Peers review of the pesticide risk assessment for the active substance tri-allate in light of confirmatory data submitted

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Abstract

The conclusions of the EFSA following the peer review of the initial risk assessment carried out by the competent authority of the rapporteur Member State, the United Kingdom, for the pesticide active substance tri-allate are reported. The context of the peer review was that requested by the European Commission following the submission and evaluation of confirmatory data. The conclusions were reached on the basis of the evaluation of the representative uses of tri-allate as a herbicide on cereals (barley and wheat). The reliable endpoints concluded as being appropriate for use in regulatory risk assessment, derived from the available studies and literature in the dossier peer reviewed, are presented. Concerns are identified.

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Keywords: tri-allate, peer review, confirmatory data, risk assessment, pesticide, herbicide

Requestor: European Commission

Question number: EFSA-Q-2018-00744

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Suggested citation: EFSA (European Food Safety Authority), Anastasiadou M, Arena M, Auteri D, Brancato A, Bura L, Carrasco Cabrera L, Chaideftou E, Chiusolo A, Crivellente F, De Lentdecker C, Egsmose M, Fait G, Greco L, Ippolito A, Istance F, Jarrah S, Kardassi D, Leuschner R, Lostia A, Lythgo C, Magrans O, Mangas I, Miron I, Molnar T, Padovani L, Parra Morte JM, Pedersen R, Reich H, Santos M, Sharp R, Szentes C, Terran A, Tiramani M, Vagenende B and Villamar-Bouza L, 2020. Conclusion on the peer review of the pesticide risk assessment for the active substance tri-allate in light of confirmatory data submitted. EFSA Journal 2020;18(9):6244, 21 pp. https://doi.org/10.2903/j.efsa.2020.6244

ISSN: 1831-4732

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Summary

Tri-allate was included in Annex I to Directive 91/414/EEC on 1 January 2010 by Commission Directive 2009/77/EC and has been deemed to be approved under Regulation (EC) No 1107/2009, in accordance with Commission Implementing Regulation (EU) No 540/2011, as amended by Commission Implementing Regulation (EU) No 541/2011. It was a specific provision of the approval that the applicant was required to submit to the European Commission further information to assess the primary plant metabolism, further information on the fate and behaviour of the soil metabolite diisopropylamine (DIPA), further information on the potential for biomagnification in aquatic food chains, information to further address the risk to fish-eating mammals and the long-term risk to earthworms by 31 December 2011.

In accordance with the specific provision, the applicant, Gowan Comércio Internacional e Servicos submitted an updated dossier in December 2011 which was evaluated by the designated rapporteur Member State (RMS), the United Kingdom, in the form of an addendum to the draft assessment report. In compliance with the guidance document SANCO 5634/2009-rev. 6.1, the RMS distributed the addendum to the Member States, the applicant and EFSA for comments on 23 September 2015. The RMS collated all comments in the format of a reporting table, which was submitted to EFSA in December 2015.

Following consideration of the comments received, the European Commission requested EFSA to organise a peer review of the evaluation by the RMS of the confirmatory data submitted in relation to residues and fate and behaviour and to deliver its conclusions on the following points:

- the plant residue definitions, including the relevance of the metabolites peak 14, conjugates M14 and M15, DIPA and TCP; and
- the relevance of livestock exposure and the need for livestock metabolism studies as well as the relevance of rotational crop residues and the need for rotational crop studies;
- the consumer risk assessment;
- to examine how the calculation of the formation fractions can be calculated if a substantial part of tri-allate is volatilised as well as the impact of any changes on predicted environmental concentration (PEC) values of tri-allate and its metabolites should be reported.

The toxicological profile, including genotoxic potential of tri-allate metabolites TCP, M14, M15 and DIPA were clarified according to the guidelines applicable at the time of the first peer review and dietary toxicological reference values were established for these metabolites. It was noted that according to current scientific knowledge, aneugenicity has not been sufficiently addressed. Nevertheless, the experts considered that according to the guidelines applicable at the time of the first peer review, the genotoxicity potential had been sufficiently assessed. No information has been provided on the metabolite referred to as ‘peak 14’. In addition, but out of the scope of this confirmatory data mandate, it was noted that a concern regarding the mutagenicity potential of the parent compound could not be excluded based on the observation of positive Ames tests not adequately followed up in vivo according to current scientific knowledge. The experts agreed that this concern should be flagged in the present conclusion.

On the basis of new wheat metabolism data, the residue definition for risk assessment derived by the first peer review was amended to include a new relevant metabolite, DIPA, that has lower toxicological reference values than tri-allate. Data on the magnitude of DIPA residues in primary and rotational crops and animal matrices are not available. Moreover, the applicant’s hypothesis on unidentified ‘peak 14’ as a structurally and toxicologically similar metabolite requires substantiation. As occurrence of significant residues of DIPA might be expected in different commodities, the investigation of effects of food processing is recommended in view of the potential of DIPA for formation of nitrosamines. Currently, a robust consumer dietary risk assessment with regard to DIPA cannot be conducted. As for metabolite TCP, the lack of residue trials in primary and rotational crops with determination of TCP conjugated residues leads to uncertainty in the risk assessment for this metabolite. Altogether the consumer risk assessment for the representative uses of tri-allate cannot be concluded.

With respect to the fate and behaviour in the environment, the groundwater metabolite TCP exceeded 0.75 μg/L for all relevant scenarios and 10 μg/L in four scenarios. The groundwater metabolite DIPA exceeded 10 μg/L for all scenarios. DIPA is a known precursor of N-nitroso-disopropylamine. The issue of possible formation of N-nitroso-disopropylamine from DIPA and under which conditions it may be produced (e.g. effect of water treatment procedures) remains also open at this stage.
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Background

Tri-allate was included in Annex I to Directive 91/414/EEC on 1 January 2010 by Commission Directive 2009/77/EC\(^1\), and has been deemed to be approved under Regulation (EC) No 1107/2009\(^2\), in accordance with Commission Implementing Regulation (EU) No 540/2011\(^3\), as amended by Commission Implementing Regulation (EU) No 541/2011\(^4\). EFSA previously finalised a Conclusion on this active substance on 26 September 2008 in the EFSA Scientific Report (2008) 181 (EFSA, 2009).

It was a specific provision of the approval that the applicant was required to submit to the European Commission further information to assess the primary plant metabolism, further information on the fate and behaviour of the soil metabolite diisopropylamine (DIPA), further information on the potential for biomagnification in aquatic food chains, information to further address the risk to fish-eating mammals and the long-term risk to earthworms by 31 December 2011.

In accordance with the specific provision, the applicant, Gowan Comércio Internacional e Servicos submitted an updated dossier in December 2011, which was evaluated by the designated rapporteur Member State (RMS), the United Kingdom, in the form of an addendum to the draft assessment report (United Kingdom, 2015). In compliance with the guidance document SANCO 5634/2009-rev. 6.1 (European Commission, 2013), the RMS distributed the addendum to Member States, the applicant and EFSA for comments on 23 September 2015. The RMS collated all comments in the format of a reporting table, which was submitted to EFSA in December 2015, leading to the conclusions published in the EFSA Technical Report (EFSA, 2016).

Following consideration of the comments received, in September 2018, the European Commission requested EFSA to organise a peer review of the evaluation of the RMS of the confirmatory data submitted in relation to residues and fate and behaviour and to deliver its conclusions on the following points:

- the plant residue definitions, including the relevance of metabolites peak 14, conjugates M14 and M15, DIPA and TCPSA;
- the relevance of livestock exposure and the need for livestock metabolism studies as well as the relevance of rotational crop residues and the need for rotational crop studies;
- the consumer risk assessment;
- to examine how the calculation of the formation fractions can be calculated if a substantial part of tri-allate is volatilised as well as the impact of any changes on predicted environmental concentration (PEC) values of tri-allate and its metabolites should be reported.

The addendum and the reporting table were discussed at the Pesticides Peer Review Experts’ Meetings on environmental fate and behaviour, mammalian toxicology and residues in November 2018, January and February 2019. Details of the issues discussed, together with the outcome of these discussions were recorded in the meeting reports.

A final consultation on the conclusions arising from the peer review took place with Member States via a written procedure in April 2019.

The conclusions laid down in this report were reached on the basis of the peer review of the RMS’s evaluation of the confirmatory data submitted in relation to mammalian toxicology, residues and environmental fate and behaviour. A key supporting document to this conclusion is the peer review report, which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the compilation of comments in the reporting table to the conclusion. The peer review report (EFSA, 2020) comprises the following documents, in which all views expressed during the course of the peer review, including minority views, can be found:

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\(^1\) Commission Directive 2009/77/EC of 1 July 2009 amending Council Directive 91/414/EEC to include chlorsulfuron, cyromazine, dimethachlor, etofenprox, lufenuron, penconazole, tri-allate and triflusulfuron as active substances. OJ No L 172, 2.7.2009, p. 23–33.

\(^2\) Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1–50.

\(^3\) Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 1–186.

\(^4\) Commission Implementing Regulation (EU) No 541/2011 of 1 June 2011 amending Implementing Regulation (EU) No 540/2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 187–188.
the reporting table (12 January 2016)\(^5\); the reports of the scientific consultation with Member State experts; the comments received on the draft EFSA conclusion.

Given the importance of the DAR including its final addendum (United Kingdom, 2019) and the peer review report, these documents are considered as background documents to this conclusion. It is recommended that this conclusion report and its background documents would not be accepted to support any registration outside the EU for which the applicant has not demonstrated to have regulatory access to the information on which this conclusion report is based.

**The active substance and the formulated product**

Tri-allate is the ISO common name for S-2,3,3-trichloroallyl diisopropyl(thiocarbamate) (IUPAC). The representative formulated product for the evaluation was 'Avadex 15G' ('Mon 7966'), a granule (GR) containing 150 g/kg tri-allate. The representative uses evaluated comprised post-sowing and pre-emergence applications with tractor mounted ground applicator to control wild oats, black-grass and meadow-grass in summer and winter barley and wheat.

**Conclusions of the evaluation**

The applicant has submitted to the Commission by the deadline of 31 December 2011 studies to provide further information to assess the primary plant metabolism, further information on the fate and behaviour of the soil metabolite diisopropylamine (DIPA), further information on the potential for biomagnification in aquatic food chains, information to further address the risk to fish-eating mammals and the long-term risk to earthworms. The assessment of the information was presented in revised confirmatory data addenda (United Kingdom, 2015), updated in January 2019 (United Kingdom, 2019).

1. **Mammalian toxicology**

In the mammalian toxicology area, additional information has been provided on tri-allate metabolites TCPSA and DIPA; their toxicological profile was discussed during the Pesticides Peer Review Experts’ meeting 190, session 2, in January 2019.

Following the request for confirmatory data, no further information was provided for the metabolite 'peak 14' (identity and/or toxicity) and further clarification regarding the significance of this compound as a residue in plant was requested (see Section 2).

The genotoxicity potential of TCPSA was already assessed in the previous conclusion (EFSA, 2009) and no concerns had been identified; accordingly the metabolite was found not relevant according to the guidance document on the assessment of the relevance of metabolites in groundwater (European Commission, 2003) up to stage 3 of step 3. It was noted that according to current scientific knowledge, the aneugenicity might not be sufficiently addressed in the chromosome aberration test and should be further assessed in the framework of the renewal process. Nevertheless, the experts considered that according to the guidelines applicable at the time of the first peer review, the genotoxicity potential had been sufficiently assessed. TCPSA presents low acute toxicity after ingestion; based on 14-day and 28-day toxicity studies in rats, it was concluded that the metabolite is of equivalent toxicity or most likely lower toxicity when compared to the parent tri-allate. Therefore, the dietary reference values of tri-allate are applicable to TCPSA. The metabolites M14 and M15 are not rat metabolites and are glycosides of TCPSA; hydrolysis of these metabolites is likely to occur in the gastrointestinal tract, resulting in the generation of their aglycon M1 (a major metabolite identified in rat metabolism) and TCPSA, respectively. It was considered that their toxicological profile is addressed by the studies performed with tri-allate and TCPSA, allowing to conclude that the dietary reference values of the parent are applicable also to these two metabolites.

Regarding the metabolite DIPA, it appears to be acutely more toxic than the parent and presents a different toxicological profile than tri-allate such as local irritation/corrosivity and secondary systemic effects (changes in clinical chemistry). Based on newly submitted genotoxicity studies, it was concluded that DIPA is unlikely to be genotoxic *in vitro*. It was noted that according to current scientific knowledge, the aneugenicity might not be sufficiently addressed in the chromosome aberration test and should be further assessed in the framework of the renewal process. Nevertheless,

\(^5\) published in the EFSA Technical Report (EFSA, 2016).
the experts considered that according to the guidelines applicable at the time of the first peer review, the genotoxicity potential had been sufficiently assessed. An acceptable daily intake (ADI) of 0.015 mg/kg body weight (bw) per day was established for the metabolite, based on the no observed adverse effect level (NOAEL) of 15 mg/kg bw per day from the 28-day study in rat, and applying an uncertainty factor (UF) of 1,000, that includes an additional UF of 10 to account for the lack of chronic, carcinogenicity and reproductive toxicity data. An acute reference dose (ARfD) of 0.15 mg/kg bw was established, based on the local and systemic NOAEL of 15 mg/kg bw per day from the 28-day study and applying the standard UF of 100. An additional UF to account for the lacking developmental toxicity study is not needed in this case, considering the corrosive effects of the compound.

It is noted that the genotoxicity assessment conducted in 2008 on the parent compound tri-allate fails to demonstrate a lack of genotoxicity potential according to the current scientific developments (EFSA Scientific Committee, 2011). Three positive Ames tests were followed up with a negative in vivo unscheduled DNA synthesis (UDS) test. It is currently well recognised that the latter test is not sufficiently sensitive to overrule the positive results observed in vitro. In addition, some carbamate-derived chemical structures have been identified in the open literature as potential genotoxic compounds in vitro. Even though this was not part of the confirmatory data process and therefore not revised by the applicant and/or the RMS, the experts agreed that this concern should be flagged in the present conclusion for further considerations during the renewal process.

2. Residues

In addition to the previously assessed metabolism studies in wheat and peas (EFSA, 2009), new metabolism data in wheat upon soil treatment with diisopropylamine (DIPA) and allyl labelled tri-allate were submitted. On the basis of the recent studies and the information provided by the section on mammalian toxicology regarding metabolites TCPSA and DIPA, the residue definition for risk assessment has been set in the confirmatory data process as:

1) Sum of tri-allate, TCPSA and TCPSA conjugates, expressed as tri-allate, and 2) DIPA

Application of the derived residue definition for risk assessment purposes should be restricted to soil applied uses in cereals since metabolism data with foliar application are not available. As the new wheat metabolism data revealed the presence of a relevant metabolite DIPA (45–60% total radioactive residue (TRR) and with lower reference values applicable than tri-allate, see Section 1 above), the provisional residue definition derived by the peer review (EFSA, 2009) was amended to include this metabolite in addition (part 2) above) to the initial proposal (part 1) above).

An unidentified metabolite ‘peak 14’ was present at levels in wheat grains which ideally should have been identified, specifically as DIPA has lower toxicological reference values than tri-allate and has the potential to form N-nitroso-diisopropylamine. The applicant’s hypothesis on ‘peak 14’ as a derivative of DIPA with a toxicological profile comparable to DIPA should be further substantiated and the presence of DIPA-derived nitrosamines should be ruled out (data gap).

It is recommended to currently maintain the residue definition for monitoring as tri-allate and to review this definition once residue trials analysing for the complete residue definition have been submitted and permit an evaluation whether tri-allate is a sufficiently good marker (< LOQ in grain).

The currently available field trials in cereals did not determine residues of TCPSA conjugates and DIPA but only of tri-allate and TCPSA (free). However, based on the findings in the wheat metabolism study, a significant increase of TCPSA total residues, i.e. including TCPSA conjugates, and quantifiable residue levels of DIPA may be expected. Therefore, the available residue trials are insufficient to conduct robust exposure and risk assessments and residue trials with analysis of DIPA and TCPSA, including its conjugates, are requested (data gap).

The soil-applied primary crop metabolism and soil degradation studies conducted with diisopropylamine labelled tri-allate complement the rotational crop metabolism study that limited the investigations to the allyl portion of the molecule. A similar metabolite picture is expected in soil-applied primary and rotational crops. This assumption should be confirmed by the previously requested (EFSA, 2009) rotational crop field trials in representative crop categories, analysing commodities for tri-allate, TCPSA (free and conjugated) and DIPA, and with particular attention to the detection of nitrosamines as DIPA is a known precursor of N-nitroso-diisopropylamine.

For the same reason of potential formation of nitrosamines, investigation of the behaviour of DIPA under conditions representative for food processing should be investigated, if significant residues will be found in residue trials with investigation of DIPA.
As residue trials with determination of the relevant residue compounds for risk assessment are not available, robust assessments of the livestock dietary burden and the potential transfer of residues into animal commodities cannot be conducted. Should the calculated animal intakes exceed the established trigger value, which is indicated by tentative estimates using metabolism data, additional livestock metabolism studies (investigating the behaviour of diisopropylamine-labelled tri-allate) might be necessary. Currently, residue definitions in animal commodities cannot be derived.

A robust consumer risk assessment according to the derived residue definition cannot be conducted without residue trials determining the actual concentrations of all relevant analytes. The RMS attempted a provisional assessment for part 1) of the residue definition, using residue data for tri-allate and free TCPSA, where available, and adding assumptions and factors to compensate for missing data in crops and animal commodities, i.e. adding several non-standard uncertainties. With this approach, the maximum estimated intakes for the sum of tri-allate, TCPSA and TCPSA conjugates, expressed as tri-allate with PRIMO rev. 2 correspond to approx. 27% of the ADI and 6% of the ARfD. As TCPSA is also a metabolite leaching to groundwater (see Section 3 on environmental fate and behaviour), a relevance assessment was triggered and the consumer exposure with regard to residues of metabolite TCPSA in groundwater abstracted for drinking water purposes was assessed on the basis of the predicted concentrations in groundwater. The estimates are based on WHO default assumptions (WHO, 2004). The intake of TCPSA residues via drinking water corresponds to 5%, 16% and 24% of the ADI applicable to TCPSA for adults, toddlers and infants, respectively.

A separate risk assessment attempt for part 2) of the residue definition for dietary risk assessment, DIPA, was based on a single residue value derived for cereal grain from the metabolism study as residue trials in cereals for DIPA are not available. Moreover, residues in rotational crops to which significant uptake of DIPA from soil is expected and potential transfer into animal commodities via feed items could not be considered without any data available. A reliable consumer risk assessment cannot be conducted for DIPA.

DIPA is also a metabolite in groundwater that triggered a relevance assessment. The consumer exposure via groundwater is predicted to be approximately 18% of the ADI of DIPA for adults, 55% for toddlers and 83% for infants. It is not known to which extent dietary intake of DIPA residues from food of plant and possibly animal origin will contribute in addition, however, significant residues in primary and rotational crops might be expected from the currently available data. When a combined exposure assessment is performed for DIPA considering exposure via food and groundwater, it cannot be excluded that exposures could exceed an acceptable level depending on the consumer group.

### 3. Environmental fate and behaviour

With respect to the fate and behaviour in the environment, the peer review of the confirmatory data assessment confirmed the formation fractions used by the RMS for the fate and behaviour modelling. The groundwater exposure assessment presented by the RMS was therefore agreed in the experts’ meeting:

For TCPSA, the 80th percentile annual average concentration exceeded 0.75 µg/L for all scenarios and 10 µg/L for the Hamburg, Jokioinen, Kremsmünster and Okehampton scenarios using the PEARL 3.3.3 model. The relevance of TCPSA was assessed following the step-wise procedure set out in the guidance document for relevance of metabolites in groundwater (see Sections 1 and 2 for toxicology and consumers risk assessment).

For DIPA, the 80th percentile annual average concentration exceeded 10 µg/L for all scenarios using the PEARL 3.3.3 model. An assessment of the relevance of the tri-allate metabolite DIPA in groundwater has been performed, but not finalised, including an exposure assessment (see Sections 1 and 2 for toxicology and consumers risk assessment and Section 5.1 for issues that could not be finalised). DIPA is a known precursor of N-nitroso-diisopropylamine. The issue of possible formation of N-nitroso-diisopropylamine from DIPA and under which conditions it may be produced (e.g. effect of water treatment procedures) remain also open at this stage.

### 4. Data gaps

Data gaps identified during this focussed peer review of confirmatory data assessment are listed below. It is noted that data gaps identified in the previously finalised EFSA Conclusion on this active substance (EFSA, 2009) that were not part of the focussed peer review process of confirmatory data remain unchanged.
The applicant’s hypothesis on ‘peak 14’ as a derivative of DIPA with a toxicological profile comparable to DIPA should be further substantiated and the presence of DIPA-derived nitrosamines should be ruled out (relevant for all representative uses, see Section 2).

Residue trials with analysis of DIPA and TCPSA, including its conjugates (relevant for all representative uses, see Section 2).

5. Concerns

5.1. Issues that could not be finalised

An issue is listed as an issue that could not be finalised where there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the Uniform Principles in accordance with Article 29(6) of Regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011, and where the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

1) Occurrence of significant residues of the relevant metabolite DIPA might be expected in different commodities for animal and human consumption. Data on the magnitude of DIPA in primary and rotational crops and potential transfer into animal matrices are not available. Moreover, the investigation of effects of food processing is recommended in view of the potential of DIPA for formation of nitrosamines. Currently, a robust consumer dietary risk assessment for the representative uses with regard to DIPA and TCPSA cannot be conducted. Consumer exposure to DIPA from groundwater abstracted for drinking water purposes leads to predicted intakes that already correspond to up to 83% of the ADI. A combined assessment for food and drinking water to exclude consumer risks and progress the relevance assessment of metabolite DIPA in groundwater cannot be finalised without further data and could, when finalised, become a concern (see Section 2).

5.2. Critical areas of concern

An issue is listed as a critical area of concern where there is enough information available to perform an assessment for the representative uses in line with the Uniform Principles in accordance with Article 29(6) of Regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011, and where this assessment does not permit to conclude that, for at least one of the representative uses, it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

An issue is also listed as a critical area of concern where the assessment at a higher tier level could not be finalised due to lack of information, and where the assessment performed at the lower tier level does not permit to conclude that, for at least one of the representative uses, it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

2) A new concern has been identified regarding the genotoxicity assessment conducted in 2008 on the parent compound tri-allate (even though this was not part of the confirmatory data process and therefore not revised by the applicant and/or the RMS). Three positive Ames tests conducted with tri-allate were followed up with a negative in vivo UDS test. It is currently well recognised that the latter test is not sufficiently sensitive to overrule the positive results observed in vitro. In addition, some carbamate-derived chemical structures have been identified in the open literature as potential genotoxic compounds. The experts agreed that this concern should be flagged in the present conclusion.

3) It is confirmed that soil metabolite TCPSA may reach levels above 10 µg/L in groundwater in vulnerable scenarios.
4) The formation and leaching of soil metabolite DIPA (known to be a precursor of nitrosamines) has been confirmed that may reach levels above 10 μg/L in all relevant scenarios for the representative uses considered.

6. **Overview of the concerns identified for each representative use considered (Table 1)**

| Representative use                        | Cereals                                      |
|------------------------------------------|----------------------------------------------|
| **Operator risk**                        | Risk identified                              |
|                                          | Assessment not finalised                      |
| **Worker risk**                          | Risk identified                              |
|                                          | Assessment not finalised                      |
| **Resident/bystander risk**              | Risk identified                              |
|                                          | Assessment not finalised                      |
| **Consumer risk**                        | Risk identified                              |
|                                          | Assessment not finalised                      |
| **Groundwater exposure to active substance** | Legal parametric value breached               |
|                                          | Assessment not finalised                      |
| **Groundwater exposure to metabolites**  | Parametric value of 10 μg/L breached         |
|                                          | Assessment not finalised                      |

The superscript numbers relate to the numbered points indicated in Sections 5.1 and 5.2.

(a): When the consideration for classification made in the context of this evaluation under Regulation (EC) No 1107/2009 is confirmed under Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008.

(b): Value for non-relevant metabolites prescribed in SANCO/221/2000-rev. 10 final, European Commission (2003).

**References**

EFSA (European Food Safety Authority), 2009. Conclusion regarding the peer review of the pesticide risk assessment of the active substance tri-allate. EFSA Scientific Report 2008;181, 100 pp. https://doi.org/10.2903/j.efsa.2009.181r

EFSA (European Food Safety Authority), 2016. Technical report on the outcome of the consultation with Member States, the applicant and EFSA on the pesticide risk assessment for tri-allate in light of confirmatory data. EFSA supporting publication 2016:EN-953, 48 pp. https://doi.org/10.2903/sp.efsa.2016.EN-953

EFSA (European Food Safety Authority), 2020. Peer review report to the conclusion regarding the peer review of the active substance tri-allate in light of confirmatory data submitted. Available online: www.efsa.europa.eu

EFSA Scientific Committee, 2011. Scientific Opinion on genotoxicity testing strategies applicable to food and feed safety assessment. EFSA Journal 2011;9(9):2379, 68 pp. https://doi.org/10.2903/j.efsa.2011.2379. Available online: www.efsa.europa.eu/efsajournal

European Commission, 2003. Guidance Document on Assessment of the Relevance of Metabolites in Groundwater of Substances Regulated under Council Directive 91/414/EEC. SANCO/221/2000-rev. 10 final, 25 February 2003.

European Commission, 2013. Guidance document on the procedures for submission and assessment of confirmatory information following approval of an active substance in accordance with Regulation (EC) No 1107/2009. SANCO 5634/2009-rev. 6.1.

United Kingdom, 2015. Addendum to the Draft Assessment Report (DAR) on tri-allate prepared by the rapporteur Member State the United Kingdom in the framework of Regulation (EC) No 1107/2009, September 2015, revised in December 2015. Available online: www.efsa.europa.eu

United Kingdom, 2019. Revised Addendum to the Draft Assessment Report (DAR) on tri-allate prepared by the rapporteur Member State the United Kingdom in the framework of Regulation (EC) No 1107/2009, January 2019. Available online: www.efsa.europa.eu

WHO (World Health Organization), 2004. Guidelines for drinking-water quality. Vol. 1. 3rd Edition, Geneva, WHO.

**Abbreviations**

1/n slope of Freundlich isotherm

λ wavelength
| Abbreviation | Description |
|--------------|-------------|
| ε            | decadic molar extinction coefficient |
| ADI          | acceptable daily intake |
| ARfD         | acute reference dose |
| bw           | body weight |
| CAS          | Chemical Abstracts Service |
| CI           | confidence interval |
| CL           | confidence limits |
| DAR          | draft assessment report |
| DAT          | days after treatment |
| DM           | dry matter |
| DT50         | period required for 50% dissipation (define method of estimation) |
| DT90         | period required for 90% dissipation (define method of estimation) |
| FOCUS        | Forum for the Co-ordination of Pesticide Fate Models and their Use |
| HPLC         | high-performance liquid chromatography |
| IEDI         | international estimated daily intake |
| IESTI        | international estimated short-term intake |
| ISO          | International Organization for Standardization |
| IUPAC        | International Union of Pure and Applied Chemistry |
| KOC          | Organic-carbon partition coefficient |
| KOM          | partition coefficient normalized to organic matter |
| LD50         | lethal dose, median dose letalis media |
| LOQ          | limit of quantification (determination) |
| M/L          | mixing and loading |
| mm           | millimetre (also used for mean measured concentrations) |
| MS           | mass spectrometry |
| MWHC         | maximum water-holding capacity |
| NOAEL        | no observed adverse effect level |
| OECD         | Organisation for Economic Co-operation and Development |
| PD           | proportion of different food types |
| PEC          | predicted environmental concentration |
| PHI          | preharvest interval |
| PIE          | potential inhalation exposure |
| SC           | suspension concentrate |
| SFO          | single first-order |
| SMILES       | simplified molecular-input line-entry system |
| TK           | technical concentrate |
| TLC          | thin-layer chromatography |
| TMDI         | theoretical maximum daily intake |
| TRR          | total radioactive residue |
| UDS          | unscheduled DNA synthesis |
| UF           | uncertainty factor |
| UV           | ultraviolet |
| WHO          | World Health Organization |
Appendix A – List of end points for the active substance and the representative formulation

Impact on Human and Animal Health

Other toxicological studies (Annex IIA, point 5.8)

| Metabolite | Studies performed on metabolites or impurities |
|------------|-----------------------------------------------|
| TCPSA      | Minor metabolite in the rat                    |
|            | *In vitro* metabolism: TCPSA was not metabolised |
|            | Rat acute oral LD$_{50}$ > 2,000 mg/kg bw in females |
|            | Negative in:                                   |
|            |   - *Salmonella* Typhimurium reverse mutation assay (Ames test) |
|            |   - *In vitro* chromosome aberration test in Chinese hamster V79 cells |
|            |   - Cell mutation assay at the thymidine kinase locus in mouse lymphoma L5178Y cells. |
|            | 14-Day range-finding study in rat with TCPSA-Na salt did not provide any signs of toxicity up to 1,413 mg/kg bw per day when administered to rats for 14-days. Clinical chemistry, haematology or microscopic examination of organs and tissues were not performed |
|            | 28-Day, rat with TCPSA-Na salt: NOAEL 1,244 mg/kg bw per day, the highest dose tested |
|            | The toxicological reference values of the parent apply to this metabolite |
| M14 Carbohydrate conjugate of M1 (major rat metabolite) | The toxicological reference values of the parent apply to this metabolite |
| M15 Carbohydrate conjugate of TCPSA | The toxicological reference values of the parent apply to this metabolite |
### DIPA

| LD$_{50}$: lethal dose, 50%; bw: body weight; NOAEL: no observed adverse effect level; ADI: acceptable daily intake; ARfD: acute reference dose. |
|---|
| Rat acute oral LD$_{50}$ = 420 mg/kg bw (both sexes combined) – Acute Tox 4, H304 'harmful if swallowed' (harmonised classification according to Annex VI of Regulation (EC) No 1272/2008). |
| Negative results in: |
| - Ames test (±S9) |
| - *In vitro* chromosome aberration test in human lymphocytes (±S9) |
| - Cell mutation assay at the thymidine kinase locus in mouse lymphoma L5178Y cells (±S9) |
| 28-Day, rat: NOAEL (local and systemic) = 15 mg/kg bw per day based on local toxicity in the gastrointestinal tract (GIT) (consistent with gavage administration of a corrosive substance) and changes in haematological and clinical chemistry parameters at 50 mg/kg bw per day |
| ADI: 0.015 mg/kg bw per day, based on the 28-day study in rats and applying an UF of 1,000 that includes an additional UF of 10 to account for the lack of chronic, carcinogenicity and reproductive toxicity data |
| ARfD: 0.15 mg/kg bw, based on the 28-day study in rats and applying an UF 100 (additional UF to account for the lacking developmental toxicity study is not needed in this case considering the corrosive effects of the compound) |
### Residues

#### Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

| Plant groups covered | Cereals (Soil application) |
|----------------------|-----------------------------|
| Rotational crops     | Allyl label only: Cereal (wheat), leafy (lettuce), root (radish) |
| Metabolism in rotational crops similar to metabolism in primary crops? | Similarity is assumed as for  
  – application mode in primary crop studies (soil application)  
  – findings in the allyl label plant studies  
  – soil degradation studies  
  DIPA uptake (major in soil) is expected but has not been directly studied (lack of second radiolabel in rotational crop study)  
  Similarity should be confirmed by rotational crop field trials |
| Processed commodities | No data, but recommended as for the potential of formation of nitrosamines from major plant metabolite DIPA |
| Residue pattern in processed commodities similar to residue pattern in raw commodities? | n/a |
| Plant residue definition for monitoring | Tri-allate (review recommended once residue trials are available analysing for the complete residue definition) |
| Plant residue definition for risk assessment | 1) Sum of tri-allate, TCPSA and TCPSA conjugates, expressed as tri-allate  
2) DIPA  
Restricted to soil applied uses |
| Conversion factor (monitoring to risk assessment) | Open. Unable to convert from tri-allate levels (< 0.01 mg/kg in grain) to the sum of tri-allate, TCPSA, free and conjugated, expressed as tri-allate or to DIPA residues |

#### Residues in succeeding crops (Annex IIA, point 6.6, Annex IIIA, point 8.5)

Open. Uptake expected and further investigation necessary to enable assessment according to the full residue definition for risk assessment

#### Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8)

1) Sum of tri-allate, TCPSA and TCPSA conjugates, expressed as tri-allate

| ADI | 0.025 mg/kg bw per day |
| TMDI (% ADI) according to national (to be specified) diets | n/a |
| IEDI (EFSA PRIMo) (% ADI) | Tentative: 27% (UK toddler) |
Factors included in IEDI

ARfD

Estimates based on levels in metabolism studies

IESTI (ESFA PRIMo) (% ARfD)

Tentative: 5.7% (potato – rotational crop)

Factors included in IESTI

Estimates based on levels in metabolism studies

ADI: acceptable daily intake; bw: body weight; TMDI: theoretical maximum daily intake; IEDI: international estimated daily intake; ARfD: acute reference dose; IESTI: international estimated short-term intake.

Additional consumer exposure via drinking water predicted for groundwater metabolite TCPSA (top three critical scenarios in bold)

| Concentration [µg/L](a) | Intakes via drinking water | [mg/kg bw per day] | [% ADI] |
|------------------------|----------------------------|--------------------|---------|
|                        | Adult | Toddler | Infant | Adult | Toddler | Infant |
| Châteaudun             | 6.301 | 0.000284 | 0.000851 | 0.001277 | 1.1 | 3.4 | 5.1 |
| Hamburg                | 19.690 | 0.000887 | 0.002660 | 0.003991 | 3.5 | 10.6 | 16.0 |
| Jokioinen              | 29.737 | 0.001339 | 0.004018 | 0.006027 | 5.4 | 16.1 | 24.1 |
| Kremsmünster           | 10.086 | 0.000454 | 0.001363 | 0.002044 | 1.8 | 5.5 | 8.2 |
| Okehampton             | 13.204 | 0.000595 | 0.001784 | 0.002676 | 2.4 | 7.1 | 10.7 |
| Piacenza               | 7.179 | 0.000323 | 0.000970 | 0.001455 | 1.3 | 3.9 | 5.8 |
| Porto                  | 5.041 | 0.000227 | 0.000681 | 0.001022 | 0.9 | 2.7 | 4.1 |
| Sevilla                | 3.170 | 0.000143 | 0.000428 | 0.000642 | 0.6 | 1.7 | 2.6 |

(a): Parent equivalents.

2) DIPA

Any data on the magnitude of residues of DIPA are not available in primary crops, rotational crops and matrices of animal origin.

|                |                |                |
|----------------|----------------|----------------|
| [mg/kg bw per day] | [ADI] | TMDI (% ADI) |
|                |                |                |
|                | 0.015          | Unable to assess without data on magnitude of residues in the relevant primary and rotational crops and in animal commodities |
| IEDI (EFSA PRIMo) (% ADI) | Unable to assess without data on magnitude of residues in the relevant primary and rotational crops and in animal commodities |
| Factors included in IEDI | n/a |
| ARfD | 0.15 mg/kg bw |
| IESTI (% ARfD) | Unable to assess without data on magnitude of residues in the relevant primary and rotational crops and in animal commodities |
| Factors included in IESTI | n/a |

ADI: acceptable daily intake; bw: body weight; TMDI: theoretical maximum daily intake; IEDI: international estimated daily intake; ARfD: acute reference dose; IESTI: international estimated short-term intake.
Additional consumer exposure via drinking water predicted for groundwater metabolite DIPA (top three critical scenarios in **bold**)

| Concentration [μg/L](a) | Intakes via drinking water [mg/kg bw per day] [% ADI] |
|--------------------------|-----------------------------------------------------|
|                          | Adult      | Toddler   | Infant   | Adult      | Toddler   | Infant   |
| Chateaudun 82.037         | 0.002735   | 0.008204  | 0.012306 | **18.2**   | **54.7**  | **82.0** |
| Hamburg 75.801            | 0.002527   | 0.007580  | 0.011370 | **16.8**   | **50.5**  | **75.8** |
| Jokioinen 83.015          | 0.002767   | 0.008302  | 0.012452 | **18.4**   | **55.3**  | **83.0** |
| Kremsmünster 56.147      | 0.001872   | 0.005615  | 0.008422 | 12.5       | 37.4      | 56.1     |
| Okehampton 55.456        | 0.001849   | 0.005546  | 0.008318 | 12.3       | 37.0      | 55.5     |
| Piacenza 65.374          | 0.002179   | 0.006537  | 0.009806 | 14.5       | 43.6      | 65.4     |
| Porto 20.169             | 0.000672   | 0.002017  | 0.003025 | 4.5        | 13.4      | 20.2     |
| Sevilla 33.101           | 0.001103   | 0.003310  | 0.004965 | 7.4        | 22.1      | 33.1     |

(a): Parent equivalents.

Fate and behaviour in the environment

Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)

- **Mineralisation after 100 days**:
  - 19.34–43.98% after 120 days at 20°C; [14C-allyl]-label (n = 4)
  - 17.36% after 120 days at 10°C; [14C-allyl]-label (n = 1)
  - 5.2–7.0% after 120 days at 20°C, [14C-isopropyl-2]-label (n = 3)
  - 2.3% after 120 days at 10°C, [14C-isopropyl-2]-label (n = 3)

- **Non-extractable residues after 100 days**:
  - 25.29–35.92% after 120 days at 20°C; [14C-allyl]-label (n = 4)
  - 19.47% after 120 days at 10°C; [14C-allyl]-label (n = 1)

| Metabolites requiring further consideration **‡** | TCPSA – 1.56–3.74% at 16–120 days at 20°C (n = 4) |
| - name and/or code, % of applied (range and maximum) | TCPSA – 3.04% at 64 days at 10°C (n = 1). [14C-allyl]-label |

**HPLC ANALYSIS**

- TCPSA – 2.82–7.38% at 4–120 days at 20°C (n = 4)
- TCPSA – 6.54% at 64 days at 10°C (n = 1). [14C-allyl]-label

**TLC ANALYSIS**

- TCPSA – 13.9–16.9% at 90–120 days at 20°C (n = 3)
- DIPA – 15.9% at 90 days at 10°C (n = 1) [14C-isopropyl-2]-label

HPLC: high-performance liquid chromatography; TLC: thin-layer chromatography.

(a): n corresponds to the number of soils.
Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

Laboratory studies

| Soil type                  | pH (CaCl₂) | t°C/50% MWHC | DT₅₀ / DT₉₀ (d) | DT₅₀ (days) 20°C pF2/10kPa | Method of calculation |
|----------------------------|------------|--------------|-----------------|--------------------------|----------------------|
| Speyer 2.2, Loamy Sand     | 5.5        | 20°C/50% MWHC| 111.7/371       | 111.7                    | 5.5                  |
| Spyer 5M, Sandy Loam       | 7.2        | 20°C/50% MWHC| 258.7/860       | 213.3                    | 6.3                  |
| Speyer 6S, Clay            | 7.1        | 20°C/50% MWHC| 267.6/889       | 171.8                    | 4.3                  |
| Geometric mean/median      |            |              | 160.0           | N/A                      | N/A                  |

Soil adsorption/desorption (Annex IIA, point 7.1.2)

| Soil type                  | OC % | Soil pH (CaCl₂) | Kₐ (mL/g) | Kₒc (mL/g) | Kᵥ (mL/g) | Kₒcᵥ (mL/g) | 1/n |
|----------------------------|------|-----------------|-----------|------------|-----------|-------------|-----|
| Speyer 2.2, Loamy Sand     | 1.93 | 5.5             | N/A       | N/A        | 0.11      | 5.7         | 0.769|
| Spyer 5M, Sandy Loam       | 1.27 | 7.2             | N/A       | N/A        | 0.18      | 14.1        | 0.863|
| Speyer 6S, Clay            | 1.66 | 7.1             | N/A       | N/A        | 1.00      | 60.2        | 0.948|
| Arithmetic mean/median      |      |                 |           |            | 0.43      | 26.7        | 0.860|
| pH dependence (yes or no)  |      |                 |           |            | No        |             |     |
PEC (ground water) (Annex IIIA, point 9.2.1)

Method of calculation and type of study (e.g. modelling, field leaching, lysimeter)

For FOCUSgw modelling, values used –

Modelling using FOCUS model(s), with appropriate FOCUSgw scenarios, according to FOCUS guidance
Model(s) used: PELMO 3.3.2, FOCUS PEARL 3.3.3
Scenarios (list of names): Châteaudun (C), Hamburg (H), Jokioinen (J), Kremsmünster (K), Okehampton (N), Piacenza (P), Porto (O), Sevilla (S), Thiva (T)
Crop: Winter Cereals
Tri-allate vapour pressure: 0.012 Pa at 20 °C
Tri-allate solubility in Water: 4.1 mg/L at 20 °C
Geometric mean tri-allate DT50lab: 106.2 days (normalised to 10 kPa or pF2, 20 °C with Q10 of 2.2)
Tri-allate KOC: arithmetic mean = 4,301 (Kom = 2,495), 1/n = 0.94
TCPSA vapour pressure: 0.00134 Pa at 20 °C
TCPSA aqueous solubility: 47,110 mg/L at 25 °C
Geometric mean TCPSA DT50lab: 16.9 days* (normalised to 10 kPa or pF2, 20 °C with Q10 of 2.2)
Formation fraction (from parent)= 0.3
TCPSA KOC: arithmetic mean = 2.6 (Kom = 1.51), 1/n = 1.01
TCPSA formation fraction: 30%
DIPA vapour pressure: 87.8 Pa at 20 °C
DIPA aqueous solubility: 110,000 mg/L (25 °C, Episuite)
Geometric mean DIPA DT50lab: 160 days (study performed at reference temperature and field capacity).
Formation fraction (from parent)= 0.66
DIPA KOC: arithmetic mean = 26.7 (Kom = 15.5), 1/n = 0.861
DIPA formation fraction: 66%
Plant uptake = 0 for parent tri-allate and the two metabolites

Application rate

Application rate: 2,250 g tri-allate/ha
No. of applications: 1
Time of application (month or season): 1 week prior to emergence (winter)

FOCUS: Forum for the Co-ordination of Pesticide Fate Models and their Use; DT50: period required for 50% dissipation; KOC: organic-carbon partition coefficient; Kom: partition coefficient normalized to organic matter.
PEC(gw) – FOCUS modelling results (80th percentile annual average concentration at 1 m)

| Scenario               | Tri-allate (µg/L) | Metabolite (µg/L) |
|------------------------|-------------------|-------------------|
|                        |                   | TCPSA  | DIPA  |
| PELMO 3.3.2/Winter cereals |                   |        |       |
| Chateaudun             | < 0.001           | 0.854  | 4.164 |
| Hamburg                | < 0.001           | 3.677  | 4.809 |
| Jokioinen              | < 0.001           | 8.503  | 7.291 |
| Kremsmunster           | < 0.001           | 1.194  | 3.758 |
| Okehampton             | < 0.001           | 3.715  | 6.121 |
| Piacenza               | < 0.001           | 1.246  | 2.847 |
| Porto                  | < 0.001           | 3.133  | 3.281 |
| Sevilla                | < 0.001           | 0.412  | 0.679 |
| Thiva                  | < 0.001           | 0.502  | 3.192 |
|                        |                   |        |       |
| PEARL 3.3.3/Winter cereals |                   |        |       |
| Chateaudun             | < 0.001           | 6.301  | 82.037|
| Hamburg                | < 0.001           | 19.690 | 75.801|
| Jokioinen              | < 0.001           | 29.737 | 83.015|
| Kremsmunster           | < 0.001           | 10.086 | 56.147|
| Okehampton             | < 0.001           | 13.204 | 55.456|
| Piacenza               | < 0.001           | 7.179  | 65.374|
| Porto                  | < 0.001           | 5.041  | 20.169|
| Sevilla                | < 0.001           | 3.170  | 33.101|
| Thiva                  | < 0.001           | 3.741  | 66.061|
### Summary of representative uses evaluated (tri-allate)

| Crop and/or situation<sup>(a)</sup> | Member state or Country | Product name | F G or I<sup>(b)</sup> | Pests or group of pests controlled<sup>(c)</sup> | Preparation Type<sup>(d), (e), (f)</sup> | Conc. of as<sup>(i)</sup> | Application Method kind<sup>(g), (h)</sup> | Growth stage & season<sup>(i)</sup> | Number min/ max<sup>(k)</sup> | Interval between applications (min) | g as/hL min/ max<sup>(l)</sup> | Water L/ha min/ max | kg as/ha min/ max<sup>(m)</sup> | PHI (days)<sup>(n)</sup> | Remarks |
|-----------------------------------|--------------------------|--------------|------------------------|----------------------------------------|---------------------------------|-----------------|---------------------------------|---------------------------------|-----------------|------------------|----------------|----------------|----------------|----------------|---------|---------|
| Cereals (barley and wheat)        | Northern Europe          | Avadex 15G   | F                      | Weeds                                  | GR                              | 150 g/kg        | Broad-cast application          | Post-sowing, pre-emergence of crop | 1               | nr               | nr             | 2.25           | nr             | Commercial harvest |

(a): For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure).
(b): Outdoor or field use (F), greenhouse application (G) or indoor application (I).
(c): e.g. biting and sucking insects, soil born insects, foliar fungi, weeds.
(d): e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR).
(e): GCPF Codes – GIFAP Technical Monograph No 2, 1989.
(f): All abbreviations used must be explained.
(g): Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench.
(h): Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plant type of equipment used must be indicated.
(i): g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypry). In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalcarb-isopropyl).
(j): Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application.
(k): Indicate the minimum and maximum number of application possible under practical conditions of use.
(l): The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200,000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha.
(m): PHI – minimum preharvest interval.
### Appendix B – Used compound codes

| Code/trivial name<sup>a</sup> | IUPAC name/SMILES notation/InChiKey<sup>b</sup> | Structural formula<sup>c</sup> |
|-------------------------------|--------------------------------------------------|----------------------------------|
| **tri-allate**                | S-2,3,3-trichloroallyl diisopropyl(thiocarbamate) | ![Structural formula for tri-allate](image) |
|                               | C/(C)(-C=C)CSC(-O)N(C(C)C)(C)(C)                 |                                   |
|                               | MWBPRDONLNCVCFOU-UHFFFAOYSA-N                   |                                   |
| **TCPSA**                     | 2,3,3-trichloro-2-propene-1-sulfonic acid        | ![Structural formula for TCPSA](image) |
|                               | C/(C)(-C=C)CSC(-O)(-O)O                          |                                   |
|                               | GLDBPELSAPAUAFU-UHFFFAOYSA-N                    |                                   |
| **M1**                        | 2,3,3-trichloro-2-propene-1-sulfinic acid        | ![Structural formula for M1](image) |
|                               | C/(C)(-C=C)CSC(-O)O                             |                                   |
|                               | GDWCRDROPERPR-UHFFFAOYSA-N                     |                                   |
| **M14**                       | (1ξ)-1,5-anhydro-6-O-oxalo-1-[[2,3,3-trichloro-2-propen-1-yl] sulfanyl]-D-glucitol | ![Structural formula for M14](image) |
|                               | O[C@@H][C@@H](O)[C@@H](O)[C@@H](O)[C@@H](O)COC(-O)(-O)OCC(-O)Cl(-O)ClCl |                                   |
|                               | NHIPHHKIVGFCEE-VVANYLSESA-N                    |                                   |
| **M15**                       | (1ξ)-1,5-anhydro-6-O-oxalo-1-[[2,3,3-trichloro-2-propen-1-yl] sulfanyl]-D-glucitol | ![Structural formula for M15](image) |
|                               | O[C@@H][C@@H](O)[C@@H](O)[C@@H](O)COC(-O)(-O)OCC(-O)Cl(-O)ClCl |                                   |
|                               | GHXNBNSPLKRSAX-PQIUPZKKSA-N                    |                                   |
| **DIPA**                      | N-isopropyl-2-propanamine                       | ![Structural formula for DIPA](image) |
|                               | CC(C)NC(C)C                                   |                                   |
|                               | UAOMVDZISHZME-UHFFFAOYSA-N                     |                                   |
| **N-nitroso-diisopropylamine**| N,N-diisopropynitrous amide                    | ![Structural formula for N-nitroso-diisopropylamine](image) |
|                               | CC(C)NC(N-0)(C)C                              |                                   |
|                               | AUIJKTGFPLMFUP-UHFFFAOYSA-N                    |                                   |

<sup>a</sup> The metabolite name in bold is the name used in the conclusion.

<sup>b</sup> ACD/Name 2017.2.1 ACD/Labs 2017 Release (File version N40E41, Build 96719, 6 September 2017).

<sup>c</sup> ACD/ChemSketch 2017.2.1 ACD/Labs 2017 Release (File version C40H41, Build 99535, 14 February 2018).