Food and Agriculture Organization of the United Nations

World Health Organization

MODULE III: Templates and instructional guides for preparation of monograph and summary documents by members and experts invited by FAO to attend a meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) on the evaluation of residues of veterinary drugs in foods

FAO JECFA Secretariat

March, 2016

Guidance for residue experts for document preparation is in blue font in text boxes in the instructional guides. Text in red indicates sections of Summary documents which are completed by the toxicology experts. These toxicology headings are included only to provide the FAO residue drafting experts with an understanding of the layout of final Committee Summary documents for inclusion in the meeting report.

Instructions for use: Save a copy of the templates (Module III – Part I), then prepare a working template by making a copy of the specific template which fits the assignment. Follow the instructions in the text boxes of the matching instructional guide for the template and for additional instructions on document preparation refer to Module II.

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Overview

This module contains a series of templates in Part II which are intended to assist drafting experts and reviewers in the preparation of documents for a JECFA Meeting, including monographs for the initial review of substances (Template 1), monographs for re-evaluation of a substance, published as an Addendum (Template 2), monographs responding to specific questions from the CCRVDF or concern forms from Codex member states (Template 3) and discussion papers (Template 4). Templates for the summary documents corresponding to these monographs and discussion papers are provided in Templates 5-8.

Drafting experts are encouraged to use the appropriate templates to assist with preparation of monographs and accompanying summary documents for their JECFA assignments. These templates do not address all potential issues that may arise from a JECFA assignment and experts may choose to delete or substitute headings or sub-headings provided in a template when this will better address the review of the material. However, when such changes are required, drafting experts are strongly encouraged to review previous JECFA monographs and accompanying summary documents (found in the meeting reports) to find a format and headings used in earlier JECFA publications which can serve as a template for their current assignment.

When such situations arise, drafting experts are encouraged to provide a template which reflects the format and layout used in their monograph and summary to be added to the collection of templates in Module III.

An instructional guide is provided for each template in Part I. Do not use the instructional guide template for monograph preparation – use it only as a source of information to assist with use of the matching template. Each instructional guide includes the template layout, with instructions in text boxes on completion of the template and also some example text and tables to assist the expert in preparing a monograph or discussion paper and the accompanying summary.

Part I: Instructional guides for use of templates

Instructional guide for Template 1 (Template for a monograph providing the initial review of a substance)

The standard paper size for JECFA documents is A4. Standard font for monograph body text is Times New Roman 12.

Substance Name

Use the substance name as listed in the call for data from the JECFA Secretariat and as given in the priority list from the CCRVDF. Use font Times New Roman, 16, bold.

First draft prepared by

Drafting expert name, city, country
and
Reviewer name, city, country

Do not include academic titles. Font is Times New Roman 12, names in bold text. Use the same format if there are additional reviewers.

Identity

Font Times New Roman 14 bold.

International Non-proprietary Names (INN):

Synonyms:

IUPAC Name:

Heading font Times New Roman 12 bold; information on substance Times New Roman 12.

Chemical abstract Service No.:

Structural formula:

Insert structural diagram here.

If inserting the figure in a text box or as an object, use the" lock anchor" feature in "layout" to anchor the structural diagram in place.

Molecular formula:

Molecular weight {or Molecular weight of the salt form (when applicable)**}:**

Always take care to specify whether information provided relates to the pure active substance or a salt form used in product formulations.

Other information on identity and properties

Section heading font Times New Roman, 14, bold.

Pure active ingredient:

Appearance:

Impurities:

Melting point:

Solubility:

Log Ko/w or Partition Coefficient:

pH:

Optical rotation:

UV_{max}:

Stability:

Sub-heading font Times New Roman, 12, bold, information on each item in Times New Roman, 12 (not bold). Use each of these sub-headings which are applicable and for which information is available. Sub-headings which are not applicable should be deleted. Additional headings may be used by a drafting expert when other pertinent information on identity and properties is available for a substance.

Residues in food and their evaluation

Section heading font Times New Roman, 14, bold.

Conditions of use

Sub-heading font Times New Roman, 12, bold italics. Body text Times New Roman, 12. Leave single space between sub-heading and body text. Provide information on the approved conditions of use in member states of the Codex Alimentarius Commission. General information on the nature of the substance should be included, such as the activity of the substance (i.e., state whether the substance is used as an anti-bacterial, a coccidiostat, etc.) and the species against which the substance is active or the condition for which it is used as a therapeutic treatment. For agents approved for other uses, such as use as a production aid, state the nature of such approved use. The information in this section should also include the nature of the formulation or formulations approved for use, the species and class of food-producing animals for which the substance is approved and may also include withdrawal periods imposed by national authorities. Any restrictions on the use should be noted. Where there is information on approved usage in a number of countries for multiple species, the

Dosage

Sub-heading font Times New Roman, 12, bold italics. Body text Times New Roman, 12. Leave single space between sub-heading and body text. Provide information on the approved formulation(s), approved route(s) of administration and dosage(s) and the food-producing animals to which they apply.

Pharmacokinetics and metabolism

Section heading font Times New Roman, 14, bold.

Pharmacokinetics in laboratory animals

Sub-heading font Times New Roman, 12, bold italics.

Rats

Mice

Species font Times New Roman, 12, bold. Body text Times New Roman, 12. Leave single space between sub-heading and body text. Use sub-headings provided in template for all species that are applicable and delete any species sub-headings when there is no information for these species.

Dog

Monkey

Other

Example of type of table that might be included in this section.

Table _. Mean pharmacokinetic parameters for (compound name) in Sprague-Dawley rat plasma after dosing by dietary admixture or gavage (reference).

Route of administration	**Days**	**Dose** (mg/kg/day)	**Sex**	**T_{max}** (h)	**C_{max}** (ng/mL)	**$AUC_{(0\text{-}24h)}$** (ng.h/mL)
Dietary admixture			M F			
			M F			
Gavage			M F			
			M F			

Pharmacokinetics in Food-producing Animals

Section sub-heading font Times New Roman, 12, bold italics.

Cattle

Pigs

Species font Times New Roman, 12, bold. Body text Times New Roman, 12. Leave single space between species sub-heading and body text. Use sub-headings provided in template for all species that are applicable and delete any species sub-headings when there is no information for these species.

Sheep

Goat (or other mammal, such as deer or rabbit)

Chicken

When there are only limited data and studies which include several species of poultry, the sub-heading "poultry" may be used instead of using a sub-heading for each individual species. In general, a separate sub-heading should be used for each species for which significant data are provided and for which an MRL recommendation will be made.

Turkey (or other poultry, such as duck, pheasant or quail)

Delete any species sub-headings which do not apply.

Salmon (or other fish species)

When data are provided for multiple species of fish or seafood, it may be appropriate either to provide a sub-heading for each named species or, when the data are limited, but cover multiple species, to use the sub-heading "fish". In general, a separate sub-heading should be used for each species for which significant data are provided and for which an MRL recommendation will be made.
When referring to "fish", use the terminology agreed by the 78th JECFA; the specific species should be named when MRLs apply only to that species. For more general application of MRLs, the term "fish" should be used when an MRL recommendation applies to multiple species of finfish. For other "seafood", the term "mollusc" should be used for species such as clams, oysters and scallops, and the term "crustacean" should be used when MRLs are recommended for species such as shrimp, prawn and crayfish.

Predictive approaches using structure activity relationships or in silico tools to predict ADME properties

Sub-heading font Times New Roman, 12, bold italics. Include this sub-heading at the end of the pharmacokinetics section of the monograph only when there are relevant studies to discuss.

Metabolism in Laboratory Animals

Sub-heading font Times New Roman, 12, bold italics.

Rats

Mice

Species sub-heading font Times New Roman, 12, bold. Body text Times New Roman, 12. Leave single space between sub-heading and body text. Use sub-headings provided in template for all species that are applicable and delete any species sub-headings when there is no information for these species.

Dog

Monkey

Other

Delete any species sub-headings which do not apply.

Metabolism in Food Producing Animals

Sub-heading font Times New Roman, 12, bold italics.

Cattle

Pigs

Sheep

Sub-heading font Times New Roman, 12, bold. Body text Times New Roman, 12. Leave single space between sub-heading and body text. Use sub-headings provided in template for all species that are applicable and delete any species sub-headings when there is no information for these species.

Goat (or other mammal, such as deer or rabbit)

Delete any species sub-headings which do not apply.

Chicken

See previous guidance on when to use the term "poultry".

Turkey (or other poultry, such as duck, pheasant or quail)

Salmon (or other fish species)

See previous guidance on terminology for fish.

Comparative metabolism

Heading font is Times New Roman, 12, bold italic. Include this sub-section when there are in vitro comparative metabolism studies to discuss and/or to provide a summation of the metabolism data provided for various species. Include a metabolic pathway figure whenever possible. Tables may also be used, as appropriate, to compare metabolism across various species or to present complex metabolic data. See the examples referred to in Module II guidance.

Tissue residue depletion studies

Heading font Times New Roman, 14, bold.

Radiolabelled residue depletion studies

Cattle

Sub-heading font Times New Roman, 12, bold italics. Only depletion studies in food animal species are usually included in this section.

Lactating dairy cows

Pigs

Sub-heading font Times New Roman, 12, bold. Body text Times New Roman, 12. Leave single space between sub-heading and body text. Use sub-headings provided in template for all species that are applicable and delete any species sub-headings when there is no information for these species.

Sheep

Goat (or other mammal, such as deer or rabbit)

Delete any species sub-headings which do not apply.

Chicken

When data are provided for multiple species, it may be appropriate either to provide a sub-heading for each named species or, when the data are limited, but cover multiple species, to use the sub-heading "poultry". In general, a separate sub-heading should be used for each species for which data are provided and for which an MRL recommendation will be made.

Turkey (or other poultry, such as duck, pheasant or quail)

Salmon (or other fish species)

When data are provided for multiple species, it may be appropriate either to provide a sub-heading for each named species or, when the data are limited, but cover multiple species, to use the sub-heading "fish". In general, a separate sub-heading should be used for each species for which data are provided and for which an MRL recommendation will be made.

Example of type of table that should be included in this section to demonstrate relationship between marker residue and total residues.

Time post-dose (h)	kidney			Liver			muscle			skin/fat		
	total (µg/kg)	marker (µg/kg)	M/T ratio (%)	total (µg/kg)	marker (µg/kg)	M/T ratio (%)	total (µg/kg)	marker (µg/kg)	M/T ratio (%)	total (µg/kg)	marker (µg/kg)	M/T ratio %
0												
24												
72												
120												
168												-

Use hours (h) or days (d) as the time unit, as appropriate.

Residue depletion studies with non-radiolabelled drug

Heading font Times New Roman, 12, bold italics. Only depletion studies in food animal species are usually included in this section.

Cattle

Lactating dairy cows

Pigs

Sheep

Delete sub-headings for species for which data were not provided. Sub-heading species names in Times New Roman 12 bold, body text in Times New Roman 12 (not bold).

Goat (or other mammal, such as deer or rabbit)

Chicken

When data are provided for multiple species, it may be appropriate either to provide a sub-heading for each named species or, when the data are limited, but cover multiple species, to use the sub-heading "poultry". In general, a separate sub-heading should be used for each species for which data are provided and for which an MRL recommendation will be made.

Turkey (or other poultry, such as duck, pheasant or quail)

Salmon (or other fish species)

When data are provided for multiple species, it may be appropriate either to provide a sub-heading for each named species or, when the data are limited, but cover multiple species, to use the sub-heading "fish", "mollusc" or "crustacean". In general, a separate sub-heading should be used for each species or classification of fish or seafood for which data are provided and for which an MRL recommendation will be made.

Example of type of table that should be included in this section to demonstrate depletion profile for each major species for which MRLs will be recommended. Include similar table for minor species for which data are available. Provide the calculated mean concentration and standard deviation for each tissue and timepoint.

Withdrawal period (d)	**Mean concentration of marker residue (name) (µg/kg)**			
	muscle	**kidney**	**liver**	**fat** *or* **skin/fat**
0	mean ± std. dev.			
1				
2				
Etc.				

Methods of analysis for residues in tissues

Heading font Times New Roman 14 bold.

When multiple approaches to analysis of the marker residue are available, a short introductory paragraph may be included. The various types of methods available are then discussed under appropriate sub-headings, by instrumental technique, such as the sample sub-headings provided. Use other appropriate sub-headings, as required.

Example: Methods suitable for screening samples for potential non-compliant residues are available. In addition, quantitative methods based on high performance liquid chromatography with tandem mass spectrometry (LC-MS/MS) and high performance liquid chromatography with fluorimetric detection (HPLC/FL) were developed and validated in compliance with GLP.

Screening methods

Sub-heading text Times New Roman, 12, bold. It may be appropriate to refer to a particular technology, such as "ELISA" or "Biosensor" in this sub-heading when such suitable screening methods are available.

Quantitative methods

Include all methods which provide a quantitative result, under sub-headings by technique. Quantitative and confirmatory sub-headings may be combined when methods provide both types of result.

Liquid chromatography (LC)

Start with the least expensive quantitative techniques, such as liquid chromatography or gas chromatography, then proceed to the MS and MS/MS-based techniques. Indicate whether a method is suitable for quantitation only or whether it also can provide confirmation. Each method should be assessed according to the criteria found in CAC/GL 71 (2009, specifically the section dealing with Analytical Methods for Residue Control.

Liquid chromatography – mass spectrometry (LC-MS)

Follow the same order when presenting GC-based methods – GC, GC-MS, GC-MS/MS or GC-MS^n.

Confirmatory methods

Include all methods which provide a confirmatory result, under sub-headings by technique.

Liquid chromatography – tandem mass spectrometry (LC-MS/MS)

A table may be included in this section to demonstrate the completeness of the validation package for each matrix for a method that will be recommended as suitable to support recommended MRLs. If information is only provided for fortified samples, do not include a sub-heading for incurred samples. When other methods are provided, such as capillary electrophoresis, include a sub-heading for this technique. State if interferences are observed and describe the method briefly. Include information on matrix effects for MS-based methods using LC separation. State if issues are identified during ruggedness testing.

	Tissue (e.g., Liver)		**Tissue (e.g., Muscle**	
	Fortified samples	**Incurred samples**	**Fortified samples**	**Incurred samples**
Intraday accuracy (% bias)				
Intraday precision (% CV)				
Interday accuracy				
Interday precision				
LOQ / LOD µg/kg				
Analytical range				
Linearity (r^2)				
Specificity/selectivity	No interference observed		No interference observed	
Matrix effect				
Ruggedness testing	Acceptable		Acceptable	
Extraction recovery	76 - 79%		81 - 83%	
Stability: • Freeze-thaw • Room temperature • Extract • Stock solution	4 cycles __ hours ___ hours __ days		4 cycles __ hours ___ hours	
Confirmatory analysis: • Incurred samples • Fortified samples	<10% <10% with __exceptions		<10% with 2 exceptions <10% with 2 exceptions	

Information on analyte stability may be provided under a separate sub-heading. The stability information may be presented in a separate table or in text or figures.

Stability of residues

Heading font Times New Roman, 12, bold. Stability studies should include analyte specific information, such as the stability of the analyte in standard solutions or during preparation of samples for analysis. There may be method-specific stability information, such as steps in a method where stability may be at risk if specific directions are not followed or during extended wait times in autosampler trays. Include information on the required conditions of storage for sample material and residue degradation during storage of samples. Warnings concerning analyte stability should be included in the opening part of this section. Method-related information on stability should be included in the evaluation of each method for which such information is provided. Sample stability during storage should be addressed under the sub-heading “Stability of residues during storage”

Appraisal

Heading font Times New Roman, 14, bold.

Systematically review the information presented in the preceding sections of the monograph, establishing the basis on which MRL recommendations will be formulated. It should be relatively short and concise, reviewing the available information for each key element, noting deficiencies in information that was provided for review and giving expert opinion, thus providing the basis for MRL recommendations in the following section of the monograph. It is not necessary to repeat tables or figures from other sections of the monograph in this section. In some cases, particularly when there are a large number of studies to discuss, it may be helpful to prepare a summary table which incorporates key information from multiple studies.
This section of the monograph will be used by readers who wish to understand the basis for the MRL recommendations, but may not be residue experts themselves. It is appropriate to include depletion curves showing the estimated daily intake and/or tolerance limits for the substance in this section.

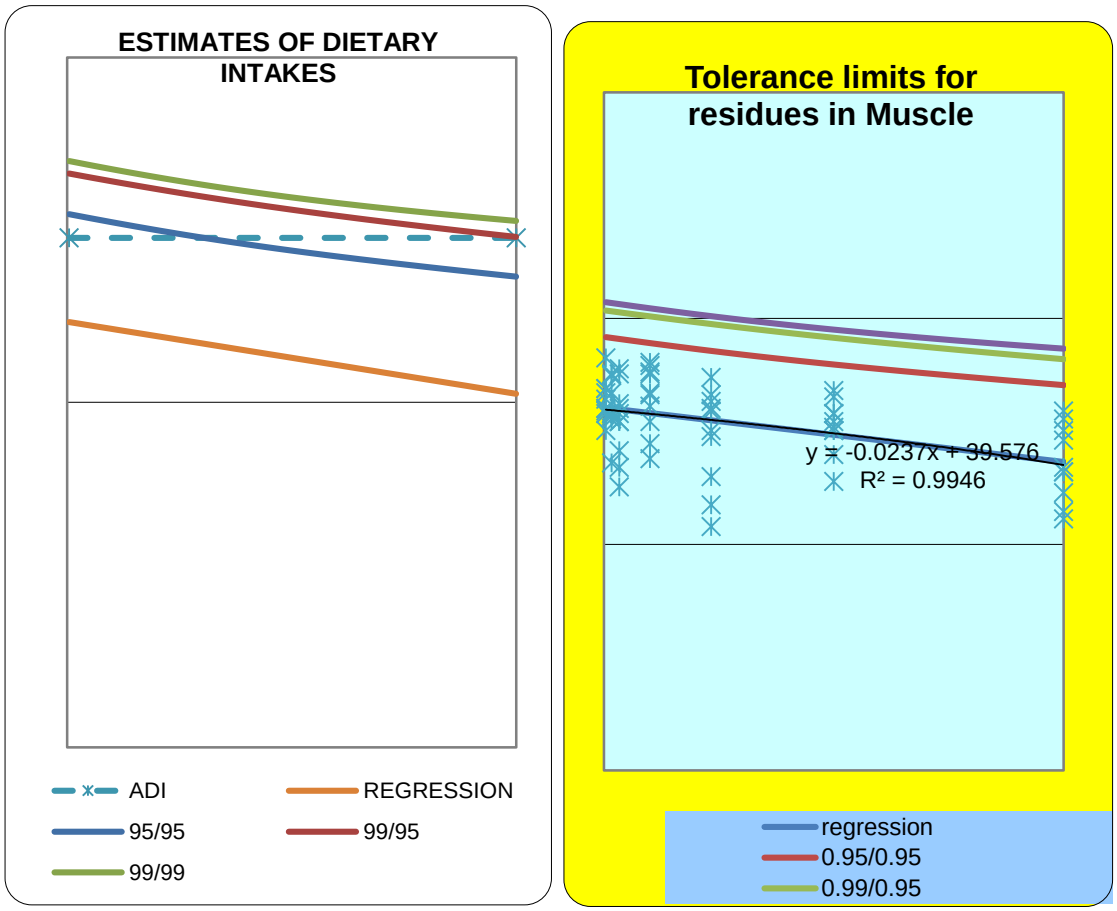
Dietary Exposure Assessment

Heading font Times New Roman, 12, bold italics.

Body text Times New Roman, 12. Include in this section information on which type of exposure assessment was used (EDI, TMDI, GEADE or other), the reason this type of assessment was chosen, including whether the exposure is based on a chronic or acute exposure (or both), the data used and the outcome. A table detailing the intake calculation should be included. It is appropriate in this section to include figures showing the tolerance limit plots on which the MRL is based and the corresponding median concentrations used in the EDI (or other) calculations of dietary exposure. The table should include the residue concentrations used and any factors used in the calculation. See Module II for additional guidance and examples. examples. Identify in the table caption whether the intake calculation is an EDI, a TMDI, a GEADE or other, such as GECDE. Indicate the number of days post-dosing at which the MRLs are recommended, based on the data provided. In the footnote to the table, indicate whether this is consistent with the shortest withdrawal time established under the GVP in a member state or if it may be inconsistent with such

Example: The Appraisal section may contain figures showing the tolerance limits and also the dietary intake estimates.

Figure 3. Estimated dietary intakes (expressed as emamectin benzoate equivalents) and tolerance limits in salmon muscle expressed as emamectin B1a.



Source: Monograph on emamectin benzoate prepared for the 78th JECFA

Example dietary intake table.

Table _: EDI based on median residues at Day _*.

Tissue	Median concentration* (µg/kg)	Standard Food Basket (kg)	MR:TR ratio [1]	Daily intake (µg)
Muscle		0.3		
Liver		0.1		
Kidney		0.05		
Fat		0.05		
Milk		1.5		
Eggs		0.1		
Honey		0.05		
TOTAL				

* Day is the shortest withdrawal period identified for GVP use in a member state.
[1] M:T ratio is the ratio of marker residue to total residue.

The EDI (or other intake calculation) is ___ µg/person per day, which represents __% of the upper bound of the ADI (or ARfD).

Maximum Residue Limits

Heading font Times New Roman, 14, bold.

In recommending MRLs for _(substance name)_ in _(name the species)_, the Committee considered the following factors:

- Body text font Times New Roman 12. When MRLs are recommended, use a statement such as given here to begin this section, followed by the bullet points which list the considerations leading to the decision. Include a statement such as the following immediately after the bullet points.

MRLs were calculated on the basis of the …..

Usually the basis for the MRL recommendations is the upper limit of the one-sided 95% confidence interval over the 95th percentile of the residue concentration (the "upper tolerance limit 95/95" or UTL 95/95) for day… There may be instances when a different basis is used and explanation should be provided for this choice in such cases.

Include next a statement of the MRL recommendations, giving the MRL recommended for each food (tissue, milk, eggs, honey) and species. State if any recommendations are for temporary MRLs.

The Committee recommended MRLs for _____.

When MRLs are not recommended or when recommendations include temporary MRLs, include the following statement.

Before re-evaluation of _(substance name)_ with the aim of recommending permanent MRLs in tissues of _(species)_, the Committee would require ….

When residue data are insufficient for the recommendation of full MRLs, finish this section with a clear statement of what additional studies are required to address the deficiencies in the data provided.

References

Heading font Times New Roman, 14, bold.

References cited in the monograph are listed in this section in alphabetical order, with author name(s) in bold, followed by the year of publication. The full name of the report or publication is given, followed by the source. For publications from the scientific literature, the full name of the journal (no abbreviations) or book is in italics. For books, include the publisher name, city and country. If a publication is not in English, include the language of publication in brackets at the end of the citation. See Module II for examples and additional details.

Instructional guide for Template 2 (Template for a monograph providing an addendum to an earlier review of a substance when new data are provided)

The standard paper size for JECFA documents is A4. Standard font for monograph body text is Times New Roman 12.

Substance Name

Use the substance name as listed in the call for data from the JECFA Secretariat and as given in the priority list from the CCRVDF. Use font Times New Roman, 16, bold.

First draft prepared by

Drafting expert name, city, country
and
Reviewer name, city, country

Do not include academic titles. Font is Times New Roman 12, names in bold text. Use the same format if there are additional reviewers.

Addendum to the monograph prepared by the __th meeting of the Committee and published in the _____.

Include this statement, giving the meeting at which the previous review was conducted and the name of the monograph publication issued by FAO. Residue monographs were published in the series FAO Food and Nutrition Paper 41/__ up to and including the 62nd JECFA, after which residue monographs were published in the series FAO JECFA Monographs.

Identity

Heading Font Times New Roman 14 bold.

International Non-proprietary Names (INN):

Synonyms:

IUPAC Name:

Chemical abstract Service No.:

Heading font Times New Roman 12 bold; information on substance Times New Roman 12.

Structural formula:

Insert structural diagram here.

If inserting the figure in a text box or as an object, use the" lock anchor" feature in "layout" to anchor the structural diagram in place.

Molecular formula:

Molecular weight {or Molecular weight of the salt form (when applicable)**}:**

Always take care to specify whether information provided relates to the pure active substance or a salt form used in product formulations.

Other information on identity and properties

Heading font Times New Roman, 14, bold.

Pure active ingredient:

Appearance:

Impurities:

Melting point:

Solubility:

Sub-heading font Times New Roman, bold, information on each item in Times New Roman, 12 (not bold). Use each of these sub-headings which are applicable and for which information is available. Sub-headings which are not applicable should be deleted. Additional headings may be used by a drafting expert when other pertinent information on identity and properties is available for a substance.

Log Ko/w or Partition Coefficient:

pH:

Optical rotation:

UV_{max}:

Stability:

The sections "Identity" and "Other information on identity and properties" are usually omitted in an addendum unless there is a major re-evaluation of the substance reported in the monograph.

Background

Heading font Times New Roman, 14, bold. Body text Times New Roman 12. This section is only included when the monograph is identified as an addendum to a previous monograph. The Background section should:

- Identify the meeting or meetings at which the substance was previously considered.
- State what decisions were taken at each previous meeting where the substance was considered by the Committee.
- Identify any requests for additional data which were made in the reports of the previous meetings and the date by which such data were requested, using the precise wording of the earlier report.
- When the substance is on the agenda for further review as a result of a specific request from CCRVDF or as a decision of the JECFA Secretariat, state the specific reason(s) for the referral, using the precise language of the referral.
- State what information has been received from the Sponsor or other sources for review by the Committee in response to the Call for Data.

Residues in food and their evaluation

Use appropriate headings and sub-headings from Template 1 to address the data that were provided for review and also to state where data were requested to address an issue, but not provided. The only heading used, for example, might be Methods of Analysis if the only data requested were for a suitable analytical method. Use fonts as directed in the Instructional Guide for Template 1.

Appraisal

Heading font Times New Roman, 14, bold. Body text is Times New Roman 12. Prepare this section as directed in the Instructional Guide for Template 1, providing an assessment of any new data and a review of the material considered previously by JECFA, as appropriate.

Dietary Exposure Assessment

Heading font Times New Roman, 12, bold italics.

Body text is Times New Roman 12. Content of this section depends on whether the new data provide the basis for an exposure assessment. If an exposure assessment is included, follow the format given in Template 1. Consult recent monographs to find an example which fits your situation.

Maximum Residue Limits

Heading font Times New Roman, 14, bold. Body text is Times New Roman 12. Content of this section depends on whether the new data lead to MRL recommendations. If MRLs are recommended, follow the format given in Template 1. If MRLs are not recommended, reasons should be provided and any additional data requirements identified. Consult recent monographs to find an example which fits your situation.

References

Heading font Times New Roman, 14, bold. Follow instructions in the Instructional Guide for Template 1 for citation format.

Instructional guide for Template 3 (Template for a monograph providing an addendum based on question from CCRVDF or a concern form from a Codex member state when no new data have been provided)

The standard paper size for JECFA documents is A4. Standard font for monograph body text is Times New Roman 12.

Substance Name

Use the substance name as listed in the call for data from the JECFA Secretariat and as given in the priority list from the CCRVDF. Use font Times New Roman, 16, bold.

First draft prepared by

Drafting expert name, city, country
and
Reviewer name, city, country

Addendum to the monograph prepared by the __th meeting of the Committee and published in the _____.

Include this statement, giving the meeting at which the previous review was conducted and the name of the monograph publication issued by FAO. Residue monographs were published in the series FAO Food and Nutrition Paper 41/__ up to and including the 62nd JECFA, after which residue monographs were published in the series FAO JECFA Monographs.

Do not include academic titles. Font is Times New Roman 12, names in bold text. Use the same format if there are additional reviewers.

Heading font Times New Roman 14, bold. This section is only included when the monograph is identified as an addendum to a previous monograph. Body text Times New Roman 12.

Background

The Background section should:

- Identify the meeting or meetings at which the substance was previously considered.
- State what decisions were taken at each previous meeting where the substance was considered by the Committee.
- When the substance is on the agenda for further review as a result of a specific request from CCRVDF or as a decision of the JECFA Secretariat, state the specific reason(s) for the referral, using the precise language of the referral.
- State what information has been received from the Sponsor or other sources for review by the Committee in response to the Call for Data.

Current evaluation

Heading font Times New Roman 14, bold.

Concern from Member State

Heading font Times New Roman 12, bold. Use this heading when the monograph is addressing a concern form submitted by a Codex member state requesting re-evaluation of data or further clarification of recommendations made by a previous meeting of JECFA. Body text Times New Roman 12.

Alternative approach proposed by the sponsor

Or

Additional comment provided by the sponsor

Heading font Times New Roman 12, bold. Use a suitably descriptive sub-heading when the sponsor has provided comment or suggestions on a previous JECFA decision, but has not provided additional data.

Appraisal

Heading font Times New Roman, 14, bold. Body text is Times New Roman 12. Review the materials provided in the question from CCRVDF, the Codex member state concern form and/or the comments from the Sponsor in the light of the previous JECFA decision. Address each issue raised and provide a critical assessment of the validity, including whether the new information provided should result in a change in the previous decision.

Dietary Exposure Assessment

See Template 1 and follow instructions as appropriate to the decision by the current Committee. When the decision involves a change in MRL recommendations, a table showing the revised exposure calculation should be included.

Maximum Residue Limits

Heading font Times New Roman, 14, bold. Body text is Times New Roman 12. Content of this section depends on whether the new data leads to MRL recommendations. If it does, follow the format given in Template 1. If MRLs are not recommended, reasons should be provided and any additional data requirements identified. Consult recent monographs to find an example which fits your situation.

References

Heading font Times New Roman, 14, bold. Follow instructions in the Instructional Guide for Template 1 for citation format.

Instructional guide for Template 4 (Template for a discussion paper published as a monograph or annex)

The standard paper size for JECFA documents is A4. Standard font for monograph body text is Times New Roman 12.

Discussion Paper Title

Title font Times New Roman 16, bold.

First draft prepared by

Drafting expert name, city, country
and
Reviewer name, city, country

Do not include academic titles. Font is Times New Roman 12, names in bold text. Use the same format if there are additional reviewers.

Introduction

Heading font Times New Roman 14, bold. Use Times New Roman 12 in body text. This section provides an explanation of why the matter is under consideration, and the process followed, such as information received in response to a request to Codex member states and interested parties by the JECFA Secretariat, an information request from the CCRVDF or discussion by JECFA of the results of an expert consultation on a topic.

Background

Heading font Times New Roman 14, bold. Use Times New Roman 12 in body text. This section provides a more detailed explanation of the issue, past JECFA work and decisions on the issue and any other relevant historical information. Depending on the topic, the Introduction may be omitted and all relevant information relating to the history of the issue may be given in the Background.

Sources of guidance

Heading font Times New Roman 14, bold. Use Times New Roman 12 in body text. In this section, discuss any existing guidance materials that are available from sources other than JECFA which may inform the decision-making process. In some cases, "Information sources" may be a more appropriate section heading.

Discussion or evaluation of the issue

Select a heading or headings which reflect the topic and the evaluation being conducted. See the papers on assessment of a new approach to dietary exposure estimates, the extrapolation of MRLs to minor species and the establishment of MRLs for honey in FAO Residue Monographs 15 prepared by the 78th JECFA for examples of typical working paper assignments.

Conclusions (or **Recommendations**)

When appropriate, include a final section summarizing Committee decisions, conclusions or recommendations for further work on the topic.

References

Heading font Times New Roman, 14, bold. Follow instructions in the Instructional Guide for Template 1 for citation format.

Instructional guide for Template 5 (Template for a summary providing the initial review of a substance)

Substance name

Use Paper size A4. Use the substance name as listed in the call for data from the JECFA Secretariat and as given in the priority list from the CCRVDF. Use font Times New Roman, 14, bold, for both.

Explanation

This opening section of the Summary provides a brief review of the nature of the referral of substance to JECFA and the registered uses provided. Use font Times New Roman 12 for body text. It may be taken from the residue summary prepared by the FAO experts or from the toxicology summary prepared by the toxicology experts or it may be prepared by a blending of the Explanation sections of the summary documents prepared by the residue and toxicology experts. This is decided by the full Committee during preparation of the draft of the final report.

Toxicological and microbiological evaluation

Or

Toxicological evaluation

Font Times New Roman, 14 bold italic.

This section is prepared by the toxicology expert, under the heading "Toxicological evaluation" or "Toxicological and microbiological evaluation". It typically includes a brief paragraph identifying sources of toxicological information used by the Committee and results of any previous toxicological reviews by JECFA.

Biochemical data

This section, prepared by the toxicology expert, contains a summary of all relevant biochemical data, with emphasis on studies leading to ADI (or ArfD) decision.

Toxicological data

In this section, prepared by the toxicology expert, all relevant toxicological studies leading to a decision on the ADI (or ArfD) are summarized.

Microbiological data

This section is prepared by the toxicology expert, under the general heading "Toxicological and microbiological evaluation" when the dossier includes microbiological studies, usually for antimicrobial substances. It typically includes a review of relevant studies on the microbiological activity of the substance, particularly when these are considered in the establishment of the ADI and/or ARfD.

Evaluation

Font Times New Roman, 14 bold italic.

This section of the Summary, prepared by the toxicology expert, contains a concise assessment of the key toxicological information reviewed by the Committee and the resulting decision on an ADI and/or ARfD.

Residue evaluation

This portion of the final Summary for a substance is prepared by the drafting expert assigned by FAO. An opening paragraph or paragraphs directly under the heading "Residue evaluation" provide(s) a basic overview of the residue information provided for review to the Committee.

Data on pharmacokinetics and metabolism in food-producing animals

Font Times New Roman,

Body text Times New Roman 12. Begin this section with a statement detailing for which species information was provided. This section should be brief and relate to residue issues to avoid extensive overlap with the summary of pharmacokinetics prepared by the toxicology expert from content of the toxicological monograph. In subsequent paragraphs, briefly summarize all relevant pharmacokinetic and metabolism studies provided for laboratory species, followed by food animal species, indicating key pharmacokinetic parameters, elimination pathway, major metabolites and marker residue for food animal species. The Committee will determine when information on laboratory species needs to be blended into the pharmacokinetic and metabolic section of the summary prepared by the toxicology expert during preparation of the final summary report when the sections prepared by the toxicology and residue drafting experts are combined.

Residue data

Font Times New Roman, 12 italic.

Body text Times New Roman 12. The focus is on the key residue-related studies in food animals which contain the data leading to the decision on MRLs. Key elements include the identification of the depletion profile and summaries of the pivotal studies used in recommending MRLs. As in the preceding section, less detail is provided than in the monograph and use of tables and figures is avoided, whenever possible.
Begin with the radiolabel studies, followed by the depletion studies with non-radiolabelled drug. The studies in this section are summarized by species, for the species for which data were provided, following the same order used in the monograph.

Analytical methods

Font Times New Roman, 12

Font Times New Roman, 12. Under this heading, summarize information on residue methods considered as suitable for the support of the proposed MRLs. When no available method is considered, state the deficiencies in the available methodology.

Maximum residue limits

Font Times New Roman, 12, bold italic.

Body text Times New Roman 12. This section, prepared by the residue experts, summarizes in bullet points the considerations leading to the decision on MRLs, then follows with the MRL recommendations. The text of the bullet points should be exactly the same as in the monograph.

Example

In recommending MRLs of (substance name) in (species) food commodities, the Committee considered the following factors:

- An ADI (or ArfD) of ….
- Where information on approved veterinary uses was provided, withdrawal times were in the range ___ days.
- Etc.

The Committee recommended MRLs for (substance name) determined as (name of marker residue) in (name species and matrices; e.g., tissues and eggs).

Next state for which species and types of foods for which MRLs are recommended. State the basis on which the MRLs were derived.

The MRLs recommended for (name species and matrices; e.g., tissues and eggs) are based on (state the basis on which MRLs were derived, such as the upper limit of the one-sided 95% confidence interval over the 95th percentile (UTL 95/95) for the __-day post-treatment data from the non-radiolabelled residue depletion study).

The recommended MRLs ….

State the MRL recommendations for each species, tissue type, and any other foods, such as milk, eggs or honey.

Dietary exposure assessment

When both chronic and acute exposure assessments are included in an evaluation, the heading may be replaced by two headings, "Chronic dietary exposure assessment" and "Acute dietary exposure assessment" (see the Ivermectin summary in the report of the 81st Meeting of JECFA) State the calculation used in the exposure assessment (EDI, TMDI, GEADE or other), explain briefly why this method of exposure assessment was selected and give the outcome of the calculation, both in intake in µg/kg per person per day and as a percentage of the upper bound of the ADI when the EDI or TMDI is calculated. If the calculation is for A GECDE, give the intakes calculated for adults, children and infants per day and the percentage of the ADI this represents for each of these representative groups. For the GEADE, give the intakes calculated for adults, children and infants per day and the percentage of the ARfD this represents for each of these representative groups.

A residue monograph was prepared.

Include this statement at the end of the section on MRLs.

Summary and conclusions

Heading font Times New Roman, 14 bold.

Studies relevant to risk assessment

Prepared by the toxicology expert. This is in table format.

Uncertainty factor

Prepared by toxicology expert.

___ (__ for interspecies variability and __ for intraspecies variability)

Toxicological effects

Prepared by toxicology expert.

A toxicological ADI of 0–__ µg/kg bw could be derived.

Microbiological effects

Include when applicable. Prepared by toxicology expert.

A microbiological ADI of 0–___ µg/kg bw could be derived.

ADI (based on toxicological effects)

Prepared by toxicology expert.

__ µg/kg bw

ARfD

Prepared by toxicology expert.

__ µg/kg bw

Residue definition

Prepared by residue expert.

Name of marker residue.

MRLs

The recommended MRLs are ….

State in a single sentence the MRL recommendations by tissue and species. See reports of recent JECFA meetings for examples.

Estimated dietary exposure

Prepared by residue expert. State in a single sentence the type of intake calculation used and the result. See reports of recent JECFA meetings for examples.

Instructional guide for Template 6 (Template for a summary providing a further review of a substance when new data are provided)

Substance name	Use Paper size A4. Use the substance name as listed in the call for data from the JECFA Secretariat and as given in the priority list from the CCRVDF. Use font Times New Roman, 14, bold, for both headings.
Explanation	

Use font Times New Roman 12 for body text. This opening section of the Summary provides a brief review of the nature of the referral of substance to JECFA, including the outcomes of any previous reviews. State when the review is the result of new data being submitted in a response to a deficiency identified in a previous review of the compound by JECFA, using the precise wording used in the previous JECFA request for additional data. When the request relates to a new or additional use for the substance, provide details of the GVP for this use. The final text may be taken from the residue summary prepared by the FAO experts or from the toxicology summary prepared by the toxicology experts or it may be prepared by a blending of the Explanation sections of the summary documents prepared by the residue and toxicology experts. This is decided by the full Committee during preparation of the draft of the final report. When the new assessment is only for residue issues, this text is prepared by the residue experts.

Use additional headings and sub-headings from Template 5 which are applicable to complete the summary.

Instructional guide for Template 7 (Template for a summary providing a further review of a substance in response to a question from CCRVDF or a concern form from a Codex member state when no new data are provided)

Substance name

Explanation

Use Paper size A4. Use the substance name as listed in the call for data from the JECFA Secretariat and as given in the priority list from the CCRVDF. Use font Times New Roman, 14, bold, for Substance name, Times New Roman 12 bold italics for Explanation and other major

Use font Times New Roman 12 for body text. This opening section of the Summary provides a brief review of the nature of the referral of substance to JECFA, including the outcomes of any previous reviews. State the question or issue referred to JECFA from CCRVDF using the specific wording from the CCRVDF request. State if there have been any additional comments rece3ived from other parties, such as a Codex member state or a Sponsor. The final text may be taken from the residue summary prepared by the FAO experts or from the toxicology summary prepared by the toxicology experts or it may be prepared by a blending of the Explanation sections of the summary documents prepared by the residue and toxicology experts. This is decided by the full Committee during preparation of the draft of the final report. When the new assessment is only for residue issues, this text is prepared by the residue experts.

Review of the ADI

Previous JECFA evaluation

Concern from sponsor

Comments by the present Committee

These are typical headings that may appear when the question posed to JECFA from CCRVDF relates to a decision on the ADI. This section is prepared by the toxicology expert.

Residue evaluation

Concern from Member State

Comments from sponsor

Maximum residue limits

These are typical headings that may appear when the question posed to JECFA from CCRVDF relates to a decision on the MRLs. This section is prepared by the residue experts. Use font Times New Roman 12 bold italic for main section heading, Times New Roman 12 italic for the sub-headings. Use instructions from Template 5, as appropriate.

Summary and conclusions

ADI

Prepared by toxicology expert.

The ADI of 0–__ µg/kg bw established by the Committee at the _____ meeting was maintained (or state the revised ADI, if that is the Committee decision).

MRLs

Prepared by residue expert.

The Committee proposed the following revised MRLs: ……..

Dietary exposure

Prepared by residue expert. State the result of the revised dietary intake calculation when revised MRLs are recommended. See template 5 for suggested text to be used.

Instructional guide for Template 8 (Template for a summary for inclusion under "General considerations")

Subject

Use Paper size A4. Times New Roman, 14, bold, for Subject, Times New Roman 12 bold italics for major section headings. Use a title for the topic which adequately identifies the issue discussed in the text (e.g., Decision-tree approach to the evaluation of residues of veterinary drugs).

Additional sub-headings (font Times New Roman 12 italic) may be used to define specific topics under the general heading for a section when they are needed, typically when the topic is complex and requires several pages of text. See examples such as "Dietary exposure to veterinary drug residues" in TRS 988, the Meeting Report for the 78th JECFA.

Keep the discussion clear and concise – identify the issue, identify work done by previous meetings of JECFA on the issue, summarize the points discussed at the current meeting and state what decisions were made by the Committee. Use font Times New Roman 12 for the body text. Any section headings should be in Times New Roman 12 bold italic, sub-headings Times New Roman 12 italic.

Part II: Templates

Template 1. Template for a monograph providing the initial review of a substance

Substance Name

First draft prepared by

Drafting expert name, city, country
and
Reviewer name, city, country

Identity

International Non-proprietary Names (INN):

Synonyms:

IUPAC Name:

Chemical abstract Service No.:

Structural formula:

Molecular formula:

Molecular weight:

Other information on identity and properties

Pure active ingredient:

Appearance:

Impurities:

Melting point:

Solubility:

Log Ko/w or Partition Coefficient:

pH:

Optical rotation:

UV_{max}:

Stability:

Residues in food and their evaluation

Conditions of use

Dosage

Pharmacokinetics and metabolism

Pharmacokinetics in laboratory animals

Rats

Mice

Dog

Monkey

Other

Pharmacokinetics in Food-producing Animals

Cattle

Pigs

Sheep

Goat

Chicken

Turkey

Salmon

Predictive approaches using structure activity relationships or in silico tools to predict ADME properties

Metabolism in Laboratory Animals

Rats

Mice

Dog

Monkey

Other

Metabolism in Food Producing Animals

Cattle

Pigs

Sheep

Goat

Chicken

Turkey

Salmon

Comparative metabolism

Tissue residue depletion studies

Radiolabelled residue depletion studies

Cattle

Lactating dairy cows

Pigs

Sheep

Goat

Chicken

Turkey

Salmon

Residue depletion studies with non-radiolabelled drug

Cattle

Lactating dairy cows

Pigs

Sheep

Goat

Chicken

Turkey

Salmon (or other fish species)

Methods of analysis for residues in tissues

Screening methods

Quantitative methods

Confirmatory methods

Appraisal

Dietary Exposure Assessment

Maximum Residue Limits

References

Template 2. Template for a monograph providing an addendum to an earlier review of a substance when new data are provided

Substance Name

First draft prepared by

Drafting expert name, city, country
and
Reviewer name, city, country

Addendum to the monograph prepared by the __th meeting of the Committee and published in the _____.

Identity

International Non-proprietary Names (INN):

Synonyms:

IUPAC Name:

Chemical abstract Service No.:

Structural formula:

Molecular formula:

Molecular weight:

Other information on identity and properties

Pure active ingredient:

Appearance:

Impurities:

Melting point:

Solubility:

Log Ko/w or Partition Coefficient:

pH:

Optical rotation:

UV_{max}:

Stability:

Background

Residues in food and their evaluation

Appraisal

Dietary Exposure Assessment

Maximum Residue Limits

References

Template 3. Template for a monograph providing an addendum based on question from CCRVDF or a concern form from a Codex member state when no new data have been provided

Substance Name

First draft prepared by

Drafting expert name, city, country
and
Reviewer name, city, country

Addendum to the monograph prepared by the __th meeting of the Committee and published in the _____.

Background

Current evaluation

Concern from Member State

Or

Alternative approach proposed by the sponsor

Or

Additional comment provided by the sponsor

Appraisal

Dietary Exposure Assessment

Maximum Residue Limits

References

Template 4. Template for a discussion paper published as a monograph or annex

Discussion Paper Title

First draft prepared by

Drafting expert name, city, country
and
Reviewer name, city, country

Introduction

Background

Sources of guidance

Discussion *or* Evaluation

Conclusions *or* Recommendations

References

Template 5. Template for a summary providing the initial review of a substance

Substance name

Explanation

Toxicological and microbiological evaluation

Or

Toxicological evaluation

Biochemical data

Toxicological data

Microbiological data

Evaluation

Residue evaluation

Data on pharmacokinetics and metabolism in food-producing animals

Residue data

Analytical methods

Maximum residue limits

Dietary exposure

A residue monograph was prepared.

Summary and conclusions

ADI

ARfD

MRLs

Dietary exposure

Template 6. Template for a summary providing a further review of a substance when new data are provided

Substance name

Explanation

(Use additional headings and sub-headings from Template 5 which are applicable to complete the summary.)

Template 7. Template for a summary providing a further review of a substance in response to a question from CCRVDF or a concern form from a Codex member state when no new data are provided

Substance name

Explanation

Review of the ADI

Previous JECFA evaluation

Concern from sponsor

Comments by the present Committee

Residue evaluation

Concern from Member State

Comments from sponsor

Maximum residue limits

Summary and conclusions

ADI

ARfD

MRLs

Dietary exposure

Template 8. Template for a summary for inclusion under “General considerations”

Subject