

**Evaluation Manual  
for the Authorisation  
of plant protection products  
according to Regulation (EC) No 1107/2009**

**EU part**

**Plant protection products**

**Chapter 5 Residues; residue dossier**

**version 2.6; April 2020**



**Board  
for the Authorisation  
of Plant Protection Products and Biocides**

**Chapter 5 Residues; residue dossier**

Category: Plant protection products

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**Changes in the Evaluation Manual**

<b>Evaluation manual PPP EU part Chapter 5 Residue dossier</b>			
<b>Version</b>	<b>Date</b>	<b>Paragraph</b>	<b>Changes</b>
2.1	October 2016	Whole document	Text from data requirements (grey boxes) deleted from the Evaluation Manual and replace with references as hyperlink to original documents. Short description of data requirements included in the text.
2.2	January 2018	General introduction and par. 1.1	Reference to Regulation (EC) 396/2005 and Annex I of this Regulation has been added.
2.3	February 2018	Appendix LoEP	New version of EFSA Primo model (revision 3) is available from 1.02. 2018. Reference to the newest version was added.
2.4	June 2019	Derivation of endpoints and reference values	MRL bijenhoning, paragraph 1.3.8. <i>Residues in honey</i> was added.
		Appendix 1	Appendix 1 has been updated: newest available version of List of Endpoints was added.
2.5	January 2020	1.	Sentence included on the administrative EFSA guidance
2.6	April 2020	6.3	Typo in link to extrapolation table has been corrected.
		6.4	Link to Animal model 2017 has been updated.
		6.6	Reference to OECD Guidance 97 (rotational crop residue studies) was added.
		6.9	New version of EFSA Primo model (revision 3.1) is available. Reference to the newest version was added.

## GENERAL INTRODUCTION

This chapter describes the data requirements for the aspect residues and how these are evaluated for the EU framework (§1 - §1.5) under [Regulation \(EC\) No 1107/2009](#).

With regard to setting of Maximum Residue Levels (MRLs), risk assessment and decision making, Regulation (EC) No 1107/2009 refers to [Regulation \(EC\) No 396/2005](#).

### 1. EU FRAMEWORK

In this document, the procedures for the evaluation and re-evaluation of active substances as laid down in the EU are described; the NL procedure for evaluation of a substance is reverted to when no EU procedure has been laid down.

This document aims to give procedures for the approval of active substances and inclusion in [Commission Implementing Regulation \(EU\) No 540/2011](#).

Notifiers preparing an assessment report for active substances need to comply with the relevant guidance, instructions and format laid down in the EFSA [Administrative guidance on submission of dossiers and assessment reports for the peer-review of pesticide active substances](#).

#### 1.1. Introduction

The use of plant protection products may result in residues in foodstuffs. Their use may directly and indirectly lead to exposure to residues via food:

- *Direct exposure via food*

Residues may remain present after the use of plant protection products on or in crops and stored products. Such crops/products are directly used for human consumption or serve as raw material for food and drink. Furthermore, exposure via drinking water may occur in case of contact with surface water during application or where pesticides or their metabolites leach to the groundwater.

- *Indirect exposure via food*

Residues in treated crops, intended for animal feeding, may result in the transmission of residues to animal products that are eventually used for human consumption (such as meat and milk).

Residue data are requested to be able to estimate the nature and level of the residues.

Residue data may relate to the following:

- \* the application of plant protection products on agricultural and horticultural crops, fully or partly intended for consumption;
- \* the application of plant protection products on crops which may via feeding to livestock lead to residues in animal products;
- \* the succeeding crops following treated crops on the same field; such consumption - crops are grown after the crop in/on which the plant protection product has been applied;
- \* the application of plant protection products on stored foodstuffs or raw materials for foodstuffs;
- \* residues in drinking water by drift of pesticides to waterways or leaching to the groundwater.

The products of plant and animal origin to which the maximum residue levels of pesticides (MRLs) set by [Regulation \(EC\) No 396/2005](#) apply are listed in Annex I to that Regulation. [Annex I](#) to the Regulation (EC) No 396/2005 is available at the commission website.

The analytical methods and corresponding validation for the crops or animal products in question, as they are used in residue research, are described in Evaluation Manual, Chapter 3: Analytical methods.

## 1.2. Data requirements

In order to qualify for inclusion of an active substance in [Commission Implementing Regulation \(EU\) No 540/2011](#), a dossier that meets the provisions laid down in [Commission Regulation \(EU\) No 283/2013](#) and [Commission Regulation \(EU\) No 284/2013](#) must be submitted for the active substance as well as for the plant protection product.

For purposes of information and of harmonization, a list of EU and OECD methods and guidelines is presented in [Commission Communications 2013/C 95/01](#)

When, according to the applicant, a certain study is not necessary, a relevant scientific justification can be provided for the non-submission of the particular study.

Experiments carried out after 25 July 1993 should have been carried out under GLP. The field part of the residue studies is exempt from this requirement, unless the research has been carried out after December 1997; the field part should in that case also have been conducted under GLP.

The analytical methods and corresponding validation for the crops or animal products in question, as used in the residue studies, must be described in each residue report or reference must be made to a separate report in which the method is described. Such a report must then also be submitted. In addition, an analytical method for enforcement must be submitted (for data requirements and evaluation criteria for these pre- and post-registration analytical methods, see Evaluation Manual: Chapter 3 Analytical methods).

Studies conducted before the application of the Regulation (EU) 283/2013, although not fully compliant with GLP requirements or with current test methods, may be integrated into the assessment, when accepted by the competent authorities as scientifically valid, thereby removing the need for repeating animal tests, especially for carcinogenicity and reprotoxicity studies. This derogation applies to studies on all vertebrate species.

### 1.2.1. *Date requirements active substance*

The data requirements regarding residues of the active substance are described in [Commission Regulation \(EU\) No 283/2013](#), section 6.

## 6. Residues in or on treated products, food and feed (283/2013; 6)

### 6.1 Storage stability of residues

The specific data requirements on stability of residues are provided in Commission Regulation (EU) No 283/ 2013 in [section 6.1](#).

### 6.2 Metabolism, distribution and expression of residues

The specific data requirements on metabolism of residues are provided in Commission Regulation (EU) No 283/ 2013 in [section 6.2](#).

Detailed circumstances in which plant metabolism is required are described in [section 6.2.1](#)

Metabolism studies must be carried out with representative crops, where test conditions should approach the intended use as much as possible: method of application (soil, seed or crop treatment), description of physical facility (field, glasshouse, chambers), number of applications, application intervals, growth stage at the moment of application and harvest, and the (non)use of a surfactant (see §1.2.2, this document) are relevant.

Metabolism studies are also required to be able to determine whether other metabolites are formed in or on the plant than after intake of the active substance in the animal (see also Evaluation Manual: Chapter 4 Human Toxicology; but which could still be toxicologically relevant for consumers).

Metabolites in plant studies that are part of the extractable fraction and which at harvest form more than 10% of the total amount of recovered radioactive residue or more than 0.05 mg/kg residue in the plant part in question should always be identified. Metabolites exceeding 0.01 mg/kg should be characterised. A scientific justification should show that the toxicology of the metabolite in question is covered by the toxicological profile in laboratory animals, or supplementary toxicological research must be carried out with the metabolite(s) formed on or in the plant in view of possible human exposure. It depends on the results of this research whether the metabolite is considered as toxicologically relevant or non-relevant and whether or not it should be included in the residue definition.

Detailed circumstances in which animal metabolism are required are described in [section 6.2.2 \(poultry\)](#), [section 6.2.3 \(lactating ruminants\)](#), [section 6.2.4 \(pigs\)](#) and [section 6.2.5 \(fish\)](#)

According to the data requirement metabolism studies in animals are required when the residue intake is expected to exceed 0.004 mg/kg bw/day or 0.1 mg/kg feed. Calculation of this amount is based on the total diet and is expressed in mg/kg dry matter.

Because the behaviour of the active substance in ruminants and poultry may differ significantly from that in the rat, metabolism research must generally be carried out in a lactating ruminant and laying poultry, except where (e.g.) the crop on which the product is applied is not fed to the particular animal group.

Where research is required, the nature of the residues in meat, fat, kidney (ruminants and swine only), liver and milk or eggs must be determined.

Where accumulation of the active substance in the animal occurs, at concentrations  $\leq 0.1$  mg/kg dry feed in the total diet per animal, data must also be submitted about the metabolism, distribution and expression of residues in livestock.

Metabolites must generally be identified when a metabolite forms more than 10% of the total amount of recovered residue or more than 0.05 mg/kg residue in the animal product in question.

A scientific justification should in such cases show that the toxicology of the metabolite in question is covered by the toxicological profile in test animals, or supplementary toxicological research must be carried out with the metabolite(s) in view of possible human exposure. It then depends on the results of this research whether or not the metabolite is considered as toxicologically relevant; this may have consequences for the residue definition.

When the metabolism in fish is required the reference should be made to [Working document on the nature of pesticide residues in fish \(SANCO/11187/2013\)](#).

### 6.3 Magnitude of residues in plants

The specific data requirement on magnitude of residues in plants are provided in Commission Regulation (EU) No 283/2013 in [section 6.3](#).

Where the requested use concerns a group of comparable crops, determination of the residues in one or more representatives of the crop groups is sometimes sufficient and results may then be extrapolated to related crops.

For crop classification we refer to the extrapolation tables presented in [Guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs \(SANCO 7525/VI/95 Rev.10.3\)](#).

The following situations are distinguished in the document SANCO 7525/VI 95 Rev.10.2:

- \* last application after the edible part has been formed
- \* last application before the edible part has been formed
- \* seed treatments
- \* post-harvest applications.

This classification also distinguishes between systemic and non-systemic plant protection products.

For consumption crops, the acreage per region (North/South Europe and World) and the average diet intake per day determine whether a crop is a 'major crop' or 'minor crop'. This classification determines the number of trials to be submitted per crop. At least 8 trials are in principle required for 'major crops', divided over 2 growing seasons and 4 different locations. At least 4 trials are sufficient for 'minor crops', where the variation on growing season and location is also taken into account.

The following special situations are to be distinguished:

- Trials spread over one year but several seasons are sufficient for storage or post-harvest applications and applications under glass (or other forms of controlled climatological conditions).
- Where no residues are found or expected above the limit of quantification, fewer trials may possibly be acceptable
- Trials from Northern and Southern Europe carried out in greenhouses are comparable as well trials carried out in tunnels and glasshouses.
- Sometimes, a substance is sensitive to photolysis, and it can be demonstrated on the basis of this and experimental data that applications in glasshouses are worst case in comparison with outdoor applications and applications in Northern Europe in comparison with Southern Europe. In such cases there should always be a complete data set for the worst-case application to be able to derive an MRL.

Not all crops are mentioned in the extrapolation tables. Where crops are not mentioned, this usually means that no data are present and that trials must be carried out with the crop in question.

#### **6.4 Feeding studies**

The specific data requirement on livestock feeding studies are provided in Commission Regulation (EU) No 283/2013 in [section 6.4](#).

Livestock feeding studies are conducted to quantify levels of residues in meat, milk, eggs and edible meat by-products. The main purpose of these studies is to provide the basis for establishing maximum residues limits (MRLs) and consequently to conduct dietary intake assessments for consumer safety.

The point under 'circumstances in which required' refers to the amount of residues in the total amount of received dry feed.

Where metabolism research in livestock shows that significant amounts of residue (<0.01 mg/kg bw) cannot occur in animal products, feeding studies are not required unless the metabolism study in livestock shows a potential for significant bioaccumulation of the pesticide in animal.

In case feeding studies are required, these must be carried out in lactating ruminants and laying poultry, except, e.g., in case the crop on which the product is applied is not fed to the animal group in question.

In cases where metabolic pathways in rodents (typically rats) differ significantly from those in ruminants (typically goats) a pig metabolism study might be required. If the metabolic pathway in the pig study is different than in the ruminant study, a pig feeding study should be conducted unless the intake by pigs is not significant.

Animals are exposed over a long period in order to reach the constant concentration reached in the course of time in the various tissues: the so-called plateau value.

To establish the speed of elimination from the system, a number of animals from the study can be used to study depuration, where animals are sacrificed some time, e.g. two weeks, after the dosing was ceased.

Fat-soluble characteristic of the residues should be taken into account when planning the feeding studies.

[EFSA document: Estimation of animal intakes and HR, STMR and MRL calculations for products of animal origin, contains introduction and instruction how to assess livestock metabolism and feeding studies and to derive MRLs for products of animal origin, when relevant.](#)

To avoid discrepancies in the MRL setting resulting from the use of different feedstuff tables and animal species, the following approach was agreed during the Standing Committee on plants, animals, food and feed (SCoPAFF) on 11 and 12 June 2015:

- The animal intake triggering the submission of animal studies remains 0.1 mg/kg DM for the active substances falling under Reg. (EU) No 544/2011 and 0.004 mg/kg bw under Reg. (EU) No 283/2013.
- Animal dietary burden and MRL setting calculations are performed according to feedstuff tables listed in the [OECD Guidance series 64/32](#) and detailed in the [OECD Guidance 73](#).

In order to harmonise and facilitate the MRL setting approach, EFSA has developed an Excel calculator: [Animal model 2017.xls](#), based on the OECD feedstuff tables and approach detailed in the [OECD Guidance 73](#).

### **6.5 Effect of processing (283/2013; 6.5)**

The specific data requirements on effect of processing are provided in Commission Regulation (EU) No 283/2013 in [section 6.5](#).

Processing studies are not required when no significant or no analytically available residues occur in the plant or animal product which would be processed. Also, when the total theoretical maximum daily intake (TMDI) is less than 10% of the ADI.



The data are required to gain insight in the extent of effect on the nature of the residue and the extent of effect on the magnitude of the residue in the processed product in comparison with the unprocessed product. In case there are significant residues ( $> 0.1$  mg/kg) and large-scale processing takes place, processing studies into the nature of the residue may be required (cooking, baking, fermentation).

Where a product consists of an edible part (flesh, pulp) and an inedible part (peel), data on the distribution of the residue over peel and flesh must be submitted.

Detailed circumstances in which nature of residues is required are described in [section 6.5.1](#).

This research in particular concerns obtaining information about the formation of specific degradation products during processing of the treated product.

Detailed circumstances in which study on distribution of the residue in inedible peel and pulp is required, are described in [section 6.5.2](#) and magnitude of residues in processed commodities are described in [section 6.5.3](#).

If the processed plant products play an important part in the diet, and if the hydrolysis study indicates that a significant transfer of residue into the processed products could occur, then studies in processed commodities to determine residue concentration or dilution factors must be carried out.

Processing studies should simulate industrial or domestic practises as closely as possible. A distinction is made in two types of magnitude of residues processing studies; balance studies and follow up studies. In balance studies, the aim of such studies is where possible to determine the distribution of the residues in all intermediate and end products and, where appropriate, the waste products arising from the processing. The basis for the follow-up studies is always dependant on the corresponding balance studies. If as a result of the balance studies the distribution of the residues is known for all intermediate and end products, then more extensive studies can be limited to important end products or intermediate products, i. e. to products which either reach the consumer direct, as an end product, or which are used as the starting product for further processing.

## **6.6 Residues in succeeding crops.**

The specific data requirements on residues in succeeding crops are provided in Commission Regulation (EU) No 283/2013 in [section 6.6](#).

Rotational food or feed crops are also referred to as succeeding or following crops and are defined as any field or aquatic crops, which may be planted after the harvest of a pesticide treated primary crop, replanted crop after failure of the pesticide treated primary crop, application of plant protection product as a soil treatment or before emergence of the crop.

Where it cannot be ruled out that residues will occur in succeeding crops, metabolism studies must be carried out, if necessary followed by field trials.

If these data show that residues may occur in succeeding crops, risk assessments must be conducted for these residues, or residues must be prevented by stipulating label restrictions. Additionally, MRLs can be set for rotational crops.

Detailed circumstances in which metabolism in rotational crops is required are described in [section 6.6.1](#) and for magnitude of residues in rotational crops in [section 6.6.2](#). Additional detailed guidance on rotational crop residue studies are provided in [OECD Guidance 97](#).

### 6.7 Proposed residue definition and maximum residue levels

The specific data requirements on proposed residue definition and maximum residue levels are provided in Commission Regulation (EU) No 283/2013 in [section 6.7](#).

### 6.8 Proposed safety intervals

The specific data requirements on proposed safety intervals are provided in Commission Regulation (EU) No 283/2013 in [section 6.8](#).

The pre-harvest interval or PHI is the term between the last application of the plant protection product and harvest, or the term between the treatment of grassland and grazing or feeding of the grass, or the term between the last application of the plant protection product and using or putting the products treated with the plant protection product on the market (in case of post-harvest treatments).

The pre-harvest interval is part of the GAP (Good Agricultural Practice) and should be mentioned in the WG (Statutory Use Instructions / Directions for Use). The submitted residue trials must be carried out according to GAP and with the proposed pre-harvest interval.

Sometimes the term 'safety interval' refers to the term between the last application and re-entry of the treated crop by man, although the term re-entry interval is more explicit and is preferred (for re-entry of treated crops see Evaluation Manual: Chapter 4 Human toxicology, risk operator (plant protection) ).

### 6.9 Estimation of the potential and actual exposure through diet and other means

The specific data requirements on estimation of exposure are provided in Commission Regulation (EU) No 283/2013 in [section 6.9](#).

The calculation of chronic and acute exposure of the consumer and risk estimation are described in Chapter 5, Residues, Risk for consumers (plant protection products).

For the calculations, EFSA calculation model Pesticide Residue Intake Model "PRIMo" [is available online](#).

### 6.10 Other studies

The specific data requirements for other studies (residue level in pollen and bee products) are provided in Commission Regulation (EU) No 283/2013 in [section 6.10](#).

#### 1.2.2. Data requirements product

The data requirements regarding residues of the plant protection are described in [Commission Regulation \(EU\) No 284/2013, section 8](#).

### 8 Residues in or on treated products, food and feed

Data and information on residues in or on treated products, food and feed in accordance with Section 6 of Part A of the Annex to [Regulation \(EU\) No 283/ 2013](#) shall be submitted, unless the applicant shows that the data and information already submitted for the active substance can be applied.

Generally, it is possible to refer to the dossier on the active substance for the requirements regarding residues of the plant protection products.

For each requirement, a justification must then be submitted why information on the active substance sufficiently answers the respective question on the plant protection product. Co-formulants that may affect uptake, distribution, life, and degradation route of the active

substance, such as surfactants and safeners, require special attention.

Co-formulants that leave toxicologically relevant residues must be investigated as well.

### **1.3. Derivation of endpoints and reference values**

Each study should be summarised and evaluated separately. The final conclusion and the endpoint per aspect (such as residue definition, MRLs, processing factors and solubility in fat) are presented in a list of endpoints (see Appendix 1).

The required residue data and the toxicological properties of the residue (active substance and/or metabolites) must enable determination of a maximum tolerable residue level, the MRL. In turn, these form the input for exposure estimation (see also Evaluation Manual: Chapter 5 Residues, Risk for consumers (plant protection products)).

#### **1.3.1. Metabolism plant and animal**

A residue definition for plant products is derived from the data from the plant metabolism studies. Residue definitions for animal products are derived from metabolism studies in livestock. The residue definitions for plant and animal products do not always correspond. The residue definition is established by taking the principles points into account:

- \* the residue definition (for enforcement) must be suitable for routine monitoring by the Food and Consumer Product Safety Authority;
- \* the residue definition (for risk assessment) should include the toxicologically relevant metabolite(s) and the components that constitute the largest part of the residue.

The extent of comparability between the metabolism in plant and animal determines whether separate toxicological research with a specific plant and/or animal metabolite is required.

The residue definition laid down for monitoring may differ from the definition laid down for risk assessment. This is the case if a suitable (routine) analytical method for a toxicologically relevant component of the residue is not available. A conversion factor is used to convert the analysed marker residue into the residue components that are relevant from a health point of view. These conversion factors may differ per product and per pre-harvest interval and are included in the list of endpoints (see Appendix 1).

#### **1.3.2. Residue trials**

The crop residue trials that serve for derivation of MRLs in plant products must be carried out in accordance with the requested directions for use and in accordance with the most critical GAP where several directions for use are concerned. It is also a requirement that the relevant residue components are analysed at the time of harvest. Where the products contain residues above the limit of quantification, consisting of an edible and a non-edible part, these must be analysed separately to be able to derive a processing factor.

#### **1.3.3. Feeding studies**

Feeding studies form the basis for derivation of MRLs in animal products and they may also yield supplementary information for establishment of the residue definition for animal products.

Here, it is important that the constant concentration reached in the course of time (the plateau) is analysed in the different matrices while giving the corresponding interval so that the MRL calculation for animal products is based on the most appropriate situation (see §1.3.7).

#### **1.3.4. Effects industrial processing or household preparations**

Evaluation of possible effect of industrial processing should be performed to establish whether or not residues and/or reaction products arise from residues in raw agricultural commodities during processing. When relevant, this process may require a separate risk assessment.

#### **1.3.5. Residues in succeeding crops**

Studies on residues in rotational crops should be performed to allow determination of nature and extent of potential residue accumulation in rotational crops from soil uptake and under realistic field conditions.

#### **1.3.6. Calculation MRL, STMR and HR for plant products**

Three mathematical values: STMR; HR and MRL can be derived from the residue trials, which can be used for risk assessment. The STMR (Supervised Trial Median Residue) is the median residue value from the residue trials at the designated PHI. The HR (Highest Residue) value is the highest value measured in a set of residue trials at the designated PHI and the MRL (Maximal Residue Level). All those values can be used for chronic and/or acute diet calculations for man and for calculation of the residue intake by livestock.

Where no residues at all are found above the LOQ (Limit of Quantification), the STMR (Supervised Trial Median Residue), HR (Highest Residue) and MRL are based on the LOQ. Where there are indications that residue levels are really zero (because the residue levels in the overdosed trials are also < LOQ) the STMR and HR are set at 0 and the MRL at the LOQ.

No MRLs are currently set for crops that are only used for animal feeding, e.g. grass.

EFSA document: [Residue trials and MRL calculations](#), includes recommendations how to set the residue trials and calculate MRLs to dossiers submitted according to the “old data requirements”(Reg. (EU) No 544/2011, EU guidelines in 1607/VI/97 rev.2) and to dossiers submitted according to the “new data requirements”(Reg. (EU) No 283/2013, EU Notice 2013/C 95/01, OECD guidelines).

To calculate the MRLs, the Member States agreed to use [OECD MRL calculator](#).

#### **1.3.7. Calculation MRL for animal products**

EFSA document [Estimation of animal intakes and HR, STMR and MRL calculations for products of animal origin](#) contains introduction and instruction how to assess livestock metabolism and feeding studies and to derive MRLs for product of animal origin.

See also: 6.4 Feeding studies (this document).

#### **1.3.8. Residues in honey**

Honey can potentially contain residues in PPPs and residues can sometimes be detected in honey during residue monitoring. It is therefore appropriate to establish safe Maximum Residue Limits (MRLs) for consumers. The MRLs have been set at a default level of 0.05 mg/kg. European data requirements ([\(Regulation \(EU\) No 283/2013, Annex 6.10\)](#) require studies on residues in pollen and bee products for human consumption:

[Technical guidelines for determining the magnitude of pesticide residues in honey and](#)

[setting Maximum Residue Levels in honey](#) (SANTE/11956/2016 rev. 9).

The Guidelines will be implemented by 1 January 2020. From 1 January 2020 the MRL honey guidelines will be applicable for all applications where use can lead to possible residues in honey.

- There are several situation where residues in honey can occur and those information should be taken by the applicant into consideration when preparing dossier
- Residues in honey can occur:
  - When a substance is applied during the flowering stage (BBCH 60-69) of a crop which is foraged by bees (Appendix II of the [Guidelines](#))
  - When a substance with systemic properties is applied prior to the following stage (before BBCH 60) including treatment of seeds, of a crop which is foraged by bees.
  - From use on non-target plants (in-field weeds and adjacent plants) when a substance is applied during the flowering period from April to September
  - From succeeding crops after application of a persistent and systemic active substance
  - Via honeydew collected from plant-sucking insects in forestry (such as *Picea spp.*, *Abies spp.*, *Pinus spp.* and *Quercus spp.*)

Currently, applications that only contain ornamental crops are not assessed by the residue aspect. From 1<sup>st</sup> January 2020 potential residues in honey and pollen need to be addressed by all applicants, including applications with (only) ornamental crops.

#### 1.4. Approval

The permissibility of an active substance or a plant protection product follows from the risk assessment for consumers, which has been elaborated in Chapter 5 Risk for consumers.

#### 1.5. Developments

The requirements for the residue dossier may change in accordance with the developments in scientific and risk assessment field.

These may lead to new research questions or amendments to of study guidelines that are already part of the residue dossier.

Developments are expected in areas such as:

- Cumulative risk assessment
- Comparative assessment

**2. APPENDICES**

Appendix 1 List of endpoints residues ..... 14

**Appendix 1 List of endpoints residues****Residues in or on treated products food and feed****Metabolism studies, methods of analysis and residue definitions in plants**

<b>Primary crops</b> (available studies)	<b>Crop groups</b>	<b>Crop(s)</b>	<b>Application(s)</b>	<b>Sampling (DAT)</b>	<b>Comment/Source</b>
	Fruit crops				Radiolabelled active substance: phenyl-UL- <sup>14</sup> C-a.s.:
	Root crops				
	Leafy crops				
	Cereals/grass				
	Pulses/oilseeds				
	Miscellaneous				
<b>Rotational crops</b> (available studies)	<b>Crop groups</b>	<b>Crop(s)</b>	<b>Application(s)</b>	<b>PBI (DAT)</b>	<b>Comment/Source</b>
	Root/tuber crops				
	Leafy crops				
	Cereal (small grain)				
	other				

Processed commodities (hydrolysis study)	Conditions	Stable?	Comment/Source
	Pasteurisation (20 min, 90°C, pH 4)	yes/no/inconclusive/not triggered	
	Baking, brewing and boiling (60 min, 100°C, pH 5)	yes/no/inconclusive/not triggered	
	Sterilisation (20 min, 120°C, pH 6)	yes/no/inconclusive/not triggered	
	Other processing conditions		

  

Can a general residue definition be proposed for primary crops?	yes/no/inconclusive	comment
Rotational crop and primary crop metabolism similar?	yes/no/inconclusive/not applicable	comment
Residue pattern in processed commodities similar to residue pattern in raw commodities?	yes/no/inconclusive/not applicable	comment
Plant residue definition for monitoring (RD-Mo)	<RD> (tentative) [metabolism group]: <RD> [metabolism group 1]: <RD> [metabolism group 2]: <RD> [processed commodities]: <RD> [honey and bee products]: <RD>	
Plant residue definition for risk assessment (RD-RA)	<RD> (tentative) [metabolism group]: <RD> [metabolism group 1]: <RD> [metabolism group 2]: <RD> [rotational crops]: <RD>	

Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs)

[processed commodities]: <RD>

[honey and bee products]: <RD>

Matrices with high water content, high oil content, high acid content and dry matrices: GC-ECD,  
LOQ 0.02 mg/kg

Confirmatory method available/missing for xxxx.

ILV available/missing for xxx.

(Reference)



**Stability of residues in plants**

Plant products (available studies)	Category	Commodity	T (°C)	Stability period		Compounds covered	Comment/Source
				Value	Unit		
	High water content						
	High oil content						
	High protein content						
	High starch content						
	High acid content						
	Processed products						
	Others						

**Magnitude of residues in plants****Summary of residues data from the supervised residue trials – Primary crops**

Commodity	Region/ Indoor (a)	Residue levels observed in the supervised residue trials (mg/kg)	Comments/Source	Calculated MRL (mg/kg)	HR <sup>(b)</sup> (mg/kg)	STMR <sup>(c)</sup> (mg/kg)	CF <sup>(d)</sup>
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## Representative uses

	NEU	Mo: - RA: -	Residue trials on <crop> compliant with GAP. Extrapolation to <crop> possible.		Mo: - RA: -	Mo: - RA: -	
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Commodity	Region/ Indoor (a)	Residue levels observed in the supervised residue trials (mg/kg)	Comments/Source	Calculated MRL (mg/kg)	HR <sup>(b)</sup> (mg/kg)	STMR <sup>(c)</sup> (mg/kg)	CF <sup>(d)</sup>
Intended uses in MRL application							
	NEU	Mo: - RA: -	Residue trials on <crop> compliant with GAP. Reduced number of trials is sufficient since, also considering metabolism studie(s), a zero residue situation is expected.				
	NEU	Mo: - RA: -					
Summary of data on residues in pollen and bee products (Regulation (EU) No 283/2013, Annex Part A, point 6.10.1)							
	NEU	Mo: - RA: -					

\* Indicates that the MRL is proposed at the limit of quantification.

Mo: residue levels expressed according to the monitoring residue definition; RA: residue levels expressed according to risk assessment residue definition.

(a): NEU: Outdoor trials conducted in northern Europe, SEU: Outdoor trials conducted in southern Europe, Indoor: indoor EU trials or Country code: if non-EU trials.

(b): Highest residue. The highest residue for risk assessment (RA) refers to the whole commodity and not to the edible portion.

(c): Supervised trials median residue. The median residue for risk assessment (RA) refers to the whole commodity and not to the edible portion.

(d): Conversion factor to recalculate residues according to the residue definition for monitoring to the residue definition for risk assessment.

**Residues in rotational crops****Overall summary**

Residues in rotational and succeeding crops expected based on confined rotational crop study?

yes/no/inconclusive/not triggered

comment

Residues in rotational and succeeding crops expected based on field rotational crop study?

yes/no/inconclusive/not triggered

Comment/source

**Summary of residues data from the rotational crops residue trials (if relevant, e.g. MRL, STMR, HR derived from rotational crops)**

Commodity	Region/ Indoor (a)	PBI (days) (b)	Residue levels observed in the supervised residue trials (mg/kg)	Comments/Source	Calculated MRL (mg/kg)	HR <sup>(c)</sup> (mg/kg)	STMR <sup>(d)</sup> (mg/kg)	CF <sup>(e)</sup>
	NEU	30	Mo: - RA: -	Rotational crops field trials conducted at a dose rate of application covering the max PECsoil for parent (or metabolite).		Mo: - RA: -	Mo: - RA: -	
		120						
		365						
	SEU	30						
		120						
		365						

\* Indicates that the MRL is proposed at the limit of quantification.

Mo: residue levels expressed according to the monitoring residue definition; RA: residue levels expressed according to risk assessment residue definition.

(a): NEU: Outdoor trials conducted in northern Europe, SEU: Outdoor trials conducted in southern Europe, Country code: if non-EU trials.

(b): Plant-back interval: The interval (days, months, years) between the final application of a pesticide product to a primary crop and the planting of a rotational crop.

(c): Highest residue. The highest residue for risk assessment (RA) refers to the whole commodity and not to the edible portion.

(d): Supervised trials median residue. The median residue for risk assessment (RA) refers to the whole commodity and not to the edible portion.

(e): Conversion factor to recalculate residues according to the residue definition for monitoring to the residue definition for risk assessment.

Processing factors

Processed commodity	Number of valid studies <sup>(a)</sup>	Processing Factor (PF)		CF <sub>P</sub> <sup>(b)</sup>	Comment/ Source
		Individual values	Median PF		
Apples, juice					Tentative <sup>(c)</sup>

PF: Processing factor (=Residue level in processed commodity expressed according to RD-Mo/ Residue level in raw commodity expressed according to RD-Mo);  
CF<sub>P</sub>: Conversion factor for risk assessment in processed commodity (=Residue level in processed commodity expressed according to RD-RA / Residue level in processed commodity expressed according to RD-Mo)  
(a): Studies with residues in the RAC at or close to the LOQ were disregarded (unless concentration may occur)  
(b): Median of the individual conversion factors for each processing residues trial.  
(c): A tentative PF is derived based on a limited dataset.

Residues in livestock

Not relevant or

Relevant groups (subgroups)	Dietary burden expressed in				Most critical subgroup <sup>(a)</sup>	Most critical commodity <sup>(b)</sup>	Trigger exceeded (Y/N)	Comments
	mg/kg bw per day		mg/kg DM					
	Median	Maximum	Median	Maximum				
Cattle (all)								
Cattle (dairy only)								
Sheep (all)								
Sheep (ewe only)								
Swine (all)								
Poultry (all)								
Poultry (layer only)								
Fish			N/A					

(a): When one group of livestock includes several subgroups (e.g. poultry “all” including broiler, layer and turkey), the result of the most critical subgroup is identified from the maximum dietary burdens expressed as "mg/kg bw per day".

(b): The most critical commodity is the major contributor identified from the maximum dietary burden expressed as "mg/kg bw per day".

**Nature of residues and methods of analysis in livestock****Metabolism studies, methods of analysis and residue definitions in livestock**

<b>Livestock</b> (available studies)	<b>Animal</b>	<b>Dose</b> (mg/kg bw/d)	<b>Duration</b> (days)	<b>Comment/Source</b>
	Laying hen			
	Lactating ruminants			e.g. Goat, cow, sheep
	Pig			
	Fish			

Time needed to reach a plateau concentration in milk and eggs (days)

Milk:	Comment
Eggs:	Comment
yes/no/inconclusive/not triggered	Comment
yes/no/inconclusive/not triggered	Comment
<div>&lt;RD&gt; (tentative)</div> <div>[metabolism group 1/tissue]: &lt;RD&gt;</div> <div>[metabolism group 2/tissue]: &lt;RD&gt;</div>	
<div>&lt;RD&gt; (tentative)</div> <div>[metabolism group 1/tissue]: &lt;RD&gt;</div> <div>[metabolism group 2/tissue]: &lt;RD&gt;</div>	
Yes/No	Comment
Milk,	

(analytical technique, matrix groups, LOQs)

Eggs,  
Muscle,  
Fat,  
Liver  
Kidney:  
HPLC-MS/MS , LOQ 0.02 mg/kg.  
Confirmatory method available/missing for xxxx.  
ILV available/missing for xxx  
(Reference)

Stability of residues in livestock

Animal products (available studies)	Animal	Commodity	T (°C)	Stability period		Compounds covered	Comment/ Source
				Value	Unit		
		Muscle				Parent	
		Muscle				Metabolite XX	
		Fat					
		Liver				Sum of parent and metabolite X	
		Kidney					
		Milk					
		Eggs					

**Magnitude of residues in livestock****Summary of the residue data from livestock feeding studies**

Animal commodity	Residues at the closest feeding level (mg/kg)		Estimated value at 1N		MRL proposal (mg/kg)	CF <sup>(c)</sup>
	Mean	Highest	STMR <sub>Mo</sub> <sup>(a)</sup> (mg/kg)	HR <sub>Mo</sub> <sup>(b)</sup> (mg/kg)		
<b>Cattle (all)</b> - Closest feeding level (x mg/kg bw; x N rate) <sup>(d)</sup>						
Muscle						
Fat						
Liver						
Kidney						
<b>Cattle (dairy only)</b> - Closest feeding level (x mg/kg bw; x N rate) <sup>(d)</sup>						
Milk <sup>(e)</sup>		n.a.				
<b>Sheep (all)</b> <sup>(f)</sup> - Closest feeding level (x mg/kg bw; x N rate) <sup>(d)</sup>						
Muscle						
Fat						
Liver						
Kidney						
<b>Sheep (ewe only)</b> <sup>(f)</sup> - Closest feeding level (x mg/kg bw; x N rate) <sup>(d)</sup>						
Milk <sup>(e)</sup>		n.a.				
<b>Swine (all)</b> <sup>(f)</sup> - Closest feeding level (x mg/kg bw; x N rate) <sup>(d)</sup>						
Muscle						
Fat						
Liver						
kidney						
<b>Poultry (all)</b> - Closest feeding level (x mg/kg bw; x N rate) <sup>(d)</sup>						
Muscle						
Fat						
Liver						
<b>Poultry (layer only)</b> - Closest feeding level (x mg/kg bw; x N rate) <sup>(d)</sup>						
Eggs <sup>(g)</sup>						

\* Indicates that the MRL is proposed at the limit of quantification.

n.a.: not applicable

n.r. : not reported

(a): Median residues expressed according to the residue definition for monitoring, recalculated at the 1N rate for the median dietary burden.



- (b): Highest residues expressed according to the residue definition for monitoring, recalculated at the 1N rate for the maximum dietary burden.
- (c): Conversion factor to recalculate residues according to the residue definition for monitoring to the residue definition for risk assessment.
- (d): Closest feeding level and N dose rate related to the maximum dietary burden.
- (e): For milk, mean was derived from samplings performed from day D1 to day D2 (daily mean of X cows).
- (f): Since extrapolation from cattle to other ruminants and swine is acceptable, results of the livestock feeding study on ruminants were relied upon to derive the MRL and risk assessment values in sheep and swine.
- (g): For eggs, mean and highest residues were derived from samplings performed from day D1 to day D2 (daily mean or daily highest of Y laying hens).

## Consumer risk assessment

ARfD

Highest IESTI, according to EFSA PRIMo (rev.x)

NESTI (% ARfD), according to (to be specified)

Assumptions made for the calculations

X mg/kg bw (source)
<b>Scenario 1 without risk mitigation measures:</b> Crop1: x% of ARfD Crop2: x% of ARfD Crop3: x% of ARfD  <b>Scenario 2 with risk mitigation measures:</b>
Highest NESTI: XX% ARfD (commodity)
<b>Scenario 1 without risk mitigation measures:</b> The calculation is based on the highest residue levels expected in raw agricultural commodities, except for XXXX were the derived processing factor was applied. The following CF for risk assessment were also applied: XXXX <b>Scenario 2 with risk mitigation measures:</b>

Or

Not relevant since no ARfD has been considered necessary.

ADI

TMDI according to EFSA PRIMo

NTMDI, according to (to be specified)

Highest IEDI, according to EFSA PRIMo (rev.x)

X mg/kg bw per day (source)
Highest TMDI: XX% ADI (MS, diet)
Highest NTMDI: XX% ADI (MS, diet)
<b>Scenario 1 without risk mitigation measures:</b> xx% ADI (diet) Contribution of crops assessed: Crop1: x% of ADI Crop2: x% of ADI Crop3: x% of ADI <b>Scenario 2 with risk mitigation measures:</b> 36% ADI (diet) Contribution of crops assessed: Crop1: x% of ADI

NEDI (% ADI), according to (to be specified)

Assumptions made for the calculations

Crop2: x% of ADI  
Crop3: x% of ADI

Highest NEDI: XX% ADI (MS, diet)

**Scenario 1 without risk mitigation measures:**

The calculation is based on the median residue levels derived for raw agricultural commodities, multiplied by the conversion factor for risk assessment, except for XXX where the processing factor for XXXX was also applied.

The contributions of commodities where no GAP was reported in the framework of the MRL review were not included in the calculation.

**Scenario 2 with risk mitigation measures:**

Consumer exposure assessment through drinking water resulting from groundwater metabolite(s) according to SANCO/221/2000 rev.10 Final (25/02/2003)

Metabolite(s)

ADI (mg/kg bw per day)

Intake of groundwater metabolites (% ADI)


Recommended MRLs

Code <sup>(a)</sup>	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/justification
<b>Enforcement residue definition:</b> <RD-Mo> <sup>(F)</sup>				
Representative uses				
				The submitted data are sufficient to derive a MRL proposal for the NEU/SEU use. Risk for consumers unlikely.
				The MRL proposal reflects the more critical residue situation of the NEU use. Risk for consumers unlikely.
				The submitted data are sufficient to derive an import tolerance (US GAP). Risk for consumers unlikely.
				The MRL proposal reflects the NEU use. For the SEU use the data were not sufficient to derive a MRL proposal. Risk for consumers unlikely.
			No change	The submitted data do not provide evidence that the existing MRL has to be modified.
			Further risk management considerations required	For the NEU use a MRL proposal of 1 mg/kg was calculated.
			No MRL proposal	
MRL application				

Code <sup>(a)</sup>	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/justification
Enforcement residue definition: 2 (if relevant, e.g. animal RD-Mo ≠ Plant RD-Mo)				

\* Indicates that the MRL is set at the limit of analytical quantification (LOQ)  
(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005  
(F): Fat soluble

