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Food safety, sustainability and innovation
Pesticides and Biocides

SANTE/10235/2016 Rev. 5.0
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COMMISSION STAFF WORKING DOCUMENT

Evaluation of data submitted to confirm Maximum Residue Levels (MRLs) following their review in accordance with article 12 of Regulation (EC) 396/2005[1] and risk management decisions in the absence of such data

finalised in the Standing Committee on Plants, Animals, Food and Feed
at its meeting on 20-21 November 2023

This document has been conceived as a technical guideline of the Commission Services. It does not represent the official position of the Commission. It does not intend to produce legally binding effects.

Only the European Court of Justice has jurisdiction to give preliminary rulings concerning the validity and interpretation of acts of the institutions of the EU pursuant to Article 267 of the Treaty.

[1] Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC, OJ L 70, 16.3.2005, p. 1–16

PREFACE

Explanations on revision 5.0:
Revision 5.0 formalises existing working procedures that are already being followed in case of absence of data to confirm MRLs. Therefore, for revision 5.0 no new implementation date is necessary.

The new revision of the working document (SANTE/10235/2016 Rev. 5.0) has been presented and discussed at the Standing Committee on Plants, Animals, Food and Feed (SCoPAFF) - Section Pesticide Residues on 20-21 November 2023.

Revision 4.1
The Transparency Regulation[2] amended the General Food Law[3] by introducing new requirements in the pre-submission phase and submission application procedure, such as:

- possibility to request for general pre-submission advice;
- obligation to notify information related to studies commissioned or carried out to support an application;
- submission of the application dossier using the format of the International Uniform Chemical Information Database (IUCLID), including non-confidential version of the dossier;
- public disclosure of non-confidential version of all information submitted in support of the application and related confidentiality decision-making process;
- public consultation on submitted application dossiers.

These new requirements, as implemented by the Practical Arrangements laid down by the European Food Safety Authority (EFSA), are reflected in the EFSA "Administrative guidance on submission of dossiers and assessment reports for the peer-review of pesticide active substances and on the MRL application procedure":
https://www.efsa.europa.eu/en/applications/pesticides/regulationsandguidance.
It is therefore advised to consult the EFSA administrative guidance for further details on the new procedure and obligations.

Since its revision 4.1, this document applies to all MRL applications submitted as of 27 March 2021. For all applications submitted before 27 March 2021, all procedural steps as described in SANTE/10235/2016 Rev. 4.0 continue to apply.

[2] Regulation (EU) 2019/1381 of the European Parliament and of the Council of 20 June 2019 on the transparency and sustainability of the EU risk assessment in the food chain and amending Regulations (EC) No 178/2002, (EC) No 1829/2003, (EC) No 1831/2003, (EC) No 2065/2003, (EC) No 1935/2004, (EC) No 1331/2008, (EC) No 1107/2009, (EU) 2015/2283 and Directive 2001/18/EC, PE/41/2019/REV/1. OJ L 231, 6.9.2019, p. 1–28.

[3] Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. OJ L 31, 1.2.2002, p. 1.

1. Introduction

Article 12 of Regulation (EC) No 396/2005 provides for a review by EFSA of the existing MRLs for all substances approved as active substances in plant protection products, and for substances non-approved on or after 2 September 2008.

In the outcome of such reviews, EFSA recommends maintaining or amending MRLs, or highlights items for the consideration of risk managers. Within the latter, EFSA derives tentative MRLs that are not fully supported by data but for which no risk to consumers could be identified. EFSA also lists the data required to confirm those MRLs.

In that case, risk managers frequently decide to maintain the existing MRL or set the MRL tentatively derived by EFSA and to add a footnote to the MRL in the Annexes to Regulation (EC) No 396/2005. The footnote indicates the information identified as unavailable and that the Commission will take such information into account in a future review of the MRL, if submitted by the given date, usually defined as 2 years following the publication of the Regulation reviewing the MRL.

This document sets out the procedures for the evaluation of data submitted to address the lack of information as indicated in the footnotes. Other information identified as unavailable by EFSA but not indicated in a footnote to the MRL is not in the scope of this document.

Such data is mentioned in the document as “confirmatory data”. It should be stressed that such data must not be confused with confirmatory information in the sense of Article 6(f) of Regulation (EC) No 1107/2009, whose evaluation is the subject of a separate guidance document.

As a matter of principle, confirmatory data should support the critical Good Agricultural Practice (cGAP) identified in the MRL review. Alternatively, an adjusted GAP may be supported, if it confirms the tentative MRL or leads to a lower MRL proposal. If the adjusted GAP leads to a higher MRL proposal, it should be evaluated following the standard procedures for setting new or modified MRLs, and this Working Document does not apply.

Member States agree that within the time period provided for submission of the confirmatory data, such data will not be considered as necessary information in a procedure to authorise a plant protection product, and its absence will not lead to a delay in the authorisation procedure, unless concerns are justified on a scientific basis. The same approach applies to the commercial availability of reference standards for substances where an 'A' footnote was added to the residue definition (see below).

However, when such information is not submitted by the interested party within the specified time period, Member States agree not to provide any new authorisations after the expiry of the deadline and until information is submitted and evaluated by EFSA in support of the tentative MRL or other lower MRL.

This document also sets out the consequences if data to address the lack of information as indicated in the footnotes is not submitted within the period specified in the footnote.

2. General procedure

- EFSA is involved in the assessment of confirmatory data in all cases, i.e. also when only residue trials are reported and no change of the MRL is needed.
- To achieve and maintain an up-to-date overview of confirmatory data requested and/or submitted, the Rapporteur Member State (RMS)/Evaluating Member State (EMS) informs EFSA (via the functional mailbox pesticides.mrl@efsa.europa.eu) upon receipt of confirmatory data, through submission of the relevant information in the same format as the overview excel sheet[4] held by EFSA and collating all the data gaps and the information whether and how they were addressed. EFSA updates the overview Excel table that is shared with Member States (read-only) on the EFSA Document Management System (DMS). EFSA will circulate on a regular basis (at least once per year) the overview table to Member States to verify completeness.

  Two main situations may arise:

2.1 Confirmatory data not submitted:

- Based on this completeness check of the overview table, if no confirmatory data is submitted by the deadline specified in the footnote to the MRL, risk managers may decide to lower the MRL to the limit of determination (LOD), taking into account that the MRL was not fully supported by data at the time of its review, and that the data gap identified at the time has not been addressed within the period specified in the footnote to the MRL.
- In such cases, the Commission mandates EFSA to prepare a Statement confirming that such data required by specific footnotes was not submitted by the applicant within the deadline and is therefore lacking.
- The Statement published by EFSA is then used by the Commission to support its draft measure lowering the MRL to the LOD, while deleting the footnote.
- In case of footnote 'A', if analytical standards have not been made available by the applicant as specified in footnote 'A' despite reminders sent to the applicant, risk managers may equally decide to lower the MRL to the limit of determination (LOD). Confirmation of availability or non-availability of analytical standards is sought by the European Union Reference Laboratories (EURLs). For more details see chapter 4.

2.2 Confirmatory data submitted:

2.2.1 General

Confirmatory data is submitted to EFSA by the RMS/EMS under the procedure set out in Chapter II of Regulation (EC) No 396/2005 (hereinafter "Article 10 application"), and the RMS/EMS prepares an Evaluation Report (ER; case 1 below). In case an application for a new use on that active substance has been received by the RMS/EMS, the RMS/EMS prepares one single ER covering both evaluations (combined submission of new use and confirmatory data; case 2 below). There are two cases:

[4] https://dms.efsa.europa.eu/otcs/cs.exe/open/15954020

Case 1: The confirmatory data are provided in the context of an application concerning only such confirmatory data:

i. Guidance documents in place at the time of setting of the confirmatory data request are applied. Reference date is the publication date of the relevant act in the Official Journal of the European Union.
ii. Data requirements used in the initial Article 12 review are applied.
iii. The same version of the animal dietary burden calculator used in the initial Article 12 review is applied, taking into account additional (more critical) uses assessed after the Article 12 review.
iv. Pesticide Residue Intake Model (PRIMo) rev. 3.1 shall be used. For the chronic exposure assessment, the Supervised Trials Median Residue (STMR) values derived for uses assessed in the framework of confirmatory data assessment shall be used. In addition, the STMR values corresponding to the MRLs established in the MRL legislation shall be used (i.e. STMR value for uses assessed in the MRL review, for MRLs modified after the MRL review, or for Codex MRLs implemented after the MRL review). The acute exposure assessment should focus on the uses subject to confirmatory data assessment. If a concern is identified for a commodity for which confirmatory data has been requested, the clock may be stopped for a maximum of 2 months, for applicant/RMS/EMS to supply information on a fall-back GAP via an updated IUCLID dossier/Evaluation Report (ER). In the updated IUCLID dossier the applicant should indicate that the update is based on a request from an authority.
v. The following Pesticide Residue Overview File (PROFile) version is applied:

PROFile version in the initial Article 12 assessment	**PROFile version to be used in the evaluation of confirmatory data**	**Main changes between the 2 assessments**
2.1	2.3	- use of the OECD calculator for plant MRL - MRL for muscle instead of meat
2.2	2.3	- MRL for muscle instead of meat
2.3	2.3	/
3.0	3.0	/

Case 2: The confirmatory data are provided in the context of an MRL application including additional new elements besides the confirmatory data:

i. Guidance documents in place at the time of the submission of the Article 10 application to the RMS/EMS is applied, also for assessing the Article 12 confirmatory data. The date of submission corresponds to the date the dossier is successfully submitted via IUCLID (passing IUCLID Business Rules).
ii. Data requirements applicable to the Article 10 application are determined in accordance with Technical Guideline SANTE/2015/10595[5]. The same data requirements then apply for assessing the Article 12 confirmatory data.
iii. The version of the animal dietary burden calculator in place at the time of the submission of the Article 10 application is applied, also for assessing the Article 12 confirmatory data.
iv. The version of PRIMo used for the Article 10 application and thus also for assessing the Article 12 confirmatory data is: PRIMo version 3.1 for all applications pending with

[5] https://food.ec.europa.eu/plants/pesticides/maximum-residue-levels/guidelines-maximum-residue-levels_en

EFSA (opinion or conclusion not yet adopted) on 01 January 2020 or submitted to EFSA as from 01 January 2020.

v. The following PROFile version is applied:

PROFile version in the initial Article 12 assessment	PROFile version to be used in the evaluation of confirmatory data	Main changes between the 2 assessments
2.1	3.0	- use of the OECD calculator for plant MRL - MRL for muscle instead of meat - OECD dietary burden calculator
2.2	3.0	- MRL for muscle instead of meat - OECD dietary burden calculator
2.3	3.0	- OECD dietary burden calculator
3.0	3.0	/

2.2.2 Detailed procedure

1) The applicant compiles the IUCLID dossier header indicating if the application supports an Article 12 confirmatory data and/or an Article 10 application. GAP documents in the IUCLID dossier should report the authorised cGAPs to be confirmed and new intended GAPs separately.
2) Following receipt of a successful submission of an IUCLID dossier, EFSA creates a folder on DMS and adds the application to the EFSA Collaboration table on DMS, clearly indicating if the application is on Article 10 (new use), or Article 12 Confirmatory data, or both. In case of a combined submission (case 2), two separate question numbers are created to ensure transparency and traceability of the different applications.
3) The RMS/EMS updates the PROFile and submits it along with the supporting ER to EFSA.
4) Following receipt of the ER, EFSA amends the status of the application in the EFSA Collaboration table to 'ER available'. This triggers the inclusion of the application in the monthly Commission mandate. In this mandate, the Commission clearly indicates what the application is referring to (new use, confirmatory data, or both).
5) EFSA specifies the deadline in the mandate acceptance letter as this is decided on a case-by-case level, depending on the amount and nature of the data.
6) Both RMS/EMS and EFSA have the possibility to stop the clock for incomplete Article 12 confirmatory data applications. Since the applicant was already given an extensive time period for addressing the confirmatory data, the clock stop period at RMS/EMS and EFSA will be limited to a maximum of 2 months each. If after 2 months, no additional data have been received, the assessment will resume and the RMS/EMS and EFSA will proceed with the finalisation of the ER and Reasoned Opinion, respectively, clearly listing (a) which confirmatory data have been addressed and (b) those confirmatory data for which insufficient information has been received and thus EMS/RMS and EFSA could not conclude if the confirmatory data requirement has been addressed. In case the ER is combining an assessment of both an Article 10 application for a new use and for Article 12 confirmatory data (case 2), the clock stop shall be limited to 2 months for

Article 12 confirmatory data and the standard 6 months for the data pertaining to the new use.

7) EFSA provides a reasoned opinion (in the case of combined submission, one reasoned opinion will cover two question numbers) and publishes the ER as a background document to the reasoned opinion. In exceptional cases, an ad hoc MS consultation might be needed before finalising the reasoned opinion. EFSA updates the overview table accordingly.
8) In case a consumer risk is identified, EMS and EFSA should report those findings. It is then the task of risk managers to find a solution.
9) The Commission submits a draft Regulation deleting the footnote and, where appropriate, amending the MRL, to the ScoPAFF.

3. Specificities for substances in the renewal process

- The following paragraphs relate to substances in the renewal process, i.e. between submission of the dossier for renewal to the RMS and submission of the RAR to EFSA. However, on a case-by-case basis, deviations from this approach can be agreed between RMS, EFSA and Commission. A separate ER should be submitted where the RAR is already finalised or at a very advanced stage, or where the renewal evaluation would be in the too distant future. Likewise, flexibility can be applied where confirmatory data was submitted shortly before the submission of the dossier for renewal.
- In the following situations, the evaluation of confirmatory data takes place within the renewal assessment:
  - ✓ When the confirmatory data contain information relevant for more than one or few commodities (e.g. metabolism studies).
  - ✓ When the confirmatory data contain information relevant for the representative uses.
  - ✓ When the confirmatory data contain information relevant for other intended (not representative) uses, but only if all requested confirmatory data is available for evaluation.
  - ✓ The renewal assessment may also conclude that no confirmatory data were submitted. In such cases a separate EFSA statement indicating a lack of confirmatory data is not necessary.
- The evaluation of confirmatory data containing information relevant for other intended (not representative) uses takes place outside the renewal assessment (i.e. in a separate Article 10 application), if only part of the requested confirmatory data is available for evaluation.
- To ensure the link with the confirmatory data request is made during the evaluation, the applicant should compile the IUCLID dossier header indicating if the renewal is submitted simultaneously in the section "*other submission related information*". For further information please refer to the IUCLID manual[6]. The assessment should be clearly reported in the Renewal Assessment Report (RAR Volume 1, residues section) and highlighted in the EFSA conclusion.
- If the confirmatory data has been submitted elsewhere (e.g. to the previous RMS) and the RAR is under preparation, the confirmatory data is forwarded to the RMS for the renewal.
- Where the renewal assessment leads to the proposal of revised residue definitions, the evaluation of confirmatory data is based on the existing residue definitions.

[6] https://www.efsa.europa.eu/en/applications/toolkit#iuclid-software

- As regards guidance documents, data requirements, animal dietary burden calculator, PRIMo and PROFile versions, the provisions for combined submission (case 2) described in the section "General procedure" apply *mutatis mutandis*.
- Where the renewal assessment leads to the proposal of revised toxicological reference values that are however not yet endorsed by risk managers, the consumer risk assessment is reported in duplicate, i.e. with both the existing and the proposed values.

4. Specificities for footnotes on missing analytical standards:

- In some cases the European Union Reference Laboratories (EURLs) highlighted that analytical standards were not commercially available and an 'A' footnote was added to the residue definition, stating that the EURLs identified the reference standard for a specific substance as commercially not available and that when re-viewing the MRL, the Commission will take into account the commercial availability of the reference standard one year after publication or, if that reference standard is not commercially available by that date, the unavailability of it.
- The Commission systematically follows up on these footnotes, by asking the EURLs whether the standards for the expired footnotes have become available in the meantime. This is done at the end of each calendar year or at the occasion of an Article 6 application of a concerned substance, whatever comes first.
- If the standard is available, the 'A' footnote associated with the residue definition is deleted.
- If the standard is still not commercially available:
  - ✓ In the meantime the applicant has made an application for a new MRL under Article 6. In such case the Commission writes a letter to the applicant, reminding that the standard has not been made available yet. The applicant is given 3 months for making the standard commercially available, during which the respective legislative proposal will be put on hold.
    - ➔ The standard is finally made available: the 'A' footnote is deleted and the new MRL could be voted provided all other conditions are fulfilled.
    - ➔ The standard is not made available: the application for the new MRL is rejected.
  - ✓ At the end of each calendar year, the Commission provides an overview on substances with an expired 'A' footnote and makes this information available to authorisation holders, informing that an additional 3 months period is given for making the standard commercially available.
    - ➔ The standard is finally made available: the 'A' footnote is deleted.
    - ➔ The standard is not made available: all MRLs are reduced to the LOD.