-6 birds
Group 037, poultry fats, other meat	500g of separable fat or 1.5-2kg if fat cannot be separated Sufficient for 50-100g fat	500g of separable fat or 2kg if fat cannot be separated	500g of separable fat or 1.5-2kg if fat cannot be separated Sufficient for 50-100g fat
Group 037, poultry fats, bulk fat	500g Equal size portions from 3 locations in container	500g Portions from at least 3 locations in container	500g Equal size portions from 3 locations in container
Group 038, Poultry edible offal, liver	250-500g 6 whole livers or sufficient to meet size requirement	200g (except as below) At least 6 whole livers or a cross-section from a container 50g Goose and duck fat liver and similar products of high value Unit from one bird or container	250-500g 6 whole livers or sufficient to meet size requirement

Group 038, Poultry edible offal, other	250-500g Parts from 6 birds. If frozen, a cross section of the container	200g Parts from 6 birds. If frozen, a cross section of the container	250-500g Parts from 6 birds. If frozen, a cross section of the container
Group 39, Poultry eggs	500g or 10 whole eggs	12 whole chicken eggs, 6 whole duck or goose eggs, 24 whole quail (or similar) eggs	500g or 10 whole eggs
Class E, type 16, secondary meat and poultry products, comminuted of single species	500g cross-section of container	500g or 2 kg if fat content <5% packaged units or cross-section of container, or units (including juices, if any) taken with a sampling device	500g cross-section of container
Class E, type 16, dried meat products	500g or 1.5-2 kg if fat content <5% and MRL is expressed on a fat basis Collect packaged units from one container	500g or 2 kg if fat content <5% packaged units or cross-section of container, or units (including juices, if any) taken with a sampling device	500g or 1.5-2 kg if fat content <5% and MRL is expressed on a fat basis Collect packaged units from one container
Class E, type 17, derived edible products of animal origin	200g	200g	200g
Class E, type 18, manufactured single ingredient product	500g or 1.5-2 kg if fat content <5% and MRL is expressed on a fat basis or 1 kg for unit sizes <1kg One can, or portion (including juices) if cans >2kg Cured, smoked, etc., take a whole unit or portion of a large unit 200g of cheese	500g or 2 kg if fat content <5% packaged units or cross-section of container, or units (including juices, if any) taken with a sampling device. 500g of cheese or 300g if units <300g	500g or 1.5-2 kg if fat content <5% and MRL is expressed on a fat basis One can, or portion (including juices) if cans >2kg Cured, smoked, etc., take a whole unit or portion of a large unit. 200g of cheese
Class E, type 19, manufactured multi-ingredient product	500g Cross-section portion of unit >2kg, or 1 whole unit or 1 kg for unit sizes <1kg	500g or 2 kg if fat content <5% packaged units or cross-section of container, or units (including juices, if any) taken with a sampling device. 300g processed cheese packed in units <300g	500g Cross-section portion of unit >2kg, or 1 whole unit 200g processed cheese

Appendix 2

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Appendix 3

Considerations by 1999 JMPR on Recommendations Arising from the Informal JMPR/JECFA Harmonization Meeting

The 1999 JMPR discussed only those recommendations addressed to the JMPR. The recommendations are listed below with comments provided.

Tissue

- *For the determination of fat-soluble pesticides/veterinary drug residues in meat/muscle for enforcement or monitoring purposes, laboratories are advised to collect and to analyse trimmable fat and to report the residue on a lipid basis, i.e. meat (fat) for JMPR and fat for JECFA. For meat without trimmable fat, the entire commodity should be analysed as meat/muscle, but only where the MRL has been set on a meat/muscle basis.*

The recommendation is in agreement with current JMPR practices of MRL setting for fat-soluble compounds.

- *For the determination of non-fat soluble pesticides/veterinary drugs residues in meat/muscle, laboratories are advised to analyse meat/muscle with trimmable fat removed, as far as is practical.*

The JMPR agrees that the practices for setting MRLs for non-fat soluble compounds for animal commodities (past and present) are in accord with the above recommendation. Data are reviewed for muscle, however the MRL is expressed as 'meat' for analytical requirements.

- *Where JMPR and JECFA have recommended MRLs for the same chemical with the same residue/marker residue definitions on the same commodity, the higher MRL should prevail.*

The JMPR is aware of this situation. However, the JMPR will evaluate the data received and report the estimated maximum residue level. The recommended MRL will take into account the CCRVDF MRL. The reviewer (JMPR/JECFA) should be alerted to the current status of the MRLs in both the CCPR and CCRVDF systems.

Milk

- *For the determination of fat-soluble pesticide/veterinary drug residues in milk, the milk fat portion of the fresh milk should be analysed, and the results should be expressed on a whole milk basis using 4% as the nominal fat content.*

The JMPR agree with the above recommendation, as this is the current practice in the evaluation of fat-soluble pesticides present in milk.

Harmonisation of residue definition

- *The working group noted disparate residue definitions by CCPR and CCRVDF for abamectin and recommended that CCRVDF/JECFA consider expansion of its residue definition to include other isomers, such as the photodegradation isomer of B1a. CCPR/JMPR should consider its need to include the various isomers as part of the periodic review of abamectin.*

The JMPR agree that residue definitions should be harmonised where possible and will consider the recommendation at the next periodic evaluation of abamectin. The scheduling of the periodic review of the compound is a matter for discussion by the CCPR priorities commmittee.

- *Cypermethrin and alpha-cypermethrin should remain as the marker residue definitions for their use as veterinary drugs for cypermethrin and alpha-cypermethrin, respectively, and cypermethrin (sum of isomers) should remain as the residue definition for the pesticide cypermethrin. Guidance should be supplied to laboratories on the designation of the measured residue as cypermethrin or alpha-cypermethrin based on the chromatography of the test substance.*

Cypermethrin is scheduled for periodic evaluation by the JMPR in September 2004 and will consider this issue further at that time. Cypermethrin is also scheduled for evaluation by JECFA in February 2000. However, it is noted that there may be enforcement problems if products containing the mixture of isomers are still registered alongside products containing a single pair of isomers, e.g. alpha-cypermethrin and zeta-cypermethrin where different MRLs exist for such products. In addition, exposure to animals may originate from both types of products and if laboratories are only monitoring for a single marker residue and not sum of isomers, problems may occur.

- *Harmonisation efforts should be undertaken on a case-by case basis where marker residue definition/residue definition differences occur between JECFA and JMPR.*

The JMPR agrees that harmonisation of residue definitions should occur where relevant. Different residue definitions are set by JMPR for enforcement and dietary intake purposes and this should be taken into account when harmonisation is considered.

- *CCPR should amend the note explaining the "V" designation for MRLs. The present description, "the MRL accommodates veterinary uses", is confusing and should be amended to "the MRL accommodates external treatments".*

The Meeting agreed to use the suggested amendment and include the amended terminology in future recommendations.

- *For compounds that are common to both, JMPR and JECFA should use the more specific animal commodity descriptions to enhance harmonisation. For example, separate MRLs for cattle muscle, goat muscle, horse muscle, pig muscle and sheep muscle are preferable to meat of cattle, goats, horses, pigs and sheep.*

The JMPR agrees that when there are existing MRLs for common pesticides resulting from

direct veterinary treatments (JMPR/JECFA), specific animal commodity MRLs (species specific) should be estimated rather than a generic MRL. This will allow JECFA to clearly see the origin of the MRL in relation to specific animal uses as opposed to MRLs set on the basis of exposure from feeding of treated feed items.

Dietary Intake Estimation and Risk Assessment

- *Each expert panel needs a better understanding of the other's procedure for food safety assessment for estimating MRLs and dietary exposure, for example. JECFA will provide JMPR with its guidance document describing the JECFA evaluation procedures when the draft version is finalised. The JMPR FAO Manual (1997) will be distributed to the JECFA members at the February 1999 meeting.*

The JMPR looks forward to the publication of the JECFA manual with interest and notes that the FAO manual has been distributed to JECFA members.

- *The JECFA/JMPR Group acknowledge the very different approaches used for dietary exposure determinations. JMPR will provide JECFA with detailed reports of its assessments, dietary intake calculations and % ADI determinations for compounds of interest to JECFA. When the data are available, JECFA will provide JMPR with median and upper limit animal commodity residue values and dietary intake calculations/% ADI determinations for compounds of interest to JMPR.*

There is a need to discuss further the two approaches of dietary intake and investigate in detail the current approaches used by JECFA. The JMPR is aware that in future intake estimates there is a need to take into account residues in animal commodities resulting from direct veterinary treatment for those pesticides which are not used on major animal feed commodities, *e.g.* thiabendazole and deltamethrin. It is noted that JECFA will provide median residue levels to the JMPR panel for inclusion in dietary intake assessments in place of the STMRs.

- *JECFA and JMPR should consider the exchange of one panel member each for a portion of the expert panel meetings to facilitate the harmonisation of MRLs and risk assessment for substances used as veterinary drugs and pesticides.*

The JMPR is willing to support exchange of panel members when there is a common interest in the review of a particular compound. The Meeting was aware that the Joint Secretaries had arranged for a JMPR Panel member to attend the JECFA meeting in 2000.

- *The Joint Secretary for JMPR will attend the JECFA meeting and the Joint Secretary for JECFA will attend the JMPR meeting, particularly when MRLs and risk assessments of substances used as veterinary drugs and as pesticides are being considered.*

The JMPR notes that this exchange may be useful.

- *Joint meetings of JMPR and JECFA should be held on an ad hoc basis to address issues of mutual interest, for example how to address MRL and ADI issues for classes of compounds with common modes of action, e.g. organophosphate compounds.*

Dietary intake assessments and other matters should be discussed at *ad hoc* meetings in the interest of continued harmonisation.

1. For compounds of mutual interest, JMPR and JECFA should have each other's recommendations/reports available when conducting evaluations. The Joint Secretaries will have responsibility for obtaining and distributing the documents and information, as appropriate.

The Joint Secretaries should have the appropriate evaluation reports and it is essential that this information is given to the Joint Secretaries at scheduling of the compounds. The Meeting recommended that the information should be provided to the panel member reviewing the compound at a very early stage. The information should include the full evaluation report.