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Targeted review of maximum residue levels (MRLs) for endosulfan

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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 endosulfan in view of the possible lowering of the MRLs. EFSA investigated the origin of the current EU MRLs. For existing EU MRLs that reflect previously authorised uses in the EU, or that are based on obsolete Codex maximum residue limits, or import tolerances that are not required any longer, EFSA proposed the lowering to the limit of quantification or to an alternative MRL. EFSA performed an indicative chronic and acute dietary risk assessment for the revised list of MRLs to allow risk managers to take the appropriate decisions. For all 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, toxicological evaluation, residue definitions, MRL setting, endosulfan, non-approved active substance

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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 endosulfan.

In accordance with the terms of reference, EFSA investigated the origin of the current EU MRLs for endosulfan, 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 endosulfan has been established as an import tolerance. EFSA also screened the quality of the toxicological reference values (TRVs) derived at EU level and by the Joint Meeting on Pesticide residues (JMPR). As EFSA identified critical issues related to the available toxicological database, EFSA organised an experts' consultation (Pesticides Peer Review Teleconference 98) to discuss the toxicological profile and the TRVs for endosulfan.

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 endosulfan in plants and livestock was previously investigated in the framework of the EU evaluation, as well as 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 endosulfan (sum of alpha and beta isomers and endosulfan sulfate, expressed as endosulfan). The residue is fat soluble.

Analytical methods are available for the enforcement of the proposed residue definition in high water content, high oil content, high acid content and dry matrices with an LOQ of 0.06 mg/kg. For tea, the LOQ was reported to be 0.03 mg/kg. The proposed residue definition can be enforced in food of animal origin with an LOQ of 0.075 mg/kg in muscle liver, fat and eggs, and an LOQ of 0.06 mg/kg in milk. According to the EURLs, a QuEChERS (or QuOil) multiresidue analytical method with an LOQ of 0.03 mg/kg for the routine analysis of endosulfan in the four main matrix groups of plant origin and in commodities of animal origin (egg, muscle, liver, milk and honey). Based on the experience gained with these matrices, a default LOQ of 0.03 mg/kg is also deemed achievable in animal fat and kidney.

The origin of all current MRLs set for endosulfan (based on formerly approved uses or on CXLs) was investigated, and the following MRLs were identified as not sufficiently substantiated: EU MRLs for tea and soya beans. No fall-back MRL was identified for soya beans, but existing CXL was identified as possible fall-back MRL for tea. Moreover, further risk management discussions are required to decide whether the existing EU MRL for tea should be lowered to the existing CXL or to the LOQ.

A screening of the quality of the TRVs set at EU level and of those established by the JMPR was performed, and the set of toxicological studies used to derive these TRVs was assessed according to the current standards. As critical issues were identified, a Member States experts' consultation took place. In view of the limitations of the toxicological data set, the experts concluded that the TRVs cannot be confirmed for endosulfan; in addition, the inconclusive assessment of the genotoxic potential prevents the derivation of revised TRVs, including the use of additional uncertainty factors. Accordingly, the EU acceptable daily intake (ADI) and JMPR ADI and acute reference dose (ARfD) derived in 1999 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 prerequisite to derive robust TRVs:

- complete genotoxicity test battery to conclude on the genotoxic potential of endosulfan;
- up-to-date search for published literature;

- additional toxicological data to perform an endocrine disruptor (ED) assessment according to the ECHA/EFSA Guidance (ECHA and EFSA, 2018);
- interspecies comparative *in vitro* metabolism study on animal species used in pivotal studies and on human material;
- DNT 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;
- if possible, an assessment of the toxicological relevance of impurities potentially present in the technical specification and in endosulfan-treated commodities;
- full re-evaluation of the toxicological data package and reporting relevant details on the studies and the results in accordance with the current OECD test guidelines.

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, while all CXLs/MRLs that were revoked or are no longer substantiated were proposed to be lowered to the appropriate LOQ or MRL proposal, as well as all other commodities for which no good agricultural practice (GAP) was reported under this review. Comparing to the EU TRVs, no exceedances were observed, and the highest chronic exposure represented 63% of the ADI (Dutch toddler) and the highest acute exposure amounted to 31% of the ARfD (tea). Nevertheless, EFSA emphasises that as the toxicological assessment revealed deficiencies regarding the toxicological studies available for endosulfan and considering that current EU TRVs do not meet the current scientific standards, the indicative risk assessment cannot be finalised and results presented in this review are indicative only.

Due to the deficiencies identified regarding the toxicological studies available for endosulfan, none of the existing EU MRLs/CXLs listed in the summary table below are recommended for inclusion in Annex II to the Regulation. If a decision to withdraw the TRVs is taken, EFSA recommends that risk managers discuss whether all MRLs currently implemented in EU Regulation should be lowered to the respective LOQs.

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): Endosulfan (sum of alpha and beta isomers and endosulfan sulfate, expressed as endosulfan)[(F)]				
0401070	Soya beans	0.5	LOQ	The existing EU MRL is not substantiated. Hence, the MRL should be lowered to the LOQ.
0401090	Cotton seeds	0.3	0.3 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 endosulfan.
0610000	Teas	30	10 (CXL) or LOQ Further consideration by risk managers needed	The existing EU MRL is not substantiated. Further risk managers discussions are needed to decide whether the existing EU MRL should be lowered to the LOQ or the existing CXL would be more appropriate. In addition, it should be discussed whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for endosulfan.
0810000	Seed spices	1	1 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. Similar recommendations as reported for cotton seeds.

Code[(a)]	Commodity	Existing MRL[(b)] (mg/kg)	Outcome of the review	
			MRL proposal (mg/kg)	Comment
0820000	Fruit spices	5	5 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. Similar recommendations as reported for cotton seeds.
0840000	Root and rhizome spices	0.5	0.5 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. Similar recommendations as reported for cotton seeds.

MRL: maximum residue limit; CXL: Codex residue limit; LOQ: limit of quantification.
(F): Fat soluble.
(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.
(b): MRL currently set under Regulation (EU) No 310/2011.

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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 10 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 endosulfan.

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 endosulfan.

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 endosulfan. 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;

[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, 16.03.2005, 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).

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:
    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 the JMPR;
10) to report information on the classification of the substance under the classification, labelling and packaging (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 endosulfan, by 22 May 2023.

[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.

Subsequently, an extension of this 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 endosulfan), 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 quality of the TRVs set in the EU and by the JMPR are assessed (ToR 7).
- 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 assessments 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 EU and 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).

EFSA has based its assessment on the following documents:

- Scientific support for preparing an EU position in the 43rd Session of the Codex Committee on Pesticide Residues (CCPR) (EFSA, 2011);
- the draft assessment report (DAR) (Spain, 1999);
- the reports and evaluations of the JMPR (FAO and WHO, 2004, 2006a,b, 2011a,b);
- the reports of the Codex Committee on pesticide residues (CCPR, 2005, 2007, 2011).

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, FR, IT, NL and SE) provided feedback regarding endosulfan 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 a main supporting document to this reasoned opinion and, thus, made publicly available. In addition, an expert consultation in the area of mammalian toxicology was conducted in March 2023; the **peer review meeting report TC 98** (EFSA, 2023a) is also considered as a main supporting document.

On the basis of the data submitted by 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 regard 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 May

2023. Comments received by 31 May 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, 2023b). 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 documents to this reasoned opinion.

1. Regulatory background information on endosulfan

The key events concerning the regulatory history of endosulfan, 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	Decision on non-inclusion of endosulfan in Annex I of Council Directive 91/414/EEC by Decision 2005/864/EC[(a)]
EFSA conclusion available	No	–
MRL review performed	No	–
EU MRL applications or other EU assessments	Yes, see comments	Implementation of EU MRLs: Existing MRLs on soybeans and teas were legally implemented in Regulation (EC) 149/2008[(b)] and have never been modified since. Implementation of CXLs adopted by CAC 2005: Following discussion in CCPR 37 (2005) (i.e. CXLs for seed spices, fruit spices and root and rhizomes spices). These CXL values were included in Regulation (EC) 839/2008[(c)] and kept in Regulation (EU) 310/2011[(d)]. Implementation of CXLs adopted by CAC 2007: Following discussion in CCPR 39 (2007) (i.e. CXLs for cotton seed). This CXL value was included in Regulation (EU) 310/2011. MRL application (Art. 43): Scientific support for preparing an EU position in the 43rd Session of the Codex Committee on Pesticide Residues (CCPR) (EFSA, 2011)
Classification under CLP Regulation	See comments	Acute Tox 2*, H300 'fatal if swallowed'; Acute Tox 4*, H312 'harmful in contact with skin'; Acute Tox 2*, H330 'fatal if inhaled'. ATP1[(e)]
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[(f)]) have not been performed. Endosulfan has been considered as ED as a hormonally active agent and endocrine modulator by scientists considering that the effects may not be necessarily adverse or are led by its neurotoxicity potential (ATSDR, 2015).
Other relevant information	–	Endosulfan is a persistent organic pollutant (POP) and is included in Annex I Part A of Regulation (EU) 2019/1021[(g)]

a.s: active substance; MRL: maximum residue limit; CXL: Codex maximum residue limit; CCPR: Codex Committee on Pesticide Residues; CAC: Codex Alimentarius Commission; CLP: classification, labelling and packaging; ED: endocrine disruptor; ECHA: European chemicals agency; ATP: 'adaptation to technical and scientific progress' Regulation.

*: 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).

(a): Commission Decision 2005/864/EC of 2 December 2005 concerning the non-inclusion of endosulfan in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance (notified under document number C(2005) 4611). OJ L 317, 3.12.2005, p. 25–28.

(b): Commission Regulation (EU) No 149/2008 of 29 January 2008 amending Regulation (EC) No 396/2005 of the European Parliament and of the Council by the establishing Annexes II, III and IV setting maximum residue levels for products covered by Annex I thereto. OJ L 58, 1.3.2008, p. 1–398.

(c): Commission Regulation (EC) No 839/2008 of 31 July 2008 amending Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards Annexes II, III and IV on maximum residue levels of pesticides in or on certain products. OJ L234, 30.8.2008, p. 1–216.
(d): Commission Regulation (EU) No 310/2011 of 28 March 2011 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 aldicarb, bromopropylate, chlorfenvinphos, endosulfan, EPTC, ethion, fenthion, fomesafen, methabenzthiazuron, methidathion, simazine, tetradifon and triforine in or on certain products. OJL 86, 1.4.2011, p. 1–50.
(e): Commission Regulation (EC) No 790/2009 of 10 August 2009 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures. OJ L 235, 5.9.2009, p. 1–439.
(f): 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.
(g): Regulation (EU) 2019/1021 of the European Parliament and of the Council of 20 June 2019 on persistent organic pollutants. OJ L 169 25.6.2019, p. 45.

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 in the framework of the EU evaluation for inclusion in Annex I to Directive 91/414/CE and studies that were submitted to the JMPR in the framework of the setting of CXLs (including 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 appl., 3 × 635 g a.s./ha, 7 days interval	Leaves and fruits: 8, 13, 21, 27, 42 and 48 Leaves: 1 or 2 after each appl.	[6,7,8,9,10-U-^{14}C]- endosulfan; α/β endosulfan = 2/1 (Spain, 1999; FAO and WHO, 2006b)
		Apple	Outdoor, foliar appl., 1 × 1.5 kg a.s./ha	Leaves and fruits: 0, 7, 14 and 21	[5a, 9a-^{14}C]-endosulfan; α/β endosulfan = 2/1 (Spain, 1999; FAO and WHO, 2006b)
		Cucumber	Outdoor, foliar appl., 3 × 530 g a.s./ha, 7 days interval	Leaves and fruits: 0, 3, 7 and 14	[5a, 9a-^{14}C]-endosulfan; α/β endosulfan = 2/1 (Spain, 1999; FAO and WHO, 2006b)
	Root crops	Sugar beet	Outdoor, foliar appl., 2 × 630 g a.s./ha, 21 days interval	14 and 21 days after 1st appl. 28 days after 2nd appl.	[6,7,8,9,10-^{14}C]- endosulfan; α/β endosulfan = 2/1 (FAO and WHO, 2006b)
	Leafy crops	–	–	–	No study available but not required since the metabolism is similar in all crop groups investigated.
	Cereals/grass	–	–	–	
	Pulses/oilseeds	Soybean	Foliar appl., 2 × 530 g a.s./ha, 23 days interval	Seeds: 38 Forage and hay: 0 and 23 days after 1st appl.	[6,7,8,9,10-^{14}C]- endosulfan; α/β endosulfan = 2/1 (FAO and WHO, 2006b)
Livestock	**Animal**		**Dose**	**Duration (day)**	**Comment/Source**
	Laying hen		1.36 mg/animal per day (11 ppm in diet)	12	^{14}C-endosulfan; α/β endosulfan = 2/1 (FAO and WHO, 2006b)
	Ruminant, lactating cows		0.64 mg/kg bw per day	5	^{14}C-endosulfan; α/β endosulfan = 2/1 (FAO and WHO, 2006b)

Livestock	Animal	Dose	Duration (day)	Comment/Source
		α and β endosulfan: 5 mg/kg in the diet endosulfan sulfate: 5 mg/kg in the diet	30	Non-radiolabelled endosulfan and endosulfan sulfate. Additional cows were sacrificed 30 days after the end of the dosing period (Spain, 1999).
	Ruminant, lactating goats	1 mg/kg bw per day	28	Non-radiolabelled endosulfan. Groups of 3 animals were sacrificed 1, 8, 15 and 21 days after the end of the dosing period (Spain, 1999).
	Ruminant, ewe	1 × 0.3 mg/kg bw per day	Milk, urine and faeces were sampled for up to 22 days after dosing Tissues: 40 days after dosing	^{14}C-endosulfan; α/β endosulfan = 2/1 (methylene labelling) administered in a single dose (Spain, 1999; FAO and WHO, 2006b).
		0.3 mg/kg bw per day	26	Non radiolabelled endosulfan (Spain, 1999; FAO and WHO, 2006b)
	Pigs	–	–	Study not required[(a)]

a.s.: active substance; DAT: days after treatment; bw: body weight; ppm: parts per million.
(a): The metabolism and residue levels in pig commodities were not discussed in the JMPR reports, but MRLs were recommended for all mammals other than marine mammals (FAO and WHO, 2006a,b), thus it is assumed that the metabolism in rats and ruminants is similar.

Metabolism studies on tomato, apple and cucumber were assessed in the framework of EU evaluation (Spain, 1999) and by the JMPR (FAO and WHO, 2006a,b). Additional metabolism studies on sugar beet and soya bean were only assessed by the JMPR (FAO and WHO, 2006a,b). In investigated crops, the parent endosulfan (alpha and beta isomers) and the metabolite endosulfan sulfate were the predominant components of the residues. Consequently, the JMPR proposed to set the residue definitions, both for enforcement and risk assessment as the sum of alpha-endosulfan, beta-endosulfan and endosulfan sulfate. The conclusions of the EU evaluation are in line with the JMPR proposal. The residue definitions are applicable to all crop groups.

The nature of endosulfan residues in livestock was investigated and assessed in the framework of the EU evaluation (Spain, 1999) and by the JMPR (FAO and WHO, 2006a,b). In the investigated metabolism studies, the parent endosulfan (alpha and beta isomers) and the metabolite endosulfan sulfate were the predominant components of the residues observed in tissues. Consequently, the JMPR proposed to set the residue definitions, both for enforcement and risk assessment as the sum of alpha-endosulfan, beta-endosulfan and endosulfan sulfate. The residue is fat soluble. The conclusions of the EU evaluation, based on a restricted number of studies and awaiting additional livestock metabolism studies which were assessed by the JMPR, were in line with the JMPR proposal.

Table 3 summarises the residue definitions derived at EU level and by the JMPR. The EU residue definitions for enforcement are the ones set in Regulation (EC) No 396/2005. EU residue definitions for risk assessment were proposed in the framework of the EU evaluation. The same residue definitions for enforcement and risk assessment were derived by the JMPR (FAO and WHO, 2006a).

Table 3: Residue definitions derived at EU level and by JMPR

Type of residue definition (RD)	Commodity group	EU residue definition	JMPR residue definitions
RD for enforcement	Plant products	Reg. 396/2005: Endosulfan (sum of alpha and beta isomers and endosulfan sulfate, expressed as endosulfan)	Sum of alpha-endosulfan, beta-endosulfan and endosulfan sulfate (FAO and WHO, 2006a)
	Animal products	Reg. 396/2005: Endosulfan (sum of alpha and beta isomers and endosulfan sulfate, expressed as endosulfan) The residue is fat soluble	Sum of alpha-endosulfan, beta-endosulfan and endosulfan sulfate. The residue is fat soluble (FAO and WHO, 2006a)
RD for risk assessment	Plant products	RMS proposal (Spain, 1999) but not peer-reviewed: sum of endosulfan (alpha and beta isomers) and endosulfan sulfate	Sum of alpha-endosulfan, beta-endosulfan and endosulfan sulfate (FAO and WHO, 2006a)
	Animal products	RMS proposal (Spain, 1999) but not peer-reviewed: sum of endosulfan (alpha and beta isomers) and endosulfan sulfate	Sum of alpha-endosulfan, beta-endosulfan and endosulfan sulfate (FAO and WHO, 2006a)

Comments: The residue definitions in plant and animal products set in Reg. 396/2005 are similar with the ones proposed in the framework of the JMPR assessment.

2.2. Analytical methods for MRLs enforcement

Analytical methods for the determination of endosulfan residues were assessed in the framework of the EU evaluation for inclusion in Annex I to Directive 91/414/CE (Spain, 1999). Analytical methods were available to enforce residues of endosulfan in high water content, high acid content, high oil content and dry commodities, but it was not possible to determine if the reported LOQ is referring to single component or to the sum of alpha-endosulfan, beta-endosulfan and endosulfan sulfate. Furthermore, the available methods used benzene for the extraction step, which is not acceptable for safety reasons. An analytical method was made available for liver and kidney, but no validation data, nor ILV were provided. Therefore, the methods reported for inclusion in Annex I to Directive 91/414/CE are not further considered for the assessment.

Analytical methods for the determination of endosulfan residues were also assessed in the framework of the JMPR evaluations (FAO and WHO, 2006b, 2011b). Analytical methods are available to enforce residues of endosulfan in all four main plant matrices with an LOQ of 0.02 mg/kg for each component of the residue definition (alpha-endosulfan, beta-endosulfan and endosulfan sulfate). An analytical method is available to enforce residues of endosulfan in tea with a summed LOQ of 0.03 mg/kg. Each component of the residue definition of endosulfan can be enforced in food of animal origin with an LOQ of 0.02 mg/kg in milk and with an LOQ of 0.025 mg/kg in egg, fat, liver and muscle. No ILV is provided in the JMPR report.

During the data collection, the EURLs provided information on a QuEChERS (or QuOil) multiresidue analytical method using GC-MS/MS technique, for the routine analysis of alpha-endosulfan, beta-endosulfan and its metabolite endosulfan sulfate with an LOQ of 0.01 mg/kg each, in high water content, high acid content, high oil content and dry commodities. Thus, a summed LOQ, considering the conversion factors, calculated to 0.03 mg/kg. No data were provided regarding the possible enforcement of endosulfan residues in complex matrices. According to the EURLs, in commodities of animal origin (egg, muscle, liver, milk and honey), alpha-endosulfan, beta-endosulfan and its metabolite endosulfan sulfate can be monitored with a default LOQ of 0.01 mg/kg and, then a summed LOQ of 0.03 mg/kg. Based on the experience gained with these matrices, individual LOQs of 0.01 mg/kg for animal fat and kidney are also deemed achievable for alpha-endosulfan, beta-endosulfan and its metabolite endosulfan sulfate (EURLs, 2022). Even lower levels were successfully validated. The EURLs also informed that separate analytical standards for alpha-endosulfan, beta-endosulfan and endosulfan sulfate are 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[(a)] (mg/kg)	Source
Plant commodities	High water	Yes (GC-ECD)	0.06	FAO and WHO (2006b)
		Yes (QuEChERS method with GC-MS/MS)	0.03	EURLs (2022)
	High oil	Yes (GC-ECD or GC-NPD)	0.06	FAO and WHO (2006b)
		Yes (QuEChERS and QuOil methods with GC-MS/MS)	0.03	EURLs (2022)
	High acid content	Yes (GC-ECD)	0.06	FAO and WHO (2006b)
		Yes (QuEChERS method with GC-MS/MS)	0.03	EURLs (2022)
	Dry	Yes (GC-ECD)	0.06	FAO and WHO (2006b)
		Yes (QuEChERS method with GC-MS/MS)	0.03	EURLs (2022)
	Other: difficult matrices (tea)	Yes (GC-ECD)	0.03	FAO and WHO (2011b)
Animal commodities	Muscle	Yes (GC-ECD)	0.075	FAO and WHO (2006b)
		Yes (QuEChERS method with GC-MS/MS)	0.03	EURLs (2022)
	Kidney	Yes (QuEChERS method with GC-MS/MS)	0.03	EURLs (2022)
	Liver	Yes (GC-ECD)	0.075	FAO and WHO (2006b)
		Yes (QuEChERS method with GC-MS/MS)	0.03	EURLs (2022)
	Fat	Yes (GC-ECD)	0.075	FAO and WHO (2006b)
		Yes (QuEChERS method with GC-MS/MS)	0.03	EURLs (2022)
	Milk	Yes (GC-ECD)	0.06	FAO and WHO (2006b)
		Yes (QuEChERS method with GC-MS/MS)	0.03	EURLs (2022)
	Eggs	Yes (GC-ECD)	0.075	FAO and WHO (2006b)
		Yes (QuEChERS method with GC-MS/MS)	0.03	EURLs (2022)
	Other: honey	Yes (QuEChERS method with GC-MS/MS)	0.03	EURLs (2022)

LOQ: limit of quantification; GC-ECD: gas chromatography with electron capture detector; GC-MS: gas chromatography with mass spectrometry; GC-MS/MS: gas chromatography with tandem mass spectrometry; GC-NPD: gas chromatography with nitrogen phosphorus detection; QUEChERS: Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method).
(a): summed LOQ (individual LOQs for α-endosulfan, β-endosulfan and endosulfan sulfate are equal to 1/3 of the summed LOQ).

2.3. Existing MRLs

The EU MRLs for endosulfan are established in Annex II and IIIb of Regulation (EC) No 396/2005. For a number of food products, Codex maximum residue limits (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 5, the existing EU MRLs 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 MRL 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 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 reported.

Table 5: Background information on current MRLs for endosulfan 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)	Comments
Soya beans	0.5	See comments	See comments	N	No fall-back GAP identified	–	Existing EU MRL was legally implemented in Regulation (EC) 149/2008 and has never been modified. The origin of this MRL is unknown. In 2006, JMPR derived a Codex MRL proposal of 1 mg/kg on soyabean seeds. The proposed CXL was adopted by CCPR 39/CAC 2007. The EU expressed reservations in the CCPR 39/CAC 2007 and the CXL has not been implemented. Existing EU MRL is not substantiated as no EU uses and no IT in place.
Cotton seeds	0.3	CXL (CAC, 2007)	Greece, Spain: Foliar appl., 1 × 0.84 kg a.s./ha, PHI 21 days Australia: Foliar appl., 1 × 0.735 kg a.s./ha, PHI 56 days	Y	n.r.	n.r.	In 2006, JMPR derived a Codex MRL proposal of 0.3 mg/kg on cotton seed. The proposed CXL was adopted by CCPR 39/CAC 2007 and was implemented in EU legislation by Reg. (EU) 310/2011.
Teas	30	See comments	See comments	N	China: Foliar appl., 1 × 0.668 kg a.s./ha, PHI 7 days (FAO and WHO, 2011b)	10	Existing EU MRL was legally implemented in Regulation (EC) 149/2008 and has never been modified. The origin of this MRL is unclear. A Codex MRL proposal of 10 mg/kg was derived based on a Chinese GAP and adopted (CAC, 2011; CCPR, 2011). The CXL proposal has not been legally implemented. However, the EU did not express reservations in CCPR and CAC. Existing EU MRL is not substantiated as there is no IT in place. It is recommended that risk managers discuss whether this EU MRL should be lowered to the level of the existing CXL or to the LOQ.

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)	Comments
Seed spices	1	CXL (CAC, 2005)	See comments	Y	n.r.	n.r.	In 2004, JMPR derived a Codex MRL proposal of 1 mg/kg on seed spices based on monitoring data (FAO and WHO, 2004). The proposed CXL was adopted by CCPR 37/CAC 2005. The EU did not express reservations in the CCPR 37/CAC 2005. The CXL was implemented in EU legislation by Reg. (EU) 839/2008.
Fruit spices	5	CXL (CAC, 2005)	See comments	Y	n.r.	n.r.	In 2004, JMPR derived a Codex MRL proposal of 5 mg/kg on fruit spices based on monitoring data (FAO and WHO, 2004). The proposed CXL was adopted by CCPR 37/CAC 2005. The EU did not express reservations in the CCPR 37/CAC 2005. The CXL was implemented in EU legislation by Reg. (EU) 839/2008.
Root and rhizome spices	0.5	CXL (CAC, 2005)	See comments	Y	n.r.	n.r.	In 2004, JMPR derived a Codex MRL proposal of 1 mg/kg on seed spices based on monitoring data (FAO and WHO, 2004). The proposed CXL was adopted by CCPR 37/CAC 2005. The EU did not express reservations in the CCPR 37/CAC 2005. The CXL was implemented in EU legislation by Reg. (EU) 839/2008.

MRL: maximum residue limit; CXL: Codex maximum residue limit; IT: import tolerance; CAC: Codex Alimentarius Commission; CCPR: Codex committee on pesticide residues: GAP: good agricultural practice; cGAP: critical good agricultural practice; a.s.: active substance; PHI: preharvest interval; n.r.: not relevant.

3. Toxicological reference values

EFSA was mandated 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 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 endosulfan reported in Table 6 were proposed by the RMS in 1999 (Spain, 1999). The JMPR derived an ADI and an ARfD which can be found in Table 7, these values have been used for the MRLs setting.

Table 6: Toxicological reference values (TRVs) set at EU level

TRV	Value	Reference	Comments
ADI	0.006 mg/kg bw per day	Spain (1999)	Based on kidney toxicity observed in a 2-year rat study and applying an UF of 100.
ARfD	–	–	Not considered at the time of the assessment

ADI: acceptable daily intake; ARfD: acute reference dose; bw: body weight; UF: uncertainty factor.

Table 7: Toxicological reference values (TRVs) set by the JMPR

TRV	Value	Reference	Comments
ADI	0.006 mg/kg bw per day	FAO and WHO (1999)	Based on kidney toxicity observed in a 2-year, rat study and applying an UF of 100. The ADI is supported by similar NOAELs from a 1-year dog, 78-week mouse and maternal and developmental toxicity in rat and rabbit.
ARfD	0.02 mg/kg bw	FAO and WHO (1999)	Based on a neurotoxicity study in rats and applying an UF of 100.

ADI: acceptable daily intake; ARfD: acute reference dose; bw: body weight; UF: uncertainty factor; NOAEL: no observed adverse effect level.

EFSA screened the completeness and the quality of the toxicological studies that were used to derive the EU and the JMPR TRVs, focusing on the question whether the studies meet current scientific standards. EFSA did not undertake a full review of the original studies, the basis of the TRVs derivation was scrutinised based on the available data reported mainly in the original DAR (Spain, 1999) and JMPR report (FAO and WHO, 1999); in addition, a developmental neurotoxicity study available to the US EPA (2007) was added to the evaluation.

During this scrutiny, EFSA identified critical issues related to the available toxicological database which were discussed with Member State experts in mammalian toxicology in the Pesticides Peer Review Teleconference 98 in March 2023 (EFSA, 2023a).

The discussions with the Member State experts focussed on the following two critical points:

- the genotoxicity data set;
- the robustness of the available data to derive toxicological reference values, i.e. the ADI, the ARfD and respective UF.

The genotoxicity data package for endosulfan contains studies assessing the three endpoints, i.e. gene mutation in bacterial and mammalian cells (*in vitro*), clastogenicity (*in vitro* and *in vivo*) and aneugenicity (*in vivo*).[9]

The studies for gene mutation and clastogenicity showed negative and positive results, both *in vitro* and *in vivo*. The studies for aneugenicity showed positive and negative results *in vivo*, positive results were seen in studies of low reliability (insufficient information available) and the negative results were inconclusive due mainly to the lack of evidence of bone marrow exposure, but additional limitations were also highlighted. Most of the studies were not performed according to good laboratory practice (GLP) or OECD test guidelines, showing significant limitations in their conduct, such as lack of repeated experiments, insufficient number of concentrations tested or cells scored, criteria used to evaluate the results not in agreement with the recommended ones and, for many studies, the test material is not well defined, i.e. the purity is not reported; in *in vivo* micronucleus tests, bone marrow exposure was

[9] See experts' consultation point 2.1 at the Pesticide Peer Review Teleconference 98 (EFSA, 2023a).

not adequately assessed. Some studies, considered relevant at the time of the assessment to clarify the gene mutation potential of the test substance, were conducted according to test guidelines which have been deleted in the meantime (*in vitro* sister chromatid exchange test TG 479 (OECD, 1986a), *in vitro* unscheduled DNA synthesis assay TG 482 (OECD, 1986b) used in two studies and an *in vivo* sex linked recessive lethal assay in *Drosophila melanogaster* TG 477 (OECD, 1984)); however, also these tests presented limitations in their conduct.

Taking into consideration all weaknesses identified in the data set, a reliable test battery is not available for endosulfan. In 1999, the RMS considered that endosulfan was unlikely to be mutagenic but recommended the submission of additional data to conclude on its clastogenic potential.

The experts also noted that the full study reports are not available, and the study summaries reported in the DAR lack details and cannot be independently reviewed.

Overall, the experts concluded that a standard test battery is not available for endosulfan, its genotoxicity profile is unclear and no conclusion can be drawn on any of the genotoxicity endpoints, mutagenicity, clastogenicity or aneugenicity.

With regard to the toxicological data package needed to derive an ADI and ARfD for endosulfan according to the current data requirements,[10] the experts identified major limitations and missing data as listed below[11]:

- an 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 is not available;
- the presence of toxicologically relevant impurities in the technical specification and consequently in endosulfan-treated commodities is unknown;
- interspecies *in vitro* comparative 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 up-to-date search for published literature is missing;
- an assessment of the endocrine disruptive potential of endosulfan was not conducted since insufficient investigations of the ED parameters are available according to the current ECHA/ EFSA Guidance (ECHA and EFSA, 2018);
- a developmental neurotoxicity (DNT) study is not available, while endosulfan belongs to the chemical class of organochlorine pesticides presenting a neurotoxic mode of action. A DNT study is available to the US EPA, but only a short summary of the outcome was retrieved.

Concerning the individual studies, these were mostly not performed according to GLP and/or OECD TG, the summaries reported in the DAR are not sufficiently detailed (e.g. with tabulated results) as would be expected in current standards and an independent review of their reliability and of the findings cannot be undertaken.

The experts expressed concern regarding the lack of a DNT study that is considered critical for the risk assessment of endosulfan. Some studies in the literature report concerns regarding the developing brain of fetuses exposed to endosulfan, but reliability could not be assessed. DNT concerns were raised due to positive results *in vitro* (hit) for oligodendrocyte differentiation in the micro molar (μM) range in neural progenitor cells (NPCs). Other publications were highlighted linking endosulfan to increased susceptibility of young populations and the developing organisms to neurotoxic effects of endosulfan, even if the DNT study reported by the US EPA where reduced pup body weight and body weight gain were observed in the absence of parental toxicity, did not show neurotoxic effects up to the highest dose tested of 29.8 mg/kg bw per day (US EPA, 2007; ATSDR, 2015).

The use of an additional uncertainty factor was discussed, as an additional UF of 10 was used by the US EPA (2002) due to the neurotoxicity concern over the developing organisms and lacking at the time the DNT study, but not by the California EPA since their assessment in 2009 included the DNT study (CDPR, 2009).

In view of the limitations of the toxicological data set, it was concluded that the existing TRVs derived at EU level cannot be confirmed for endosulfan. In addition, the inconclusive assessment of the genotoxic potential prevents the derivation of revised TRVs, including the use of additional

[10] 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.

[11] See experts' consultation point 2.2 at the Pesticide Peer Review Teleconference 98 (EFSA, 2023a).

uncertainty factors. The JMPR values suffer from the same limitations as they appear to be based on the same toxicological studies, at least with regard to the genotoxicity data package.

Accordingly, the ADI and ARfD derived by the JMPR and by the RMS in 1999 do not comply with the current scientific standards.

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 current residue definition for risk assessment, i.e. endosulfan (sum of alpha and beta isomers and endosulfan sulfate, expressed as endosulfan). 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, 2019). 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. For the acute exposure assessment, the calculation is based on the highest residue levels (HR) expected in raw agricultural commodities (or the STMR for cotton seeds and tea). For spices, STMR and HR were estimated by JMPR based on monitoring data.
  - For commodities for which the CXLs/MRLs were revoked or are no longer substantiated, the appropriate LOQ was used as input value for the exposure calculation.
  - 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.

The acute and chronic exposure calculations were compared to current EU TRVs, noting that during the experts' meeting on mammalian toxicology held in March 2023, the experts concluded that these TRVs do not comply with the current scientific standards (see Section 3).

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

In both scenarios, the highest chronic exposure was calculated for Dutch toddler, representing 63% of the ADI. The contribution of the MRLs set at the LOQ to the exposure represents 62% of the ADI. The highest acute exposure was calculated for tea, representing 31% of the ARfD.

EFSA highlights that the toxicological assessment revealed deficiencies regarding the toxicological studies available for endosulfan (EFSA, 2023a). Therefore, considering the high level of uncertainty affecting the TRVs currently set in EU Regulation, the risk assessment as requested in ToR 5 cannot be finalised and the results presented in this review are indicative only.

Conclusions and recommendations

The metabolism of endosulfan in plants and livestock was previously investigated in the framework of the EU evaluation, as well as 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 endosulfan (sum of alpha and beta isomers and endosulfan sulfate, expressed as endosulfan). The residue is fat soluble.

Analytical methods are available for the enforcement of the proposed residue definition in high water content, high oil content, high acid content and dry matrices with a summed LOQ of 0.06 mg/kg. For tea, the LOQ was reported to be 0.03 mg/kg. The proposed residue definition can be enforced in food of animal origin with an LOQ of 0.075 mg/kg in muscle liver, fat and eggs, and an LOQ of 0.06 mg/kg in milk. According to the EURLs, a QuEChERS (or QuOil) multiresidue analytical method with an LOQ of 0.03 mg/kg for the routine analysis of endosulfan in the four main matrix groups of plant origin and in commodities of animal origin (egg, muscle, liver, milk and honey). Based on the experience gained with these matrices, a default LOQ of 0.03 mg/kg is also deemed achievable in animal fat and kidney.

The origin of all current MRLs set for endosulfan (based on formerly approved uses or on CXLs) was investigating, and the following MRLs were identified as not sufficiently substantiated: EU MRLs for tea and soya beans. No fall-back MRL was identified for soya beans, but existing CXL was identified as possible fall-back MRL for tea. Moreover, further risk management discussions are required to decide whether the existing EU MRL for tea, should be lowered to the existing CXL or to the LOQ.

A screening of the quality of the TRVs set at EU level and of those established by the JMPR was performed, and the set of toxicological studies used to derive these TRVs was assessed according to the current standards. As critical issues were identified, a Member States experts' consultation took place. In view of the limitations of the toxicological data set, the experts concluded that the TRVs cannot be confirmed for endosulfan, in addition, the inconclusive assessment of the genotoxic potential prevents the derivation of revised TRVs, including the use of additional uncertainty factors. Accordingly, the EU ADI and JMPR ADI and ARfD derived in 1999 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 prerequisite to derive robust TRVs:

- complete genotoxicity test battery to conclude on the genotoxic potential of endosulfan;
- up-to-date search for published literature;
- additional toxicological data to perform an ED assessment according to the ECHA/EFSA Guidance (ECHA and EFSA, 2018);
- interspecies comparative *in vitro* metabolism study on animal species used in pivotal studies and on human material;
- DNT 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;
- if possible, an assessment of the toxicological relevance of impurities potentially present in the technical specification and in endosulfan-treated commodities;
- full re-evaluation of the toxicological data package and reporting relevant details on the studies and the results in accordance with the current OECD test guidelines.

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, while all CXLs/ MRLs that were revoked or are no longer substantiated were proposed to be lowered to the appropriate LOQ or MRL proposal, as well as all other commodities for which no GAP was reported under this review. Comparing to the EU TRVs, no exceedances were observed. The highest chronic exposure represented 63% of the ADI (Dutch toddler) and the highest acute exposure amounted to 31% of the ARfD (tea). Nevertheless, EFSA emphasises that, as the toxicological assessment revealed deficiencies regarding the toxicological studies available for endosulfan and considering that current EU TRVs do not meet the current scientific standards, the risk assessment cannot be finalised, and the results presented in this review are indicative only.

Due to the deficiencies identified regarding the toxicological studies available for endosulfan, none of the existing EU MRLs/CXLs listed in the table below (Table 8) are recommended for inclusion in Annex II to the Regulation. If a decision to withdraw the TRVs is taken, EFSA recommends that risk managers discuss whether all MRLs currently implemented in EU Regulation should be lowered to the respective LOQs.

Table 8: Summary table

Code[(a)]	Commodity	Existing MRL (mg/kg)[(b)]	Outcome of the review	
			MRL proposal (mg/kg)	Comment
Residue definition for enforcement (plants and animal products): Endosulfan (sum of alpha and beta isomers and endosulfan sulfate, expressed as endosulfan)[(F)]				
0401070	Soya beans	0.5	LOQ	The existing EU MRL is not substantiated. Hence, the MRL should be lowered to the LOQ.

Code[(a)]	Commodity	Existing MRL (mg/kg)[(b)]	Outcome of the review	
			MRL proposal (mg/kg)	Comment
0401090	Cotton seeds	0.3	0.3 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 endosulfan.
0610000	Teas	30	10 (CXL) or LOQ Further consideration by risk managers needed	The existing EU MRL is not substantiated. Further risk managers discussions are needed to decide whether the existing EU MRL should be lowered to the LOQ or the existing CXL would be more appropriate. In addition, it should be discussed whether the existing MRL needs to be lowered as the risk assessment could not be finalised, lacking robust TRVs for endosulfan.
0810000	Seed spices	1	1 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. Similar recommendations as reported for cotton seeds.
0820000	Fruit spices	5	5 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. Similar recommendations as reported for cotton seeds.
0840000	Root and rhizome spices	0.5	0.5 or LOQ Further consideration by risk managers needed	The existing MRL is sufficiently substantiated. Similar recommendations as reported for cotton seeds.

MRL: maximum residue limit; CXL: Codex residue limit; LOQ: limit of quantification.
(F): Fat soluble.
(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.
(b): MRL currently set under Regulation (EU) No 310/2011.

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Abbreviations

ADI	acceptable daily intake
ARfD	acute reference dose
a.s.	active substance
ATSDR	Agency for Toxic Substances and Disease Registry, US Department of Health and Human Services, Public Health Services
bw	body weight
CAC	Codex Alimentarius Commission
CCPR	Codex Committee on Pesticide Residues
CDPR	California Department of Pesticide Regulation, California Environmental Protection Agency
cGAP	critical good agricultural practice
CLP	classification, labelling and packaging
CXL	Codex maximum residue limit
DAT	days after treatment
DAR	draft assessment report (prepared under Council Directive 91/414/EEC)
DNT	developmental neurotoxicity
ECHA	European Chemicals Agency
ED	endocrine disruptor
EURLs	European Reference Laboratories
FAO	Food and Agriculture Organization of the United Nations
GAP	good agricultural practice
GC-ECD	gas chromatography with electron capture detector
GC-MS	gas chromatography with mass spectrometry
GC-MS/MS	gas chromatography with tandem mass spectrometry
GLP	good laboratory practices
ha	hectare
hL	hectolitre
HR	highest residue
IT	import tolerance
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
LC-MS/MS	liquid chromatography - mass spectrometry
LOQ	limit of quantification (determination)
MRL	maximum residue limit
MS	Member States
NOAEL	no observed adverse effect level
n.r.	not relevant
OJ	Official Journal of the European Union
OECD	Organisation for Economic Co-operation and Development
PHI	preharvest interval
ppm	parts per million (10^{-6})
PRIMo	(EFSA) Pesticide Residues Intake Model
QuEChERS	Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method)
RMS	Rapporteur Member State
SCoPAFF	Standing Committee on Plants, Animals, Food and Feed
STMR	supervised trials median residue
TG	test guideline
ToR	terms of reference
TRV	toxicological reference value
UF	uncertainty factor
US EPA	United States Environmental Protection Agency
WHO	World Health Organization

Appendix A – Summary of the fall-back GAPs collected from Member States

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

Appendix B – Pesticide Residue Intake Model (PRIMo)

- PRIMo_EU_(Sc. 1)

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

Endosulfan (F)

LOQs (mg/kg) range from:	0.03	to:	0.10
Toxicological reference values			
ADI (mg/kg bw per day):	0.006	ARfD (mg/kg bw):	0.02
Source of ADI:	JMPR	Source of ARfD:	JMPR
Year of evaluation:	2006	Year of evaluation:	2006

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 : ---

	Calculated exposure (% of ADI)	MS Diet	Exposure (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)
TMDI/NEDI/IEDI calculation (based on average food consumption)	63%	NL toddler	3.76	30%	Milk: Cattle	5%	Apples	4%	Maize/corn	62%	0.8%
	34%	UK infant	2.05	19%	Milk: Cattle	4%	Tea (dried leaves of Camellia sinensis)	2%	Potatoes	30%	4%
	34%	NL child	2.04	12%	Milk: Cattle	4%	Sugar beet roots	3%	Apples	33%	1%
	32%	DE child	1.90	10%	Milk: Cattle	6%	Apples	2%	Wheat	31%	0.9%
	29%	FR child 3 15 yr	1.73	11%	Milk: Cattle	2%	Wheat	2%	Sugar beet roots	27%	2%
	28%	FR toddler 2 3 yr	1.67	15%	Milk: Cattle	2%	Apples	2%	Wheat	28%	0.3%
	25%	IE adult	1.51	9%	Tea (dried leaves of Camellia sinensis)	2%	Milk: Cattle	2%	Sweet potatoes	16%	9%
	24%	UK toddler	1.45	10%	Milk: Cattle	2%	Wheat	2%	Tea (dried leaves of Camellia sinens	22%	2%
	23%	GEMS/Food G11	1.37	4%	Milk: Cattle	3%	Tea (dried leaves of Camellia sinensis)	2%	Potatoes	20%	3%
	22%	GEMS/Food G06	1.35	4%	Wheat	3%	Tea (dried leaves of Camellia sinensis)	2%	Tomatoes	19%	4%
	22%	GEMS/Food G07	1.33	3%	Tea (dried leaves of Camellia sinensis)	3%	Milk: Cattle	2%	Wheat	19%	4%
	21%	GEMS/Food G08	1.24	3%	Milk: Cattle	2%	Wheat	2%	Tea (dried leaves of Camellia sinens	19%	2%
	20%	DK child	1.23	6%	Milk: Cattle	3%	Rye	2%	Wheat	20%	
	20%	GEMS/Food G10	1.22	3%	Milk: Cattle	2%	Tea (dried leaves of Camellia sinensis)	2%	Wheat	18%	2%
	20%	DE women 14-50 yr	1.20	6%	Milk: Cattle	2%	Sugar beet roots	2%	Tea (dried leaves of Camellia sinens	18%	2%
	20%	FR adult	1.19	10%	Tea (dried leaves of Camellia sinensis)	2%	Milk: Cattle	1%	Wine grapes	10%	10%
	20%	GEMS/Food G15	1.18	4%	Milk: Cattle	2%	Wheat	2%	Potatoes	19%	1%
	20%	DE general	1.17	6%	Milk: Cattle	2%	Sugar beet roots	2%	Tea (dried leaves of Camellia sinens	17%	2%
	19%	RO general	1.13	6%	Milk: Cattle	3%	Wheat	2%	Potatoes	19%	
	19%	SE general	1.12	6%	Milk: Cattle	2%	Bovine: Muscle/meat	2%	Potatoes	19%	
	18%	ES child	1.10	6%	Milk: Cattle	2%	Wheat	1%	Oranges	18%	
	17%	NL general	1.02	4%	Milk: Cattle	2%	Tea (dried leaves of Camellia sinensis)	1%	Sugar beet roots	15%	2%
	15%	FR infant	0.88	8%	Milk: Cattle	1.0%	Potatoes	0.8%	Apples	15%	0.0%
	13%	FI adult	0.77	9%	Coffee beans	0.6%	Potatoes	0.4%	Rye	13%	
	11%	UK vegetarian	0.64	3%	Tea (dried leaves of Camellia sinensis)	2%	Milk: Cattle	1%	Wheat	7%	3%
	10%	PT general	0.63	3%	Potatoes	2%	Wheat	1%	Wine grapes	10%	
	10%	UK adult	0.62	4%	Tea (dried leaves of Camellia sinensis)	1%	Milk: Cattle	0.8%	Wheat	7%	4%
	10%	ES adult	0.61	2%	Milk: Cattle	1%	Wheat	0.6%	Oranges	10%	
	9%	DK adult	0.53	3%	Milk: Cattle	0.6%	Tea (dried leaves of Camellia sinensis)	0.6%	Potatoes	8%	0.6%
	9%	FI 3 yr	0.52	2%	Potatoes	0.7%	Bananas	0.6%	Wheat	9%	
	8%	IT toddler	0.49	3%	Wheat	0.8%	Other cereals	0.7%	Tomatoes	8%	
	8%	LT adult	0.49	2%	Milk: Cattle	2%	Potatoes	0.9%	Apples	8%	
	7%	FI 6 yr	0.41	2%	Potatoes	0.5%	Wheat	0.4%	Bananas	7%	
	6%	IT adult	0.36	2%	Wheat	0.6%	Tomatoes	0.4%	Apples	6%	
	5%	PL general	0.29	2%	Potatoes	1%	Apples	0.4%	Tomatoes	5%	
	4%	IE child	0.25	2%	Milk: Cattle	0.6%	Wheat	0.3%	Potatoes	4%	0.1%

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Endosulfan (F) 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 of IESTI calculation only for crops with GAPs under assessment

Unprocessed commodities

Results for children No. of commodities for which ARfD/ADI is exceeded (IESTI): ---				**Results for adults** No. of commodities for which ARfD/ADI is exceeded (IESTI): ---			
IESTI				**IESTI**			
Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
31%	Tea (dried leaves of	10/4.1	6.3	10%	Tea (dried leaves of	10/4.1	2.1
10%	Vanilla pods	5/3.2	2.0	2%	Cardamom	5/3.2	0.32
2%	Fennel seed	1/0.63	0.49	2%	Cardamom	5/3.2	0.32
2%	Juniper berry	5/3.2	0.32	0.8%	Tamarind	5/3.2	0.15
0.7%	Peppercorn (black, green	5/3.2	0.14	0.5%	Peppercorn (black, green	5/3.2	0.10
0.4%	Allspice/pimento	5/3.2	0.08	0.3%	Caraway	5/3.2	0.06
0.3%	Caraway	5/3.2	0.06	0.3%	Anise/aniseed	1/0.63	0.06
0.2%	Cardamom	5/3.2	0.03	0.3%	Anise/aniseed	1/0.63	0.06
0.10%	Ginger	0.5/0.24	0.02	0.3%	Anise/aniseed	1/0.63	0.06
0.06%	Anise/aniseed	1/0.63	0.01	0.3%	Anise/aniseed	1/0.63	0.06
0.06%	Anise/aniseed	1/0.63	0.01	0.3%	Anise/aniseed	1/0.63	0.06
0.03%	Nutmeg	1/0.63	0.01	0.3%	Anise/aniseed	1/0.63	0.06
0.03%	Turmeric/curcuma	0.5/0.24	0.01	0.2%	Allspice/pimento	5/3.2	0.03
0.02%	Cumin seed	1/0.63	0.00	0.1%	Liquorice	0.5/0.24	0.02
0.02%	Cumin seed	1/0.63	0.00	0.1%	Liquorice	0.5/0.24	0.02
Expand/collapse list							
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): ---				**Results for adults** No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---			
IESTI				**IESTI**			
Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
7%	Tea (dried leaves of Camelli	10/0.04	1.4	4%	Tea (dried leaves of	10/0.04	0.83
2%	Ginger/jam	0.5/0.1	0.30	0.6%	Ginger/jam	0.5/0.1	0.13
				0.02%	Turmeric (Curcuma)/boiled	0.5/0.24	0.00
				0.01%	Cumin seed/processed (not	1/0.03	0.00
Expand/collapse list							

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

- PRIMo_EU_(Sc. 2)

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

Endosulfan (F)

LOQs (mg/kg) range from: 0.03 to: 0.10

Toxicological reference values

ADI (mg/kg bw per day):	0.006	ARfD (mg/kg bw):	0.02
Source of ADI:	JMPR	Source of ARfD:	JMPR
Year of evaluation:	2006	Year of evaluation:	2006

Input values

Details – chronic risk assessment

Supplementary results – chronic risk assessment

Details – acute risk assessment/children

Details – acute risk assessment/adults

Comments:

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)
	63%	NL toddler	3.76	30%	Milk: Cattle	5%	Apples	4%	Maize/corn	62%	0.8%
	34%	UK infant	2.05	19%	Milk: Cattle	4%	Tea (dried leaves of Camellia sinensis)	2%	Potatoes	30%	4%
	34%	NL child	2.04	12%	Milk: Cattle	4%	Sugar beet roots	3%	Apples	33%	1%
	32%	DE child	1.91	10%	Milk: Cattle	6%	Apples	2%	Wheat	31%	0.9%
	29%	FR child 3 15 yr	1.73	11%	Milk: Cattle	2%	Wheat	2%	Sugar beet roots	27%	2%
	28%	FR toddler 2 3 yr	1.67	15%	Milk: Cattle	2%	Apples	2%	Wheat	28%	0.3%
	25%	IE adult	1.51	9%	Tea (dried leaves of Camellia sinensis)	2%	Milk: Cattle	2%	Sweet potatoes	16%	9%
	24%	UK toddler	1.45	10%	Milk: Cattle	2%	Wheat	2%	Tea (dried leaves of Camellia sinensi	22%	2%
	23%	GEMS/Food G11	1.37	4%	Milk: Cattle	3%	Tea (dried leaves of Camellia sinensis)	2%	Potatoes	20%	3%
	22%	GEMS/Food G06	1.34	4%	Wheat	3%	Tea (dried leaves of Camellia sinensis)	2%	Tomatoes	19%	4%
	22%	GEMS/Food G07	1.33	3%	Tea (dried leaves of Camellia sinensis)	3%	Milk: Cattle	2%	Wheat	19%	3%
	21%	GEMS/Food G08	1.24	3%	Milk: Cattle	2%	Wheat	2%	Tea (dried leaves of Camellia sinensi	19%	2%
	20%	DK child	1.23	6%	Milk: Cattle	3%	Rye	2%	Wheat	20%	
	20%	GEMS/Food G10	1.22	3%	Milk: Cattle	2%	Tea (dried leaves of Camellia sinensis)	2%	Wheat	18%	2%
	20%	DE women 14-50 yr	1.20	6%	Milk: Cattle	2%	Sugar beet roots	2%	Tea (dried leaves of Camellia sinensi	18%	2%
	20%	FR adult	1.19	10%	Tea (dried leaves of Camellia sinensis)	2%	Milk: Cattle	1%	Wine grapes	10%	10%
	20%	GEMS/Food G15	1.18	4%	Milk: Cattle	2%	Wheat	2%	Potatoes	19%	1%
	20%	DE general	1.17	6%	Milk: Cattle	2%	Sugar beet roots	2%	Tea (dried leaves of Camellia sinensi	17%	2%
	19%	RO general	1.13	6%	Milk: Cattle	3%	Wheat	2%	Potatoes	19%	
	19%	SE general	1.12	6%	Milk: Cattle	2%	Bovine: Muscle/meat	2%	Potatoes	19%	
	18%	ES child	1.10	6%	Milk: Cattle	2%	Wheat	1%	Oranges	18%	
	17%	NL general	1.02	4%	Milk: Cattle	2%	Tea (dried leaves of Camellia sinensis)	1%	Sugar beet roots	15%	2%
	15%	FR infant	0.88	8%	Milk: Cattle	1.0%	Potatoes	0.8%	Apples	15%	0.0%
	13%	FI adult	0.77	9%	Coffee beans	0.6%	Potatoes	0.4%	Rye	13%	
	11%	UK vegetarian	0.64	3%	Tea (dried leaves of Camellia sinensis)	2%	Milk: Cattle	1%	Wheat	7%	3%
	10%	PT general	0.63	3%	Potatoes	2%	Wheat	1%	Wine grapes	10%	
	10%	UK adult	0.62	4%	Tea (dried leaves of Camellia sinensis)	1%	Milk: Cattle	0.8%	Wheat	7%	4%
	10%	ES adult	0.61	2%	Milk: Cattle	1%	Wheat	0.6%	Oranges	10%	
	9%	DK adult	0.53	3%	Milk: Cattle	0.6%	Tea (dried leaves of Camellia sinensis)	0.6%	Potatoes	8%	0.6%
	9%	FI 3 yr	0.52	2%	Potatoes	0.7%	Bananas	0.6%	Wheat	9%	
	8%	IT toddler	0.49	3%	Wheat	0.8%	Other cereals	0.7%	Tomatoes	8%	
	8%	LT adult	0.49	2%	Milk: Cattle	2%	Potatoes	0.9%	Apples	8%	
	7%	FI 6 yr	0.41	2%	Potatoes	0.5%	Wheat	0.4%	Bananas	7%	
	6%	IT adult	0.36	2%	Wheat	0.6%	Tomatoes	0.4%	Apples	6%	
	5%	PL general	0.29	2%	Potatoes	1%	Apples	0.4%	Tomatoes	5%	
	4%	IE child	0.25	2%	Milk: Cattle	0.6%	Wheat	0.3%	Potatoes	4%	0.1%

Conclusion:

The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.

The long-term intake of residues of Endosulfan (F) 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 of IESTI calculation only for crops with GAPs under assessment

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)
31%	Tea (dried leaves of	10/4.1	6.3
0.4%	Fennel seed	0.1/0.1	0.08
0.3%	Vanilla pods	0.1/0.1	0.06
0.05%	Juniper berry	0.1/0.1	0.01
0.04%	Ginger	0.1/0.1	0.01
0.02%	Peppercorn (black, green	0.1/0.1	0.00
0.01%	Allspice/pimento	0.1/0.1	0.00
0.01%	Turmeric/curcuma	0.1/0.1	0.00
0.01%	Caraway	0.1/0.1	0.00
0.01%	Anise/aniseed	0.1/0.1	0.00
0.01%	Anise/aniseed	0.1/0.1	0.00
0.01%	Nutmeg	0.1/0.1	0.00
0.01%	Nutmeg	0.1/0.1	0.00
0.00%	Cumin seed	0.1/0.1	0.00
0.00%	Cumin seed	0.1/0.1	0.00

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)
10%	Tea (dried leaves of	10/4.1	2.1
0.05%	Anise/aniseed	0.1/0.1	0.01
0.05%	Anise/aniseed	0.1/0.1	0.01
0.05%	Anise/aniseed	0.1/0.1	0.01
0.05%	Anise/aniseed	0.1/0.1	0.01
0.05%	Anise/aniseed	0.1/0.1	0.01
0.05%	Anise/aniseed	0.1/0.1	0.01
0.05%	Anise/aniseed	0.1/0.1	0.01
0.05%	Anise/aniseed	0.1/0.1	0.01
0.05%	Anise/aniseed	0.1/0.1	0.01
0.02%	Tamarind	0.1/0.1	0.00
0.02%	Peppercorn (black, green	0.1/0.1	0.00
0.01%	Caraway	0.1/0.1	0.00
0.01%	Allspice/pimento	0.1/0.1	0.00

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)
7%	Tea (dried leaves of Camelli	10/0.04	1.4
2%	Ginger/jam	0.1/0.1	0.30

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)
4%	Tea (dried leaves of	10/0.04	0.83
0.6%	Ginger/jam	0.1/0.1	0.13
0.02%	Cumin seed/processed (not	0.1/0.1	0.00
0.01%	Turmeric (Curcuma)/boiled	0.1/0.1	0.00

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

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: Endosulfan (sum of alpha and beta isomers and endosulfan sulfate, expressed as endosulfan)(F)					
Soya beans	0.5	0.03*	LOQ	0.03*	LOQ
Cotton seeds	0.3	Scenario 1: 0.06(a)	STMR (CXL)	Scenario 1: 0.06(a)	STMR (CXL)
		Scenario 2: 0.03*	LOQ	Scenario 2: 0.03*	LOQ
Teas	30	4.1	STMR (CXL)	4.1	STMR (CXL)
Seed spices	1	Scenario 1: 0.03	STMR (CXL)	Scenario 1: 0.63	HR (CXL)
		Scenario 2: 0.1*	LOQ	Scenario 2: 0.1*	LOQ
Fruit spices	5	Scenario 1: 0.12	STMR (CXL)	Scenario 1: 3.2	HR (CXL)
		Scenario 2: 0.1*	LOQ	Scenario 2: 0.1*	LOQ
Root and rhizome spices	0.5	Scenario 1: 0.1	STMR (CXL)	Scenario 1: 0.24	HR (CXL)
		Scenario 2: 0.1*	LOQ	Scenario 2: 0.1*	LOQ
Other crops/commodities	See Reg. (EU) 310/2011	LOQ(b)			

STMR: median residue value; HR: highest residue; CXL: Codex maximum residue limit; LOQ: limit of quantification.
*: Indicates that the input value is proposed at the limit of quantification.
(F): The active substance is fat soluble.
(a): In the JMPR report, an STMR of 0.02 mg/kg was proposed as the sum of individual components (α-endosulfan, β-endosulfan and endosulfan sulfate) was not considered for the compounds below the LOQ. The proposed STMR of 0.06 mg/kg is derived by summing the individual compound even considering the ones below the LOQ.
(b): An LOQ of 0.06 mg/kg was applied to herbs, and of 0.1 mg/kg to coffee beans, herbal infusions, cocoa beans, carobs, hops and spices. A default LOQ of 0.03 mg/kg for all other commodities was applied.