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REASONED OPINION

Targeted review of maximum residue levels (MRLs) for profenofos

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Abstract

In accordance with Article 43 of Regulation (EC) 396/2005, EFSA received a request from the European Commission to review the existing maximum residue levels (MRLs) for the non-approved active substance profenofos in view of the possible lowering of the MRL. EFSA investigated the origin of the current EU MRLs. Existing EU MRLs are based on Codex Maximum Residue Limits still in place or reflect temporary MRLs set from monitoring data. EFSA performed an indicative chronic and acute dietary risk assessment for the list of MRLs to allow risk managers to take the appropriate decisions. For some commodities, further risk management discussions are required to decide which of the risk management options proposed by EFSA should be implemented in the EU MRL legislation.

KEYWORDS

consumer risk assessment, MRL setting, non-approved active substance, profenofos, residue definitions, toxicological evaluation

CONTENTS

SUMMARY

The European Commission submitted a request to EFSA for a targeted review of maximum residue limits (MRLs) for 10 active substances no longer approved in the EU, but for which MRLs greater than the limit of quantification (LOQ) are still in place and for which Member States have identified potential consumer health risks. Separate reasoned opinions should be provided in accordance with Article 43 of Regulation (EC) 396/2005, for each of the substances included in this mandate, one of them being profenofos.

In accordance with the terms of reference, EFSA investigated the origin of the current EU MRLs for profenofos, and whether they are sufficiently substantiated. An EU MRL is considered substantiated if it is sufficiently supported by data and established for uses still authorised or based on Codex Maximum Residue Limit (CXL) or import tolerance that are still in place and relevant. Accordingly, MRLs that were derived for previously authorised EU uses are obsolete and should be lowered to the LOQ. For those commodities for which the existing EU MRLs are based on a CXL, EFSA investigated whether the CXLs are still in place and whether they are sufficiently supported by data. Obsolete or insufficiently supported Codex MRLs are also candidates for being lowered to the LOQ. To identify possible import tolerances, EFSA consulted Member States on Good Agricultural Practices authorised in third countries that were evaluated at national level which might justify maintaining certain MRLs as import tolerances. Following this Member State consultation, EFSA concluded that none of the existing EU MRL for profenofos has been established as an import tolerance. EFSA also screened the quality of the toxicological reference values (TRVs) derived by the Joint Meeting on Pesticide residues (JMPR) according to current data requirements and standards.

EFSA prepared a draft reasoned opinion that was shared with Member States and the European Reference Laboratories (EURLs) for consultation via a written procedure. Comments received were considered during the finalisation of this reasoned opinion. The following conclusions are derived.

The metabolism of profenofos in plant and animal was previously investigated by the JMPR. According to the results of the metabolism studies assessed, the residue definition for enforcement and risk assessment, both for plant and animal products, is profenofos. The EU residue definition defines the residue as fat soluble.

Analytical methods are available for the enforcement of the proposed residue definition in high-water content, high-oil content and dry matrices, as well as in coffee beans with an LOQ of 0.01 mg/kg, in high-acid content matrices with an LOQ of 0.02 mg/kg, and in seed and fruit spices with an LOQ of 0.1 mg/kg. Profenofos can be enforced in food of animal origin with an LOQ of 0.01 mg/kg in muscle, milk and eggs and an LOQ of 0.05 mg/kg in fat, kidney and liver. According to the EURLs, analytical methods are available for the routine analysis of profenofos in high-water content, high-acid content, high-oil content and dry commodities with an LOQ of 0.01 mg/kg, and in commodities that are difficult to analyse with a proposed LOQ of 0.02 mg/kg. In the four main matrix groups, even lower LOQs were achievable. Profenofos can also be monitored in commodities of animal origin (egg, muscle, liver and milk) at an LOQ of 0.01 mg/kg. Based on the experience gained with these animal matrices, the default LOQ of 0.01 mg/kg is deemed achievable also for animal fat and kidney.

The origin of all current MRLs set for profenofos was investigated, and all MRLs, based on monitoring data or on CXLs, were identified as sufficiently substantiated.

The TRVs set by the JMPR were assessed according to the current data requirements and standards. It was concluded that the TRVs cannot be confirmed for profenofos since the data available were insufficient compared to current standards, and uncertainty factors could not be established. Accordingly, the acceptable daily intake (ADI) and acute reference dose (ARfD) derived in 2007 do not comply with the current scientific standards. Therefore, EFSA recommends that risk managers discuss whether these TRVs should be withdrawn. The following data would be required to finalise the toxicological assessment which is a pre-requisite to derive robust TRVs:

- submission of the available studies with a full evaluation of the toxicological data package and reporting relevant details on the studies and the results in accordance with the current guidelines, including an assessment of the reliability and relevance of each individual study;
- assessment of the validity of analytical methods used in feed, body fluids and tissues, air and any additional matrices used in support of the toxicological studies;
- assessment of the presence of toxicologically relevant impurities in the technical specification and in profenofos-treated commodities;
- interspecies comparative in vitro metabolism study on animal species used in pivotal studies and on human material;
- additional toxicological data to perform an ED assessment according to the 2018 ECHA/EFSA Guidance;
- an up-to-date search for published literature.

Chronic and acute exposure calculations were performed using revision 3.1 of PRIMo, considering commodities for which CXLs and EU MRLs were found to be sufficiently substantiated. Comparing to the TRVs established by JMPR, no exceedances were observed, and the highest chronic exposure represented 17% of the ADI (GEMS/Food G06) and the highest acute exposure amounted to 27% of the ARfD (tomatoes). Nevertheless, EFSA emphasises that as the TRVs could not be confirmed, the risk assessment cannot be finalised and results presented under the current review are indicative only. Besides, there is further uncertainty about the risk assessment, considering that lower TRVs were derived by a Member State but could not be confirmed in the current assessment.

The summary table below reports the outcome of the review. If a decision on the withdrawing of TRVs is taken, EFSA recommends that risk managers discuss whether the MRLs currently implemented in EU Regulation should be lowered to the respective LOQs (except for the temporary MRLs set for herbs and edible flowers and rose).

Summary table

Code[a]	Commodity	Existing MRL[b] (mg/kg)	Outcome of the review	
			MRL proposal (mg/kg)	Comment
Residue definition for enforcement (plants and animal products): profenofos[F]				
0163030	Mangoes	0.2	0.2 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. However, further risk management discussions are needed to decide whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for profenofos
0231010	Tomatoes	10	10 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. However, further risk management discussions are needed to decide whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for profenofos
0256000	Herbs and edible flowers	0.03[c]	0.03	The existing temporary MRL, based on EU monitoring data, is sufficiently substantiated
0401090	Cotton seeds	3	3 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. However, further risk management discussions are needed to decide whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for profenofos
0631030	Rose	0.1[d]	0.1	The existing temporary MRL, based on EU monitoring data, is sufficiently substantiated
0810040	Coriander	0.1	0.1 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. It is based on monitoring data. Further risk management discussions are needed to decide whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for profenofos
0810050	Cumin	5	5 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. It is based on monitoring data. Further risk management discussions are needed to decide whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for profenofos
0810070	Fennel	0.1	0.1 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. It is based on monitoring data. Further risk management discussions are needed to decide whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for profenofos
0820010 0820020 0820030 0820050 0820060 0820070 0820080 0820090	Fruit spices (except cardamom)	0.07	0.07 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. It is based on monitoring data. Further risk management discussions are needed to decide whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for profenofos
0820040	Cardamom	3	3 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. It is based on monitoring data. Further risk management discussions are needed to decide whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for profenofos

Code[a]	Commodity	Existing MRL[b] (mg/kg)	Outcome of the review	
			MRL proposal (mg/kg)	Comment
1011000 1012000 1013000 1014000 1015000 1016000 1017000	Commodities from swine, bovine, sheep, goat, equine, poultry, other farmed terrestrial animals (except milk and eggs)	0.05	0.05 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. However, further risk management discussions are needed to decide whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for profenofos

Abbreviations: MRL, maximum residue limit; LOQ, limit of quantification; TRV, toxicological reference value.

[F]Fat soluble.

[a]Commodity code number according to Annex I of Regulation (EC) No 396/2005.

[b]MRL currently set under Regulation (EU) 2023/377.

[c]Temporary MRL, derived from recent monitoring data showing that residues of profenofos still occur in herbs and edible flowers. Further monitoring data is necessary to compare the evolution of the occurrence of profenofos in herbs and edible flowers. When re-viewing the MRL, the Commission will take into account the information, if it is submitted by 22/2/2030, or, if that information is not submitted by that date, the lack of it.

[d]Temporary MRL, derived from recent monitoring data showing that residues of profenofos occur in rose petals. Further monitoring data is necessary to compare the evolution of the occurrence of profenofos in rose petals. When re-viewing the MRL, the Commission will take into account the information, if it is submitted by 25 July 2029, or, if that information is not submitted by that date, the lack of it.

BACKGROUND

In March 2021, a Member State submitted to the European Commission the results of a screening performed on all maximum residue levels (MRLs) of active substances used in plant protection products that are not approved in the EU. The list contained 904 substances; for 297 of them, at least one MRL was set at a level above the limit of quantification (LOQ).

For 219 of these substances, the MRLs are not related to the uses of the substances in plant protection products (e.g. MRLs reflect the use of biocides or veterinary medical product, or MRLs are set to account for their occurrence in certain food due to environmental persistence, or their natural occurrence). For the other 78 substances, the MRLs were established either based on formerly approved uses in the EU, on import tolerance requests, or on Codex maximum residue limits (CXLs).

Some of these substances were never approved in the EU, or their approval was withdrawn before 2008, and therefore they did not fall within the scope of the systematic review of all existing MRLs under Article 12 of Regulation (EC) No 396/2005.[1]

A second Member State conducted additional analysis, identifying potential consumer risk for some of the MRLs set for these active substances.

Based on these analyses, the European Commission conducted a prioritisation exercise to identify substances for which existing MRLs should be reviewed with high priority. The prioritisation was also discussed and agreed with Member States during several meetings of the Standing Committee on Plants, Animals, Food and Feed (SCoPAFF), section Phytopharmaceuticals – Pesticides residues (September 2021,[2] November 2021,[3] and February 2022[4]). The SCoPAFF agreed that ten active substances, for which potential consumer risks were identified, should be assessed by EFSA as a priority. One of the substances identified for being assessed with high priority is profenofos.

The European Commission proposed to mandate EFSA to provide a targeted review of MRLs for the substances concerned without delay. Due to the urgency of the subject, EFSA was invited to consider, if appropriate, delivering a separate reasoned opinion for each of the substances included in this mandate, as to be able to start providing outcomes to the Commission as soon as possible and successively. In this reasoned opinion EFSA covered the targeted review of the MRLs for profenofos.

Terms of Reference (as provided by the requestor)

EFSA was requested by the European Commission, according to Article 43 of Regulation (EC) No 396/2005, to prepare a reasoned opinion on profenofos. In particular, the following tasks should be performed:

1. to investigate the origin of the current EU MRLs (e.g. MRL based on formerly approved uses in the EU, on import tolerance requests, or on CXLs). This analysis should allow to verify if the CXLs/import tolerances are still justified[5] and to identify MRLs that do not correspond to import tolerances or currently established CXLs (non-verified CXL/import tolerances);
2. to consult Member States on information about Good Agricultural Practices authorised in third countries and already evaluated at MS level, which might support maintaining the existing import tolerances or setting of new (lowered) import tolerances, if this is necessary in view of consumer protection;
3. to identify fall-back MRLs for MRLs that do not correspond to a verified CXLs/import tolerance; these fall-back MRLs could be either a lower import tolerance or a lower CXL established more recently. If no fall-back MRL can be identified, the MRL should be considered for lowering to the appropriate LOQ;
4. to consult the EU Reference Laboratories (EURLs) on the LOQs achievable during routine analyses for all commodities;
5. to perform an indicative screening of the chronic and acute consumer exposure related to the existing EU MRLs reflecting the verified CXLs/import tolerances, fall-back MRLs and/or proposed revised LOQ MRLs, using the newest version of the Pesticide Residues Intake Model (PRIMo) based on the available residue definitions for risk assessment and, if not available, residue definitions for enforcement derived at EU level or by JMPR. The following scenarios should be calculated:

[1]Regulation (EC) No 396/2005 of the 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.

[2]Standing Committee on Plants, Animals, Food and Feed Section Phytopharmaceuticals – Pesticide Residues 23-24 September 2021 (https://food.ec.europa.eu/system/files/2021-10/sc_phyto_20210923_ppr_sum.pdf).

[3]Standing Committee on Plants, Animals, Food and Feed Section Phytopharmaceuticals – Pesticide Residues 22 - 23 November 2021 (https://food.ec.europa.eu/system/files/2021-12/sc_phyto_20211122_ppr_sum_0.pdf).

[4]Standing Committee on Plants, Animals, Food and Feed Section Phytopharmaceuticals – Pesticide Residues 22 - 23 February 2022 (https://food.ec.europa.eu/system/files/2022-08/sc_phyto_20220222_ppr_sum.pdf).

[5]A CXL is considered justified if it is still in place (i.e. if it has not been withdrawn). An import tolerance is to be considered justified if the GAP in the country of origin is still authorised and the MRL in the country of origin is established at a level corresponding to the EU MRL (taking into account the potential difference in the RDs).

a. Scenario 1:

(i) Values at the appropriate LOQ: all MRLs that are based on former EU uses and all CXLs that were revoked by the Codex Committee on Pesticide Residues (CCPR) should be lowered to the appropriate LOQ;
(ii) Non-LOQ values to be considered: CXLs that were previously taken over in EU legislation, CXLs that were covered by still existing (higher) EU MRLs to be considered at the value of the CXL, MRLs based on existing import tolerances;

b. Scenario 2:

(i) Like scenario 1, but lowering all CXLs that were evaluated by EFSA before and including 2009[6] and all import tolerances established before and including 2007,[7] respectively, to the appropriate LOQ.

6. to derive the input values for commodities of animal origin for the consumer exposure calculation from the relevant assessment where the MRLs for animal products were derived. However, if the respective risk assessment values (HR/STMR) cannot be retrieved from the available sources, the exposure shall be calculated with the existing MRL. If the existing MRL is no longer justified and no fall-back MRL can be retrieved, the existing MRL should be considered for being lowered to the LOQ; in this case the risk assessment screening should be performed with the LOQ;
7. to examine the available information in order to screen the quality of the toxicological reference values (TRVs) set at EU level and of those established by JMPR. This screening should also consider the completeness of the set of toxicological studies used to derive the TRVs, as to assess if it would be acceptable according to the current standards. In case deficiencies are identified, these should be highlighted along with the resulting uncertainties;
8. to examine the available information in order to screen the quality of the residue definitions for risk assessment set at EU level and of those established by JMPR. In case deficiencies are identified, these should be highlighted along with the resulting uncertainties;
9. to compare the indicative chronic and acute dietary exposure to the toxicological reference values derived at EU level or, if not available, to the toxicological reference values derived by JMPR;
10. to report information on the classification of the substance under the CLP Regulation[8] and whether the active substance meets the criteria for endocrine disruptors;
11. to assess, in all cases, the contribution of MRLs at the LOQ to the exposure in all exposure scenarios;
12. to recommend MRLs that do not pose an unacceptable risk to consumers, where possible, and advise risk managers on alternative options. Where relevant, EFSA should indicate whether the achievable LOQs are sufficiently protective for consumers;
13. to share its draft reasoned opinion for consultation with Member States (MSs) and EURLs before finalising it.

EFSA accepted the mandate and to deliver its assessment by finalising separate reasoned opinions for each of the substances included in this mandate, including profenofos, by 22 May 2023. Subsequently, an extension of the deadline to 31 October 2023 was agreed with the European Commission.

Assessment

To address the complex Terms of Reference (ToR), EFSA used the following approach:

- In Section 1 (Regulatory background information on profenofos), information on classification of the active substance under CLP regulation and on endocrine properties is reported (addressing ToR 10).
- In Section 2.1 (Nature of residues and residue definitions), a screening of the quality of residue definitions is reported (addressing ToR 8).
- In Section 2.2 Analytical methods for MRLs enforcement), information on analytical methods for MRLs enforcement provided by the EURLs on the LOQs achievable during routine residues analysis is reported (ToR 4). In addition, EFSA summarised the information on the analytical methods assessed previously by EFSA.
- In Section 2.3 (Existing MRLs), information on the origin of the current MRL is reported in tabular format (ToR 1). In the same section, information provided by MSs on good agricultural practices (GAPs) authorised in third countries and previously evaluated in view of setting import tolerances can be found (ToR 2). This information, together with information on existing CXLs, is used to derive possible fall-back MRLs (ToR 3) that are also reported in the table, if available.
- In Section 3 (Toxicological reference values), the appropriateness of the TRVs set by the JMPR in 2007 is assessed according to the current EU data requirements[9] and standards (ToR 7).

[6]The first EFSA scientific report in preparation of CCPR was prepared in 2010.

[7]The first evaluations of import tolerances under Regulation (EC) No 396/2005 which fully entered into force on 1.9.2008.

[8]Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006.OJ L 353, 31.12.2008, p. 1

[9]Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market. OJ L 93, 3.4.2013, p. 1–84.

- In Section 4 (Consumer risk assessment), an indicative screening of the chronic and acute consumer exposure is presented (ToR 5 and 6). The dietary exposure assessment Scenario 1 and Scenario 2 are performed as requested in ToR 5 (a) and (b) respectively. This section also addresses ToR 11 (contribution of MRLs at the LOQ to the total exposure) and ToR 9 (comparison of the dietary exposure with the TRVs derived at JMPR level), however, noting that following the experts' meeting on mammalian toxicology, it was concluded that the TRVs do not comply with the current scientific standards.
- In the Conclusions and recommendations section, EFSA presents the MRL proposals that are unlikely to pose an unacceptable risk to consumers, where possible, and the ones for which further consideration is required (ToR 12).

No draft assessment report (DAR) and no EFSA conclusion are available. Therefore, EFSA has based its assessment on the following documents:

- the scientific reports on the scientific support for preparing an EU position in the 48th and in the 51st sessions of the Codex Committee on Pesticide Residues (CCPR) (EFSA, 2016, 2019b);
- the reports and evaluations of the JMPR (FAO and WHO, 2007, 2008, 2015, 2018);
- the reports of the Codex Committee on Pesticide residues (CCPR, 2009, 2016).

As requested by the terms of reference (ToR 2), Member States were invited to submit by 18 October 2022 the Good Agricultural Practices (GAPs) that are authorised in third countries and already evaluated at national level, in the format of specific GAP forms, as well as the supporting residue data, in the format of an evaluation report. In the framework of this consultation seven Member States (CZ, DE, ES, IT, FR, NL and SE) provided feedback regarding profenofos and notified that no import tolerances were in place. The EU Reference Laboratories (EURLs) were also consulted (ToR 4) to provide an evaluation report on the availability of analytical methods for enforcement and the LOQs achievable during routine analysis in plants and animal commodities. The **EURLs report on analytical methods** (EURLs, 2022) submitted during the collection of data is considered as main supporting document to this reasoned opinion and, thus, made publicly available.

On the basis of the data submitted by the MSs, the EURLs, the data available in the Joint Meeting on Pesticide residues (JMPR) Evaluation reports and taking into account the conclusions derived by EFSA in previous opinions and the screening of the available toxicological data with regards to their completeness and quality according to current standards, EFSA prepared a draft reasoned opinion, which was circulated to Member States and EURLs for consultation via a written procedure in September 2023. Comments received by 26 September 2023 were considered during the finalisation of this reasoned opinion (ToR 13).

Further supporting document to this reasoned opinion is the **Member States consultation report** (EFSA, 2023). The exposure calculations for all crops reported in the framework of this review performed using the EFSA Pesticide Residues Intake Model (**PRIMo**) are also key supporting documents made publicly available as background document to this reasoned opinion.

1 | REGULATORY BACKGROUND INFORMATION ON PROFENOFOS

The key events concerning the regulatory history of profenofos, the background information, together with the relevant published documents are summarised in Table 1.

TABLE 1 Background information.

Process	Status	Comments, references
Approval status	Not approved	Non-inclusion of profenofos in Annex I of Council Directive 91/414/EEC by Commission Regulation (EC) 2076/2002[b]
EFSA conclusion available	No	–
MRL review performed	No	–
EU MRL applications or other EU assessments	Yes, see comments	Implementation of certain CXLs adopted by CAC 2009: Following discussion in CCPR 41 (2009), CXLs for mangoes, tomatoes and cotton seeds were included in Regulation (EC) 459/2010[c] and have never been modified since. Implementation of EU MRLs: EU MRLs were set on the basis of monitoring data on herbs and edible flowers in Regulation (EU) 2023/377[d] and on rose in Regulation (EU) 899/2012[e] and 2022/1290.[f] Codex MRL assessments (Art. 43): EFSA Scientific support for preparing an EU position in the 48th and 51st Sessions of the Codex Committee on Pesticide Residues (CCPR) (EFSA, 2016, 2019b)
Classification under CLP Regulation	See comments	Acute Tox 4[a], H302 'harmful if swallowed' Acute Tox 4[a], H312 'harmful in contact with skin' Acute Tox 4[a], H332 'harmful if inhaled' (CLP00[f]) Profenofos does not fall under cut off criteria
Endocrine effects of a.s.	Not assessed	ED assessment according to ECHA and EFSA guidance (ECHA and EFSA, 2018) and scientific criteria (Commission Regulation (EC) No 2018/605[g]) have not been performed. A full data package is needed to carry it out

Abbreviations: a.s, active substance; CAC, Codex Alimentarius Commission; CCPR, Codex Committee on Pesticide Residues; CLP, classification, labelling and packaging; CXL, Codex maximum residue limit; ECHA, European chemicals agency; ED, endocrine disruptor; MRL, maximum residue limit.

[a]Indicates a minimum classification that must be classified in a more severe hazard category in the event that further information is available which shows that the hazard(s) meet the criteria for classification in the more severe category (see Annex VI, section 1,2,1 of CLP Regulation).

[b]Commission Regulation (EC) No 2076/2002 of 20 November 2002 extending the time period referred to in Article 8(2) of Council Directive 91/414/CE and concerning the non-inclusion of certain active substances in Annex I to that Directive and the withdrawal of authorisations for plant protection products containing these substances. OJL 319, 23.11.2002, p. 3–11.

[c]Commission Regulation (EU) No 459/2010 of 27 May 2010 amending Annexes II, III and IV to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for certain pesticides in or on certain products. OJ L 129, 28.5.2010, p. 3–49.

[d]Commission Regulation (EU) No 2023/377 of 15 February 2023 amending Annexes II, III, IV and V to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for benzalkonium chloride (BAC), chlorpropham, didecyldimethylammonium chloride (DDAC), flutriafol, metazachlor, nicotine, profenofos, quizalofop-P, sodium aluminium silicate, thiabendazole and triadimenol in or on certain products. OJ L 55, 22.2.2023, p. 1–84.

[e]Commission Regulation (EU) No 899/2012 of 21 September 2012 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for acephate, alachlor, anilazine, azocyclotin, benfuracarb, butylate, captafol, carbaryl, carbofuran, carbosulfan, chlorfenapyr, chlorthal-dimethyl, chlorthiamid, cyhexatin, diazinon, dichlobenil, dicofol, dimethipin, diniconazole, disulfoton, fenitrothion, flufenzin, furathiocarb, hexaconazole, lactofen, mepronil, methamidophos, methoprene, monocrotophos, monuron, oxycarboxin, oxydemeton-methyl, parathion-methyl, phorate, phosalone, procymidone, profenofos, propachlor, quinclorac, quintozene, tolylfluanid, trichlorfon, tridemorph and trifluralin in or on certain products and amending that Regulation by establishing Annex V listing default values. OJ L 273, 6.10.2012, p. 1–75.

[f]Commission Regulation (EU) 2022/1290 of 22 July 2022 amending Annexes II, III and IV to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for ametoctradin, chlormequat, dodine, nicotine, profenofos and Spodoptera exigua multicapsid nucleopolyhedrovirus (SeMNPV) isolate BV-0004 in or on certain products. OJ L 196, 25.7.2022, p. 74–114.

[f]Annex VI of Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. OJ L 353, 31.12.2008, p. 1–1355.

[g]Commission Regulation (EU) 2018/605 of 19 April 2018 amending Annex II to Regulation (EC) No 1107/2009 by setting out scientific criteria for the determination of endocrine disrupting properties. OJ L 101, 20.4.2018, p. 33–36.

2 | RESIDUE DEFINITIONS AND EXISTING EU MRLS

2.1 | Nature of residues and residue definitions

As requested in point 8 of the Terms of Reference, EFSA summarised in this section the information used to derive the residue definitions for plant and animal products. Table 2 covers the studies submitted to JMPR in the framework of the setting of CXLs (studies not assessed at EU level).

TABLE 2 Available metabolism studies.

Primary crops	Crop groups	Crop(s)	Application(s)	Sampling (DAT)	Comment/Source
	Fruit crops	Tomato	Outdoor, foliar (spray appl.), 3 × 0.722–0.822 kg a.s./ha (int. 1 week)	Tomatoes and leaves: 0, 4, 7 and 14	[U-^{14}C-phenyl]-profenofos (FAO and WHO, 2008)
	Leafy crops	Lettuce	Outdoor, 1 local appl. of 1 mg of a.s. on 2 leaves of lettuce plants	0, 7, 14 and 21	[U-^{14}C-phenyl]-profenofos (FAO and WHO, 2008) Only treated leaves were sampled
		Brussels sprout	Foliar (spray appl.), 3 × 1.1 kg a.s./ha (int. 2 weeks)	0d after 1st, 2nd and 3rd appl. Before 2nd and 3rd appl. 21d after 3rd appl.	[U-^{14}C-phenyl]-profenofos (FAO and WHO, 2008)
	Pulses/ oilseeds	Cotton	Indoor, foliar (spray appl.), 1 × 1.7 kg a.s./ha	Leaves and stem: 0 and 42 d Leaves and stems, fibre and seed samples: 12 weeks	[U-^{14}C-phenyl]-profenofos (FAO and WHO, 2008)
			Outdoor, foliar (spray appl.), 3 × 2.2 kg a.s./ha (int. 2 weeks)	Cotton plants: 0 d. After 1st, 2nd and 3rd appl Leaves, seed and fibre: 3 and 7 weeks after 3rd appl	[U-^{14}C-phenyl]-profenofos (FAO and WHO, 2008)
			Outdoor, foliar (spray appl.), 6 applications on a weekly basis at a rate of 2.2 kg a.s./ha for a total of 6.7 kg a.s./ha	61 and 83 day	[U-^{14}C-phenyl]-profenofos (FAO and WHO, 2008)

(Continues)

TABLE 2 (Continued)

Livestock	Animal	Dose	Duration (days)	Comment/Source
	Laying hen	5 mg/kg in the feed	14	[phenyl-^{14}C]-profenofos (FAO and WHO, 2008) The study does not include significant identification of the residues
		1 mg/kg and 10 mg/kg in the feed	8	[phenyl-^{14}C]-profenofos (FAO and WHO, 2008)
	Ruminant, lactating goat	5 mg/kg in the feed	9	[phenyl-^{14}C]-profenofos (FAO and WHO, 2008) Metabolites were not identified
		100 mg/kg in the feed	4	[phenyl-^{14}C]-profenofos (FAO and WHO, 2008)
	Pigs	–	–	Study not required as metabolism in rat and ruminant was found to be similar (FAO and WHO, 2008)

Abbreviations: a.s., active substance; DAT, days after treatment; ha, hectare.

Metabolism studies on tomato, lettuce, Brussels sprout and cotton were assessed by the JMPR (FAO and WHO, 2008). Parent profenofos is the major component of the total radioactive residue (TRR) in most crops until 2–3 weeks after application (63% TRR in tomato fruits 14 days after last application, 61% TRR in lettuce 21 days after treatment, 6.5% TRR in cotton seeds 83 days after last application). In Brussels sprout, no profenofos was detected in sprouts 21 days after last application. Metabolite CGA 55960 was identified at 10% TRR in lettuce. Metabolite CGA 55960 glucosyl sulfate was identified at 17.3% TRR in cotton seeds 83 days after last application but concentration of this metabolite is expected to be below the LOQ level. Consequently, the residue definition for monitoring and risk assessment in plant commodities was recommended as profenofos (FAO and WHO, 2008). The residue definitions are applicable to all crop groups.

The nature of profenofos residues in livestock was investigated and assessed by the JMPR (FAO and WHO, 2008). Profenofos was rapidly absorbed and eliminated after oral administration and was only found in significant amount in goat liver and fat. In lactating goat, the main components of residue were CGA 55960 sulfate in milk, kidney and muscle (85%, 40% and 56% TRR, respectively), CGA 55960 in liver (25% TRR) and parent profenofos in fat (44% TRR). In laying hens, the major residue components were CGA 55960 in fat (77–89% TRR) and in liver (71%–75% TRR) and CGA 55960 sulfate in muscle (75%–85% TRR) and eggs (88%–98% TRR). However, according to feeding studies, parent and metabolites are expected to be present below the LOQ. Consequently, the residue definition for monitoring and risk assessment in animal commodities was recommended as profenofos (FAO and WHO, 2008). Based on the log P_{ow} of 4.4 at 25°C, profenofos itself may be considered fat soluble. However, in animal metabolism studies TRR in fat (0.07 mg eq/kg) was lower than in kidney (up to 2.5 mg eq/kg), liver (0.51 mg eq/kg) and milk (0.41 mg eq/kg). The study results indicated that the parent was rapidly decomposed to water soluble metabolites, and those metabolites were excreted. Therefore, the meeting decided that the residues would not be fat soluble (FAO and WHO, 2008).

Table 3 summarises the residue definitions for enforcement and risk assessment derived by the JMPR. The EU residue definitions for enforcement are set in Regulation (EC) No 396/2005.

TABLE 3 Residue definitions derived by JMPR and set at EU level.

Type of residue definition (RD)	Commodity group	EU residue definition	JMPR residue definitions
RD for enforcement	Plant products	Profenofos	Profenofos (FAO and WHO, 2008)
	Animal products	Profenofos The residue is fat soluble	Profenofos The residue is not fat soluble (FAO and WHO, 2008)
RD for risk assessment	Plant products	Not assessed at EU level	Profenofos (FAO and WHO, 2008)
	Animal products	Not assessed at EU level	Profenofos (FAO and WHO, 2008)

Comments: The residue definitions for plant and animal products set in Reg. (EC) 396/2005 refer to the ones established in the framework of JMPR assessments. The JMPR defines the residues as not fat soluble, whereas the EU residue definition defines the residues as fat soluble.

2.2 | Analytical methods for MRLs enforcement

Analytical methods for the determination of profenofos residues were assessed in the framework of the JMPR evaluations (FAO and WHO, 2008, 2015, 2018). Analytical methods are available to enforce residues of profenofos in high-water content, high-oil content and dry commodities, as well as in coffee beans with an LOQ of 0.01 mg/kg, and in high-acid content commodities with an LOQ of 0.02 mg/kg. A method was reported to monitor profenofos in seed and fruit spices with an LOQ of 0.1 mg/kg.

Profenofos can be enforced in food of animal origin with an LOQ of 0.01 mg/kg in muscle, milk and eggs and an LOQ of 0.05 mg/kg in fat, kidney and liver (FAO and WHO, 2008).

During the data collection, the EURLs provided information on a QuEChERS multi-residue analytical method using GC–MS/MS and LC–MS/MS technique, with an LOQ of 0.01 mg/kg for the routine analysis of profenofos in high-water content, high-acid content, high-oil content and dry commodities. In these four matrix groups, even lower levels were achievable. A QuEChERS method using LC–MS/MS technique is also available for commodities that are difficult to analyse (e.g. spices, cocoa, tea); based on the results obtained and the fact that profenofos can be analysed with a good sensitivity, an LOQ of 0.02 mg/kg is proposed to enforce matrices that are difficult to analyse. According to the EURLs, in commodities of animal origin (muscle, liver, milk and egg), profenofos can be monitored with a default LOQ of 0.01 mg/kg. Based on the experience gained with these animal matrices, an LOQ of 0.01 mg/kg for animal fat and kidney is also deemed achievable (EURLs, 2022). The EURLs informed that analytical standard for profenofos is commercially available.

Table 4 provides an overview of the analytical methods available and their respective LOQs.

TABLE 4 Analytical methods available.

Commodity group		Analytical method available	LOQ (mg/kg)	Source
Plant commodities	High water	Yes (QuEChERS method with GC–MS/MS and LC–MS/MS)	0.01	EURLs (2022)
		Yes (LC–MS/MS)	0.01	FAO and WHO (2018)
	High oil	Yes (QuEChERS method with GC–MS/MS and LC–MS/MS; QuOil method with LC–MS/MS)	0.01	EURLs (2022)
		Yes (LC–MS/MS)	0.01	FAO and WHO (2018)
	High acid	Yes (QuEChERS method with GC–MS/MS and LC–MS/MS)	0.01	EURLs (2022)
		Yes (DFG Method S19 with GC–FPD and GC–MSD; GC-NPD; GC-ECD)	0.02	FAO and WHO (2008)
	Dry	Yes (QuEChERS method with GC–MS/MS and LC–MS/MS)	0.01	EURLs (2022)
		Yes (LC–MS/MS)	0.01	FAO and WHO (2018)
	Seed and fruit spices	Yes (QuEChERS method with GC–MS/MS and LC–MS/MS)	0.1	FAO and WHO (2015)
	Coffee beans	Yes (LC–MS/MS)	0.01	FAO and WHO (2018)
	Commodities difficult to analyse (e.g. spices, cocoa, tea)	Yes (QuEChERS method with LC–MS/MS)	0.02	EURLs (2022)
Animal commodities	Muscle	Yes (SweET method with GC–MS/MS, Q-EMR method with GC–MS/MS)	0.01	EURLs (2022)
		Yes (DFG Method S19 with GC–FPD and GC–MSD)	0.01	FAO and WHO (2008)
	Kidney	–	0.01[a]	EURLs (2022)
		Yes (GC–ECD, GC–FPD)	0.05	FAO and WHO (2008)
	Liver	Yes (QuEChERS method with GC–MS/MS and LC–MS/MS)	0.01	EURLs (2022)
		Yes (GC–ECD, GC–FPD)	0.05	FAO and WHO (2008)
	Fat	–	0.01[a]	EURLs (2022)
		Yes (GC–ECD, GC–FPD)	0.05	FAO and WHO (2008)
	Milk	Yes (SweET method with GC–MS/MS)	0.01	EURLs (2022)
		Yes (DFG Method S19 with GC–FPD and GC–MSD; GC–ECD; GC-FPD)	0.01	FAO and WHO (2008)
	Eggs	Yes (SweET method with GC–MS/MS, Q-EMR method with GC–MS/MS and GC-Orbitrap)	0.01	EURLs (2022)
		Yes (DFG Method S19 with GC–FPD and GC–MSD)	0.01	FAO and WHO (2008)

Abbreviations: GC–ECD, gas chromatography with electron capture detector; GC-FPD, gas chromatography with flame photometric detection; GC–MSD, gas chromatography with mass selective detection; GC–NPD, gas chromatography with nitrogen-phosphorus detection; GC–MS/MS, gas chromatography with tandem mass spectrometry; LC–MS/MS, liquid chromatography with tandem mass spectrometry; LOQ, limit of quantification; QuEChERS, Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method); SweET, Swedish ethyl acetate method.

[a]Although no validation data are available for this specific commodity within the EURLs, it is assumed that the reported LOQ would be achievable based on the experience gained with profenofos in other matrices.

2.3 | Existing MRLs

The EU MRLs for profenofos are established in Annex II and IIIb of Regulation (EC) No 396/2005. For a number of food products, CXLs have been taken over in the EU legislation. It should be noted that in the framework of the current review, Member States did not notify import tolerances in place.

EFSA reported in Table, the existing EU MRLs set above the LOQ for the respective crop/crop groups, including information on the source of the MRLs together with the relevant GAPs and the references to the assessment where the MRL proposal was derived. In response to ToR 1 which requests to provide an analysis whether the existing EU MRL, the CXL or the import tolerance established for a crop is sufficiently substantiated, EFSA applied the following criteria:

A CXL is considered substantiated if:

- it is still in place (CXL has not been withdrawn from the Codex system);
- the CXL is sufficiently supported by data;
- the enforcement residue definition is identical with the EU residue definition.

An import tolerance is considered substantiated if:

- the GAP in the country of origin is still authorised;
- the import tolerance is sufficiently supported by data;
- the MRL in the country of origin is established at a level corresponding to the EU MRL (taking into account the potential difference in the RDs);
- in case the residue definition in the country of origin is different, the import tolerance is substantiated if sufficient information is available to derive an MRL for the EU RD.

An existing EU MRLs is not substantiated if:

- it is based on a previously authorised EU use;
- it is based on a previous CXL that has been revoked/withdrawn;
- it is based on an import tolerance that is no longer relevant as the use in the country of origin is not confirmed.

In addition, a temporary MRL set in accordance with Art. 16 of Regulation (EC) No 396/2005 is considered substantiated, provided that the deadline for the reassessment of the temporary MRL has not yet expired.

In order to address ToR 3, 5 and 6, in cases where the current CXLs or import tolerances are not sufficiently substantiated, Table 5 includes information on possible fall-back GAPs and the associated fall-back MRLs. In the last column of this table, additional considerations relevant for taking risk management decisions are also reported.

EFSA highlights that for coffee beans, a CXL of 0.04 mg/kg is currently in place (adopted by CCPR 51/CAC 2019), which is covered by the current EU MRL set at the LOQ of 0.05 mg/kg.

TABLE 5 Background information on current MRLs for profenofos established at a level above the LOQ, and verification whether these values are sufficiently substantiated.

Commodity	Existing MRL (mg/kg)	Source of existing MRL	cGAP for existing MRL	Existing MRL substantiated? (Y/N)	Fall-back GAP	Fall-back MRL (mg/kg)	Comment
Mangoes	0.2	CXL (CAC, 2009)	Thailand: foliar, 4×0.075 kg a.s./hl, PHI 21 days	Y	n.r.	n.r.	In 2008, JMPR derived a Codex MRL proposal of 0.2 mg/kg on mangoes The proposed CXL was adopted by CCPR 32/CAC 2009 and was implemented in EU legislation by Reg. (EC) 459/2010
Tomatoes	10	CXL (CAC, 2009)	South Africa: foliar, 0.25–0.75 kg a.s./ha, PHI 4 days (number of applications not specified)	Y	n.r.	n.r.	In 2008, JMPR derived a Codex MRL proposal of 10 mg/kg on tomatoes The proposed CXL was adopted by CCPR 32/CAC 2009 and was implemented in EU legislation by Reg. (EC) 459/2010
Herbs and edible flowers	0.03	EU MRL (Reg. (EU) 2023/377)	See comments	Y	n.r.	n.r.	On the basis of EU monitoring data carried out between 2012 and 2015, EU temporary MRLs of 0.5 mg/kg on herbs and edible flowers were legally implemented in Regulation (EU) 899/2012, and its validity was further extended Based on recent EU monitoring data the MRL was decreased to 0.03 mg/kg in Reg. (EU) 2023/377, specifying that it is appropriate to continue to monitor the levels of profenofos in 'herbs and edible flowers' and to review this MRL based on monitoring data submitted to the Commission within 7 years from the publication of this Regulation
Cotton seeds	3	CXL (CAC, 2009)	USA: foliar, 2–4×0.14–0.86 kg a.s./ha, PHI 14 days	Y	n.r.	n.r.	In 2008, JMPR derived a Codex MRL proposal of 3 mg/kg on cotton seeds The proposed CXL was adopted by CCPR 32/CAC 2009 and was implemented in EU legislation by Reg. (EC) 459/2010
Rose	0.1	EU MRL (Reg. (EU) 899/2012)	See comments	Y	n.r.	n.r.	On the basis of EU monitoring data carried out between 2012 and 2015, an EU temporary MRL of 0.1 mg/kg on rose was legally implemented in Regulation (EU) 899/2012, and its validity was further extended Recent EU monitoring data showed that residues of profenofos still occur in rose petals, and the EU temporary MRL was maintained in Reg. (EU) 2022/1290, specifying that it is appropriate to continue to monitor the levels of profenofos in rose petals and to extend the validity of that temporary MRL for 7 years from the publication of this Regulation
Coriander	0.1	CXL (CAC, 2016)	See comments	Y	n.r.	n.r.	In 2015, JMPR derived a Codex MRL proposal of 0.1 mg/kg on coriander seed based on monitoring data (FAO and WHO, 2015). The proposed CXL was adopted by CCPR 48/CAC 2016 and was implemented in EU legislation by Reg. (EU) 2017/626
Cumin	5	CXL (CAC, 2016)	See comments	Y	n.r.	n.r.	In 2015, JMPR derived a Codex MRL proposal of 5 mg/kg on cumin seed based on monitoring data (FAO and WHO, 2015). The proposed CXL was adopted by CCPR 48/CAC 2016 and was implemented in EU legislation by Reg. (EU) 2017/626
Fennel	0.1	CXL (CAC, 2016)	See comments	Y	n.r.	n.r.	In 2015, JMPR derived a Codex MRL proposal of 0.1 mg/kg on fennel seed based on monitoring data (FAO and WHO, 2015). The proposed CXL was adopted by CCPR 48/CAC 2016 and was implemented in EU legislation by Reg. (EU) 2017/626

(Continues)

TABLE 5 (Continued)

Commodity	Existing MRL (mg/kg)	Source of existing MRL	cGAP for existing MRL	Existing MRL substantiated? (Y/N)	Fall-back GAP	Fall-back MRL (mg/kg)	Comment
Fruit spices (except cardamom)	0.07	CXL (CAC, 2016)	See comments	Y	n.r.	n.r.	In 2015, JMPR derived a Codex MRL proposal of 0.07 mg/kg on fruit spices (except cardamom) based on monitoring data (FAO and WHO, 2015). The proposed CXL was adopted by CCPR 48/CAC 2016 and was implemented in EU legislation by Reg. (EU) 2017/626
Cardamom	3	CXL (CAC, 2016)	See comments	Y	n.r.	n.r.	In 2015, JMPR derived a Codex MRL proposal of 3 mg/kg on cardamom based on monitoring data (FAO and WHO, 2015). The proposed CXL was adopted by CCPR 48/CAC 2016 and was implemented in EU legislation by Reg. (EU) 2017/626
Commodities from swine, bovine, sheep, goat, equine, poultry, other farmed terrestrial animals, except milk and eggs	0.05	CXL (CAC, 2009)	Mean/max. dietary burden beef cattle (US, Australia): 0.11/0.11 ppm Mean/max. dietary burden poultry (US): 0.04/0.04 ppm (FAO and WHO, 2008)	Y	n.r.	n.r.	In 2008, JMPR derived a Codex MRL proposal of 0.05* mg/kg on edible offal (mammalian and poultry) and on meat (from mammals other than marine animals and from poultry). The CXL was implemented in the EU legislation by Reg. (EU) 898/2012

Abbreviations: a.s., active substance; CAC, Codex Alimentarius Commission; CCPR, Codex committee on pesticide residues; cGAP, critical good agricultural practice; CXL, Codex maximum residue limit; GAP, good agricultural practice; ha, hectare; PHI, pre-harvest interval; MRL, maximum residue limit; n.r., not relevant; ppm, parts per million.

*Indicates that the Codex MRL is set at the limit of quantification.

3 | TOXICOLOGICAL REFERENCE VALUES

EFSA was mandated to examine the available information in order to screen the quality of the TRVs set at EU level and of those established by the JMPR and to assess the completeness of the set of toxicological studies used to derive the TRVs according to the current standards. In case deficiencies are identified, these should be highlighted along with the resulting uncertainties (ToR 7).

The TRVs for profenofos reported in Table 6 were derived by the JMPR in 2007; the active substance was never peer reviewed at the EU level.

TABLE 6 Toxicological reference values (TRVs) set by the JMPR.

TRV	Value	Reference	Comments
Group ADI	0.03 mg/kg bw per day	FAO and WHO (2007)	Based on an overall NOAEL of 2.9 mg/kg bw per day for inhibition of brain AChE activity in 3 short-term studies in dogs and applying an UF of 100 This ADI is supported by the NOAEL of 5.1 mg/kg bw per day for inhibition of maternal and pup brain AChE activity in a DNT study in rats and a NOAEL of 4.5 mg/kg bw per day for inhibition of brain AChE activity in a 2-year study in mice
Group ARfD	1 mg/kg bw	FAO and WHO (2007)	Based on a NOAEL of 100 mg/kg bw for clinical signs of neurotoxicity seen ≥ 200 mg/kg bw and inhibition of brain AChE activity at 400 mg/kg bw in studies of acute neurotoxicity in rats and applying an UF of 100

Abbreviations: bw, body weight; AChE, acetylcholinesterase; ADI, acceptable daily intake; ARfD, acute reference dose; DNT, developmental neurotoxicity; NOAEL, no observed adverse effect level; UF, uncertainty factor.

It is noted that TRVs derived by Germany in 2019 were used by EFSA as one possible risk assessment scenario in the scientific report for preparing the EU position for the CCPR (EFSA, 2019b). These values are not considered further in the current assessment since the data supporting them are not available to EFSA.

EFSA screened the completeness and the appropriateness of the toxicological data reported in the JMPR monograph (FAO and WHO, 2007) used to derive the TRVs, focusing on the question whether the information is sufficient to assess whether they meet current quality (i.e. reliability and reporting) standards and the EU data requirements. The original studies are not available to EFSA.

The JMPR reports that all pivotal studies with profenofos were certified as complying with good laboratory practice (GLP).

With regards to the toxicological data package needed to derive an ADI and ARfD, the following data gaps were identified according to the current data requirements:

- an assessment of the validity of the analytical methods used in feed, body fluids and tissues, air and any additional matrices used in support of the toxicological studies;
- the presence of toxicologically relevant impurities in the technical specification and in profenofos-treated commodities cannot be assessed;
- an interspecies comparative in vitro metabolism study performed on animal species used in pivotal studies and on human material is not available to determine the relevance of the toxicological animal data to humans and whether additional testing of potential unique human metabolites would be required;
- an assessment of the endocrine disruptive potential of profenofos cannot be performed since insufficient investigations of the ED parameters are available according to the current ECHA/EFSA Guidance (ECHA and EFSA, 2018);
- an up-to-date search for published literature.

With regards to the JMPR monograph, it is not considered a source of information that can be independently reviewed due to the lack of details reported on the methods and results of the toxicological studies, such as the presentation of the tabulated results. An assessment of the relevance and reliability of each study when compared to the current OECD test guidelines would also be needed. For instance, in the JMPR assessment, a summary table presents the results of the genotoxicity studies with profenofos. No information is reported on the tested material, deviations from OECD test guidelines and overall conduct and results of the studies, and therefore a reliability/relevance assessment cannot be undertaken for the individual studies. With regards to developmental neurotoxicity (DNT), it is noted that it is a critical study for the risk assessment of profenofos, which belongs to the chemical class of organophosphorus insecticides presenting a neurotoxic mode of action, and for which the inhibition of brain acetylcholinesterase activity has been identified as the most sensitive parameter in all the tested species. DNT studies are complex to interpret and with the information reported in the JMPR monograph it is not possible to conclude on the no observed adverse effect level/lowest observed adverse effect level (NOAEL/LOAEL) for the study with an acceptable uncertainty.

Considering the data gaps and uncertainties identified, it is concluded that the data available are insufficient to assess the strength of the toxicological reference values compared to current standards, and uncertainty factors could not be established.

4 | CONSUMER RISK ASSESSMENT

In order to address ToR 5 (a) and (b) (Scenario 1, scenario 2), ToR 6 and ToR 11, EFSA calculated the chronic and acute dietary exposure, based on the residue definition for risk assessment derived by JMPR, i.e. profenofos. Chronic and acute exposure calculations for all crops reported in the framework of this review were performed using revision 3.1 of the EFSA PRIMo (EFSA, 2018, 2019a). All input values included in the exposure calculations are summarised in Appendix C.

- **Scenario 1**:
  - All CXLs and EU MRLs that are sufficiently substantiated were considered for the exposure assessment, using the relevant risk assessment value for the current MRL. For the chronic exposure assessment, the calculation is based on the supervised trials median residue levels (STMR) derived for raw agricultural commodities or the MRL for herbs and edible flowers, rose and fruit spices except cardamom. For the acute exposure assessment, the calculation is based on the highest residue levels (HR) expected in raw agricultural commodities, except for cotton seeds for which the STMR and for herbs and edible flowers, rose and fruit spices, except cardamom for which the MRL was used. For cumin and cardamom, STMR and HR were estimated by JMPR based on monitoring data.
  - All other commodities where no GAP was reported in the framework of the MRL review were included in the calculation with the appropriate LOQ.

- **Scenario 2:**
  - Like scenario 1, but lowering all CXLs that were never evaluated by EFSA and implemented in EU before and including 2009 to the appropriate LOQ.

In the absence of TRVs derived at EU level, the acute and chronic exposure calculations were compared to the TRVs derived by JMPR (FAO and WHO, 2007), noting that data were not sufficient to assess whether the TRVs comply with the current scientific standards (see Section 3). Thus, the risk assessment requested in ToR 5 and presented in this review is indicative only.

Screenshots of the report sheet of the indicative PRIMo calculations for scenarios 1 and 2 are presented in Appendix B.

The highest chronic exposure was calculated for GEMS/Food G06 representing 17% of the ADI in scenario 1, and for Dutch toddler representing 4% of the ADI in scenario 2. The contribution of the MRLs set at the LOQ to the exposure represents 1% of the ADI for scenario 1 and 4% for scenario 2. The highest acute exposure was calculated for tomatoes, representing 27% of the ARfD in scenario 1, and for potatoes, representing 0.2% of the ARfD in scenario 2.

CONCLUSIONS AND RECOMMENDATIONS

The metabolism of profenofos in plant and animal was previously investigated by the JMPR. According to the results of the metabolism studies assessed, the residue definition for enforcement and risk assessment, both for plant and animal products, is profenofos. The EU residue definition defines the residue as fat soluble.

Analytical methods are available for the enforcement of the proposed residue definition in high-water content, high-oil content and dry matrices, as well as in coffee beans with an LOQ of 0.01 mg/kg, in high-acid content matrices with an LOQ of 0.02 mg/kg, and in seed and fruit spices with an LOQ of 0.1 mg/kg. Profenofos can be enforced in food of animal origin with an LOQ of 0.01 mg/kg in muscle, milk and eggs and an LOQ of 0.05 mg/kg in fat, kidney and liver. According to the EURLs, analytical methods are available for the routine analysis of profenofos in high-water content, high-acid content, high-oil content and dry commodities with an LOQ of 0.01 mg/kg, and in commodities that are difficult to analyse with a proposed LOQ of 0.02 mg/kg. In the four main matrix groups, even lower LOQs were achievable. Profenofos can also be monitored in commodities of animal origin (egg, muscle, liver and milk) at an LOQ of 0.01 mg/kg. Based on the experience gained with these animal matrices, the default LOQ of 0.01 mg/kg is deemed achievable also for animal fat and kidney.

The origin of all current MRLs set for profenofos was investigated, and all MRLs, based on monitoring data or on CXLs, were identified as sufficiently substantiated.

A screening of the appropriateness of the TRVs set by the JMPR was performed, and the set of toxicological studies used to derive these TRVs was assessed according to the current data requirements and standards. It was concluded that the TRVs cannot be confirmed for profenofos since the data available were insufficient compared to current standards, and uncertainty factors could not be established. Accordingly, the ADI and ARfD derived in 2007 do not comply with the current scientific standards. Therefore, EFSA recommends that risk managers discuss whether these TRVs should be withdrawn. The following data would be required to finalise the toxicological assessment which is a pre-requisite to derive robust TRVs:

- submission of the available studies with a full evaluation of the toxicological data package and reporting relevant details on the studies and the results in accordance with the current guidelines, including an assessment of the reliability and relevance of each individual study;
- assessment of the validity of analytical methods used in feed, body fluids and tissues, air and any additional matrices used in support of the toxicological studies;
- assessment of the presence of toxicologically relevant impurities in the technical specification and in profenofos-treated commodities;
- interspecies comparative in vitro metabolism study on animal species used in pivotal studies and on human material;
- additional toxicological data to perform an ED assessment according to the ECHA/EFSA Guidance (ECHA and EFSA, 2018);
- an up-to-date search for published literature.

Chronic and acute exposure calculations were performed using revision 3.1 of PRIMo, considering commodities for which CXLs and EU MRLs were found to be sufficiently substantiated. Comparing to the TRVs established by JMPR, no exceedances were observed and the highest chronic exposure represented 17% of the ADI (GEMS/Food G06) and the highest acute exposure amounted to 27% of the ARfD (tomatoes). Nevertheless, EFSA emphasises that as the TRVs could not be confirmed, the risk assessment cannot be finalised and results presented under the current review are indicative only. Besides, there is further uncertainty about the risk assessment considering that lower TRVs were derived by a Member State but could not be confirmed in the current assessment.

The outcome of the review is presented in Table 7 below. If a decision on the withdrawing of TRVs is taken, EFSA recommends that risk managers discuss whether all MRLs currently implemented in EU Regulation should be lowered to the respective LOQs (except for the temporary MRLs set for herbs and edible flowers and rose).

TABLE 7 Summary table.

Code[a]	Commodity	Existing MRL[b] (mg/kg)	Outcome of the review	
			MRL proposal (mg/kg)	Comment
Residue definition for enforcement (plants and animal products): profenofos[F]				
0163030	Mangoes	0.2	0.2 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. However, further risk management discussions are needed to decide whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for profenofos
0231010	Tomatoes	10	10 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. However, further risk management discussions are needed to decide whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for profenofos
0256000	Herbs and edible flowers	0.03[c]	0.03	The existing temporary MRL, based on EU monitoring data, is sufficiently substantiated
0401090	Cotton seeds	3	3 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. However, further risk management discussions are needed to decide whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for profenofos
0631030	Rose	0.1[d]	0.1	The existing temporary MRL, based on EU monitoring data, is sufficiently substantiated
0810040	Coriander	0.1	0.1 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. It is based on monitoring data. Further risk management discussions are needed to decide whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for profenofos
0810050	Cumin	5	5 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. It is based on monitoring data. Further risk management discussions are needed to decide whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for profenofos

(Continues)

TABLE 7 (Continued)

Code[a]	Commodity	Existing MRL[b] (mg/kg)	Outcome of the review	
			MRL proposal (mg/kg)	Comment
0810070	Fennel	0.1	0.1 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. It is based on monitoring data. Further risk management discussions are needed to decide whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for profenofos
0820010 0820020 0820030 0820050 0820060 0820070 0820080 0820090	Fruit spices (except cardamom)	0.07	0.07 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. It is based on monitoring data. Further risk management discussions are needed to decide whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for profenofos
0820040	Cardamom	3	3 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. It is based on monitoring data. Further risk management discussions are needed to decide whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for profenofos
1011000 1012000 1013000 1014000 1015000 1016000 1017000	Commodities from swine, bovine, sheep, goat, equine, poultry, other farmed terrestrial animals (except milk and eggs)	0.05	0.05 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. However, further risk management discussions are needed to decide whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for profenofos

Abbreviations: MRL, maximum residue limit; LOQ, limit of quantification; TRV, toxicological reference value.

[F]Fat soluble.

[a]Commodity code number according to Annex I of Regulation (EC) No 396/2005.

[b]MRL currently set under Regulation (EU) 2023/377.

[c]Temporary MRL, derived from recent monitoring data showing that residues of profenofos still occur in herbs and edible flowers. Further monitoring data is necessary to compare the evolution of the occurrence of profenofos in herbs and edible flowers. When re-viewing the MRL, the Commission will take into account the information, if it is submitted by 22/2/2030, or, if that information is not submitted by that date, the lack of it.

[d]Temporary MRL, derived from recent monitoring data showing that residues of profenofos occur in rose petals. Further monitoring data is necessary to compare the evolution of the occurrence of profenofos in rose petals. When re-viewing the MRL, the Commission will take into account the information, if it is submitted by 25 July 2029, or, if that information is not submitted by that date, the lack of it.

ABBREVIATIONS

a.s.	active substance
ADI	acceptable daily intake
ARfD	acute reference dose
bw	body weight
CAC	Codex Alimentarius Commission
CCPR	Codex Committee on Pesticide Residues
cGAP	critical good agricultural practice
CLP	classification, labelling and packaging
CXL	Codex maximum residue limit
DAT	days after treatment
DAR	draft assessment report
DCTO	dicyclohexyloxostannane
ECHA	European Chemicals Agency
ED	endocrine disruptor
EURL	European Reference Laboratories
FAO	Food and Agriculture Organization of the United Nations
GAP	Good Agricultural Practice
GC–FPD	gas chromatography with flame photometric detector
GC–MS/MS	gas chromatography with tandem mass spectrometry
HR	highest residue
JMPR	Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
LC–MS/MS	liquid chromatography with tandem mass spectrometry
LOAEL	lowest observable adverse effect level

LOQ	limit of quantification
MCTA	metabolites cyclohexylhydroxostannane
MRL	maximum residue level
MS	Member State
NOAEL	no observed adverse effect level
PHI	pre-harvest interval
PRIMo	(EFSA) Pesticide Residues Intake Model
QuEChERS	Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method)
SCoPAFF	Standing Committee on Plants, Animals, Food and Feed (formerly: Standing Committee on the Food Chain and Animal Health; SCFCAH)
STMR	supervised trials median residue
ToR	terms of reference
TRV	toxicological reference values

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CONFLICT OF INTEREST

If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact interestmanagement@efsa.europa.eu.

REQUESTOR

European Commission

QUESTION NUMBER

EFSA-Q-2022-00451

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APPENDIX A

Summary of the fall-back GAPs collected from Member States

Not applicable, as Member States reported no import tolerances for profenofos.

APPENDIX B

Pesticide Residue Intake Model (PRIMo)

- PRIMo_(Sc. 1)

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

Profenofos

LOQs (mg/kg) range from:	0.01	to:	0.05
Toxicological reference values			
ADI (mg/kg bw/day):	0.03	ARfD (mg/kg bw):	1
Source of ADI:	JMPR	Source of ARfD:	JMPR
Year of evaluation:	2007	Year of evaluation:	2007

Input values

Details – chronic risk assessment | Supplementary results – chronic risk assessment

Details – acute risk assessment/children | Details – acute risk assessment/adults

Comments: Scenario 1

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

TMDI/NEDI/IEDI calculation (based on average food consumption)	Calculated exposure (% of ADI)	MS Diet	Expsoure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity/ group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	Exposure resulting from MRLs set at the LOQ (in % of ADI)	Exposure resulting from commodities not under assessment (in % of ADI)
	17%	GEMS/Food G06	5.16	16%	Tomatoes	0.4%	Cotton seeds	0.2%	Wheat	1%	
	10%	RO general	2.97	8%	Tomatoes	0.4%	Milk: Cattle	0.2%	Swine: Muscle/meat	1%	
	9%	NL toddler	2.65	4%	Tomatoes	2%	Milk: Cattle	0.4%	Apples	4%	
	8%	GEMS/Food G10	2.32	6%	Tomatoes	0.2%	Poultry: Muscle/meat	0.2%	Milk: Cattle	1%	
	7%	GEMS/Food G15	2.07	5%	Tomatoes	0.2%	Swine: Muscle/meat	0.2%	Milk: Cattle	1%	
	7%	GEMS/Food G08	2.02	5%	Tomatoes	0.3%	Swine: Muscle/meat	0.2%	Milk: Cattle	1%	
	7%	IT toddler	2.00	6%	Tomatoes	0.2%	Wheat	0.1%	Other cereals	0.5%	
	7%	DE child	2.00	4%	Tomatoes	0.7%	Milk: Cattle	0.4%	Apples	2%	
	7%	GEMS/Food G07	1.99	5%	Tomatoes	0.2%	Milk: Cattle	0.2%	Cotton seeds	1%	
	6%	ES child	1.83	4%	Tomatoes	0.4%	Milk: Cattle	0.2%	Bovine: Muscle/meat	1%	
	6%	FR child 3 15 yr	1.81	4%	Tomatoes	0.8%	Milk: Cattle	0.2%	Bovine: Muscle/meat	2%	
	6%	GEMS/Food G11	1.75	4%	Tomatoes	0.3%	Milk: Cattle	0.2%	Swine: Muscle/meat	1%	
	5%	IT adult	1.62	5%	Tomatoes	0.1%	Wheat	0.0%	Apples	0.4%	
	5%	SE general	1.55	3%	Tomatoes	0.7%	Bovine: Muscle/meat	0.4%	Milk: Cattle	1%	
	5%	NL child	1.52	2%	Tomatoes	0.8%	Milk: Cattle	0.3%	Sugar beet roots	2%	
	5%	DE women 14-50 yr	1.40	3%	Tomatoes	0.4%	Milk: Cattle	0.2%	Sugar beet roots	1%	
	5%	PT general	1.36	4%	Tomatoes	0.2%	Potatoes	0.1%	Wheat	0.7%	
	4%	ES adult	1.32	3%	Tomatoes	0.2%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.6%	
	4%	FR toddler 2 3 yr	1.31	2%	Tomatoes	1.0%	Milk: Cattle	0.2%	Bovine: Muscle/meat	2%	
	4%	UK toddler	1.29	3%	Tomatoes	0.7%	Milk: Cattle	0.2%	Bovine: Muscle/meat	1%	
	4%	DE general	1.29	3%	Tomatoes	0.4%	Milk: Cattle	0.2%	Swine: Muscle/meat	1%	
	4%	DK child	1.28	2%	Tomatoes	0.4%	Milk: Cattle	0.4%	Swine: Muscle/meat	1%	
	4%	PL general	1.24	4%	Tomatoes	0.1%	Potatoes	0.1%	Apples	0.3%	
	4%	UK infant	1.18	2%	Tomatoes	1%	Milk: Cattle	0.2%	Bovine: Muscle/meat	2%	
	4%	FI adult	1.07	2%	Tomatoes	0.9%	Coffee beans	0.0%	Potatoes	1%	
	3%	LT adult	1.03	3%	Tomatoes	0.2%	Swine: Muscle/meat	0.1%	Milk: Cattle	0.5%	
	3%	UK vegetarian	0.96	3%	Tomatoes	0.1%	Milk: Cattle	0.1%	Wheat	0.5%	
	3%	IE adult	0.95	2%	Tomatoes	0.1%	Milk: Cattle	0.1%	Sweet potatoes	1%	
	3%	NL general	0.93	2%	Tomatoes	0.3%	Milk: Cattle	0.2%	Swine: Muscle/meat	0.9%	
	3%	DK adult	0.92	2%	Tomatoes	0.2%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.5%	
	3%	FI 3 yr	0.90	2%	Tomatoes	0.2%	Potatoes	0.0%	Bananas	0.6%	
	3%	FR adult	0.90	2%	Tomatoes	0.1%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.7%	
	2%	UK adult	0.75	2%	Tomatoes	0.1%	Bovine: Muscle/meat	0.1%	Milk: Cattle	0.4%	
	2%	FI 6 yr	0.71	2%	Tomatoes	0.1%	Potatoes	0.0%	Cocoa beans	0.5%	
	2%	FR infant	0.45	0.6%	Milk: Cattle	0.4%	Tomatoes	0.1%	Potatoes	0.9%	
	0.6%	IE child	0.17	0.2%	Tomatoes	0.1%	Milk: Cattle	0.0%	Wheat	0.3%	

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Profenofos is unlikely to present a public health concern.

Acute risk assessment/children	Acute risk assessment/adults/general population
Details – acute risk assessment/children	Details – acute risk assessment/adults

The acute risk assessment is based on the ARfD.
The calculation is based on the large portion of the most critical consumer group.

Show results for all crops

Unprocessed commodities

Results for children
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
27%	Tomatoes	10/4.7	273
0.6%	Mangoes	0.2/0.07	5.5
0.2%	Potatoes	0.01/0.01	1.5
0.2%	Melons	0.01/0.01	1.5
0.1%	Pears	0.01/0.01	1.4
0.1%	Oranges	0.01/0.01	1.3
0.1%	Milk: Cattle	0.01/0.01	1.2
0.1%	Watermelons	0.01/0.01	1.2
0.1%	Apples	0.01/0.01	1.1
0.1%	Pineapples	0.01/0.01	1.0
0.10%	Bananas	0.01/0.01	0.97
0.10%	Peaches	0.01/0.01	0.95
0.08%	Poultry: Muscle/meat	0.05/0.05	0.85
0.08%	Grapefruits	0.01/0.01	0.79
0.07%	Table grapes	0.01/0.01	0.73

Expand/collapse list

Total number of commodities exceeding the ARfD/ADI in children and adult diets
(IESTI calculation)

Results for adults
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
7%	Tomatoes	10/4.7	75
0.2%	Mangoes	0.2/0.07	1.8
0.06%	Poultry: Muscle	0.05/0.05	0.59
0.04%	Head cabbages	0.01/0.01	0.42
0.04%	Watermelons	0.01/0.01	0.41
0.04%	Melons	0.01/0.01	0.39
0.04%	Milk: Cattle	0.01/0.01	0.39
0.03%	Swedes/rutabagas	0.01/0.01	0.34
0.03%	Table grapes	0.01/0.01	0.34
0.03%	Oranges	0.01/0.01	0.31
0.03%	Cardamom	3/3.06	0.31
0.03%	Pears	0.01/0.01	0.31
0.03%	Potatoes	0.01/0.01	0.30
0.03%	Pineapples	0.01/0.01	0.30
0.03%	Bovine: Muscle	0.05/0.05	0.28

Processed commodities

Results for children
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
2%	Tomatoes/juice	10/1.3	25
1%	Tomatoes/sauce/puree	10/1.3	12
0.1%	Sugar beets (root)/sugar	0.01/0.12	1.1
0.1%	Potatoes/fried	0.01/0.01	0.93
0.1%	Pumpkins/boiled	0.01/0.01	0.89
0.1%	Witloofs/boiled	0.01/0.01	0.89
0.1%	Broccoli/boiled	0.01/0.01	0.79
0.1%	Cauliflowers/boiled	0.01/0.01	0.70
0.1%	Escaroles/broad-leaved endives/boiled	0.01/0.01	0.66
0.1%	Potatoes/dried (flakes)	0.01/0.05	0.59
0.1%	Leeks/boiled	0.01/0.01	0.57
0.1%	Apples/juice	0.01/0.01	0.54
0.1%	Oranges/juice	0.01/0.01	0.53
0.1%	Turnips/boiled	0.01/0.01	0.51
0.1%	Parsnips/boiled	0.01/0.01	0.51

Expand/collapse list

Results for adults
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
1%	Tomatoes/sauce/puree	10/1.3	11
0.06%	Pumpkins/boiled	0.01/0.01	0.55
0.04%	Sugar beets (root)/sugar	0.01/0.12	0.44
0.04%	Cauliflowers/boiled	0.01/0.01	0.42
0.04%	Beetroots/boiled	0.01/0.01	0.39
0.03%	Celeries/boiled	0.01/0.01	0.34
0.03%	Apples/juice	0.01/0.01	0.33
0.02%	Broccoli/boiled	0.01/0.01	0.24
0.02%	Coffee beans/extraction	0.05/0.01	0.24
0.02%	Courgettes/boiled	0.01/0.01	0.23
0.02%	Parsnips/boiled	0.01/0.01	0.21
0.02%	Kohlrabies/boiled	0.01/0.01	0.21
0.02%	Wine grapes/juice	0.01/0.01	0.21
0.02%	Escaroles/broad-leaved	0.01/0.01	0.20
0.02%	Florence fennels/boiled	0.01/0.01	0.19

Conclusion:
No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short-term intake of residues of Profenofos is unlikely to present a public health risk.

For processed commodities, no exceedance of the ARfD/ADI was identified.

- PRIMo_(Sc. 2)

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

Profenofos

LOQs (mg/kg) range from:	0.01	to:	0.05
Toxicological reference values			
ADI (mg/kg bw/day):	0.03	ARfD (mg/kg bw):	1
Source of ADI:	JMPR	Source of ARfD:	JMPR
Year of evaluation:	2007	Year of evaluation:	2007

Input values

Details – chronic risk assessment | Supplementary results – chronic risk assessment

Details – acute risk assessment/children | Details – acute risk assessment/adults

Comments: Scenario 2

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

TMDI/NEDI/IEDI calculation (based on average food consumption)	Calculated exposure (% of ADI)	MS Diet	Expsoure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity/ group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	Exposure resulting from: MRLs set at the LOQ (in % of ADI)	Exposure resulting from: commodities not under assessment (in % of ADI)
	4%	NL toddler	1.24	2%	Milk: Cattle	0.4%	Apples	0.2%	Maize/corn	4%	
	2%	NL child	0.67	0.8%	Milk: Cattle	0.3%	Sugar beet roots	0.2%	Apples	2%	
	2%	DE child	0.66	0.7%	Milk: Cattle	0.4%	Apples	0.1%	Wheat	2%	
	2%	UK infant	0.62	1%	Milk: Cattle	0.1%	Potatoes	0.1%	Eggs: Chicken	2%	
	2%	FR toddler 2 3 yr	0.57	1.0%	Milk: Cattle	0.1%	Apples	0.1%	Wheat	2%	
	2%	FR child 3 15 yr	0.56	0.8%	Milk: Cattle	0.2%	Wheat	0.1%	Sugar beet roots	2%	
	2%	UK toddler	0.46	0.7%	Milk: Cattle	0.1%	Wheat	0.1%	Potatoes	2%	
	1%	DK child	0.42	0.4%	Milk: Cattle	0.2%	Rye	0.1%	Wheat	1%	
	1%	GEMS/Food G11	0.42	0.3%	Milk: Cattle	0.1%	Potatoes	0.1%	Soyabeans	1%	
	1%	RO general	0.38	0.4%	Milk: Cattle	0.2%	Wheat	0.1%	Potatoes	1%	
	1%	GEMS/Food G07	0.38	0.2%	Milk: Cattle	0.1%	Wheat	0.1%	Potatoes	1%	
	1%	SE general	0.38	0.4%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.1%	Potatoes	1%	
	1%	ES child	0.38	0.4%	Milk: Cattle	0.1%	Wheat	0.1%	Cocoa beans	1%	
	1%	GEMS/Food G06	0.38	0.2%	Wheat	0.1%	Tomatoes	0.1%	Milk: Cattle	1%	
	1%	GEMS/Food G15	0.38	0.2%	Milk: Cattle	0.2%	Wheat	0.1%	Potatoes	1%	
	1%	GEMS/Food G08	0.38	0.2%	Milk: Cattle	0.1%	Wheat	0.1%	Potatoes	1%	
	1%	DE women 14-50 yr	0.38	0.4%	Milk: Cattle	0.2%	Sugar beet roots	0.1%	Apples	1%	
	1%	GEMS/Food G10	0.37	0.2%	Milk: Cattle	0.1%	Wheat	0.1%	Soyabeans	1%	
	1%	DE general	0.37	0.4%	Milk: Cattle	0.1%	Sugar beet roots	0.1%	Apples	1%	
	1%	FI adult	0.35	0.9%	Coffee beans	0.0%	Potatoes	0.0%	Rye	1%	
	1%	IE adult	0.34	0.1%	Milk: Cattle	0.1%	Sweet potatoes	0.1%	Wheat	1%	
	1%	NL general	0.30	0.3%	Milk: Cattle	0.1%	Sugar beet roots	0.1%	Potatoes	1%	
	1.0%	FR infant	0.29	0.6%	Milk: Cattle	0.1%	Potatoes	0.1%	Apples	1.0%	
	0.7%	FR adult	0.22	0.1%	Milk: Cattle	0.1%	Wine grapes	0.1%	Wheat	0.7%	
	0.7%	ES adult	0.21	0.2%	Milk: Cattle	0.1%	Wheat	0.0%	Oranges	0.7%	
	0.7%	PT general	0.21	0.2%	Potatoes	0.1%	Wheat	0.1%	Wine grapes	0.7%	
	0.6%	FI 3 yr	0.18	0.2%	Potatoes	0.0%	Bananas	0.0%	Wheat	0.6%	
	0.6%	DK adult	0.17	0.2%	Milk: Cattle	0.0%	Potatoes	0.0%	Wheat	0.6%	
	0.6%	LT adult	0.17	0.1%	Milk: Cattle	0.1%	Potatoes	0.1%	Apples	0.6%	
	0.5%	IT toddler	0.16	0.2%	Wheat	0.1%	Other cereals	0.0%	Tomatoes	0.5%	
	0.5%	UK vegetarian	0.15	0.1%	Milk: Cattle	0.1%	Wheat	0.0%	Potatoes	0.5%	
	0.5%	FI 6 yr	0.14	0.1%	Potatoes	0.0%	Cocoa beans	0.0%	Wheat	0.5%	
	0.5%	UK adult	0.14	0.1%	Milk: Cattle	0.1%	Wheat	0.0%	Potatoes	0.5%	
	0.4%	IT adult	0.12	0.1%	Wheat	0.0%	Tomatoes	0.0%	Apples	0.4%	
	0.3%	PL general	0.10	0.1%	Potatoes	0.1%	Apples	0.0%	Tomatoes	0.3%	
	0.3%	IE child	0.08	0.1%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes	0.3%	

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Profenofos is unlikely to present a public health concern.

Acute risk assessment/children	Acute risk assessment/adults/general population
Details – acute risk assessment/children	Details – acute risk assessment/adults

The acute risk assessment is based on the ARfD.
The calculation is based on the large portion of the most critical consumer group.

Show results for all crops

Unprocessed commodities

Results for children
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
0.2%	Potatoes	0.01/0.01	1.5
0.2%	Melons	0.01/0.01	1.5
0.1%	Pears	0.01/0.01	1.4
0.1%	Oranges	0.01/0.01	1.3
0.1%	Milk: Cattle	0.01/0.01	1.2
0.1%	Watermelons	0.01/0.01	1.2
0.1%	Apples	0.01/0.01	1.1
0.1%	Pineapples	0.01/0.01	1.0
0.10%	Bananas	0.01/0.01	0.97
0.10%	Peaches	0.01/0.01	0.95
0.08%	Mangoes	0.01/0.01	0.79
0.08%	Grapefruits	0.01/0.01	0.79
0.07%	Table grapes	0.01/0.01	0.73
0.07%	Cucumbers	0.01/0.01	0.66
0.06%	Carrots	0.01/0.01	0.63

Expand/collapse list

Results for adults
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
0.04%	Head cabbages	0.01/0.01	0.42
0.04%	Watermelons	0.01/0.01	0.41
0.04%	Melons	0.01/0.01	0.39
0.04%	Milk: Cattle	0.01/0.01	0.39
0.03%	Swedes/rutabagas	0.01/0.01	0.34
0.03%	Table grapes	0.01/0.01	0.34
0.03%	Oranges	0.01/0.01	0.31
0.03%	Cardamom	3/3.06	0.31
0.03%	Pears	0.01/0.01	0.31
0.03%	Potatoes	0.01/0.01	0.30
0.03%	Pineapples	0.01/0.01	0.30
0.03%	Yams	0.01/0.01	0.28
0.03%	Apples	0.01/0.01	0.28
0.03%	Cucumbers	0.01/0.01	0.28
0.03%	Aubergines/egg plants	0.01/0.01	0.27

Total number of commodities exceeding the ARfD/ADI in children and adult diets
(IESTI calculation)

Processed commodities

Results for children
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
0.1%	Sugar beets (root)/sugar	0.01/0.12	1.1
0.1%	Potatoes/fried	0.01/0.01	0.93
0.1%	Pumpkins/boiled	0.01/0.01	0.89
0.1%	Witloofs/boiled	0.01/0.01	0.89
0.1%	Broccoli/boiled	0.01/0.01	0.79
0.1%	Cauliflowers/boiled	0.01/0.01	0.70
0.1%	Escaroles/broad-leaved endives/boiled	0.01/0.01	0.66
0.1%	Potatoes/dried (flakes)	0.01/0.05	0.59
0.1%	Leeks/boiled	0.01/0.01	0.57
0.1%	Apples/juice	0.01/0.01	0.54
0.1%	Oranges/juice	0.01/0.01	0.53
0.1%	Turnips/boiled	0.01/0.01	0.51
0.1%	Parsnips/boiled	0.01/0.01	0.51
0.1%	Sweet potatoes/boiled	0.01/0.01	0.50
0.0%	Florence fennels/boiled	0.01/0.01	0.45

Expand/collapse list

Results for adults
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
0.1%	Pumpkins/boiled	0.01/0.01	0.55
0.04%	Sugar beets (root)/sugar	0.01/0.12	0.44
0.04%	Cauliflowers/boiled	0.01/0.01	0.42
0.04%	Beetroots/boiled	0.01/0.01	0.39
0.03%	Celeries/boiled	0.01/0.01	0.34
0.03%	Apples/juice	0.01/0.01	0.33
0.02%	Broccoli/boiled	0.01/0.01	0.24
0.02%	Coffee beans/extraction	0.05/0.01	0.24
0.02%	Courgettes/boiled	0.01/0.01	0.23
0.02%	Parsnips/boiled	0.01/0.01	0.21
0.02%	Kohlrabies/boiled	0.01/0.01	0.21
0.02%	Wine grapes/juice	0.01/0.01	0.21
0.02%	Escaroles/broad-leaved	0.01/0.01	0.20
0.02%	Florence fennels/boiled	0.01/0.01	0.19
0.02%	Turnips/boiled	0.01/0.01	0.19

Conclusion:
No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short-term intake of residues of Profenofos is unlikely to present a public health risk.
For processed commodities, no exceedance of the ARfD/ADI was identified.

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APPENDIX C

Input values for the exposure calculations

Commodity	Existing MRL (mg/kg)	Chronic risk assessment		Acute risk assessment	
		Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: profenofos[F]					
Mangoes	0.2	Scenario 1: 0.06	STMR (CXL)	Scenario 1: 0.07	HR (CXL)
		Scenario 2: 0.01[b]	LOQ	Scenario 2: 0.01[b]	LOQ
Tomatoes	10	Scenario 1: 1.3	STMR (CXL)	Scenario 1: 4.7	HR (CXL)
		Scenario 2: 0.01[b]	LOQ	Scenario 2: 0.01[b]	LOQ
Herbs and edible flowers	0.03	Scenario 1 and 2: 0.03	MRL	Scenario 1 and 2: 0.03	MRL
Cotton seeds	3	Scenario 1: 0.35	STMR (CXL)	Scenario 1: 0.35	STMR (CXL)
		Scenario 2: 0.01[b]	LOQ	Scenario 2: 0.01[b]	LOQ
Rose	0.1	Scenario 1 and 2: 0.1	MRL	Scenario 1 and 2: 0.1	MRL
Coriander seed	0.1	Scenario 1 and 2: 0.1	STMR (CXL)	Scenario 1 and 2: 0.1	HR (CXL)
Cumin	5	Scenario 1 and 2: 0.635	STMR (CXL)	Scenario 1 and 2: 4.12	HR (CXL)
Fennel	0.1	Scenario 1 and 2: 0.1	STMR (CXL)	Scenario 1 and 2: 0.1	HR (CXL)
Fruit spices (except cardamom)	0.07	Scenario 1 and 2: 0.07	CXL	Scenario 1 and 2: 0.07	CXL
Cardamom	3	Scenario 1 and 2: 0.3	STMR (CXL)	Scenario 1 and 2: 3.06	HR (CXL)
Commodities from swine, bovine, sheep, goat, equine, poultry, other farmed terrestrial animals	0.05	Scenario 1: 0.05	STMR (CXL)	Scenario 1: 0.05	HR (CXL)
		Scenario 2: 0.01[b]	LOQ	Scenario 2: 0.01[b]	LOQ
Other crops/commodities	See Reg. (EU) 2023/377	LOQ[b]			

Abbreviations: CXL, Codex maximum residue limit; HR, highest residue; MRL, maximum residue limit; LOQ, limit of quantification; STMR, median residue value.

[F]The active substance is fat soluble.

[a]An LOQ of 0.05 mg/kg was considered for tea, coffee, herbal infusions, cocoa beans, carobs, hops and spices (except coriander, cumin, fennel and fruit spices) and honey. An LOQ of 0.02 mg/kg was considered for eggs. A default LOQ of 0.01 mg/kg was applied to all other commodities.

[b]Indicates that the input value is proposed at the limit of quantification.