CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion regarding the peer review of the pesticide risk assessment of the active substance tri-allate

Issued on 26 September 2008

SUMMARY

Tri-allate is one of the 84 substances of the third stage Part B of the review programme covered by Commission Regulation (EC) No 1490/2002[1]. This Regulation requires the European Food Safety Authority (EFSA) to organise upon request of the EU-Commission a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within six months a conclusion on the risk assessment to the EU-Commission.

The United Kingdom being the designated rapporteur Member State submitted the DAR on tri-allate in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 6 August 2007. The peer review was initiated on 4 October 2007 by dispatching the DAR for consultation of the Member States and the sole applicant Gowan Comércio Internacional e Servicos. Subsequently, the comments received on the DAR were examined and responded by the rapporteur Member State in the reporting table. This table was evaluated by the EFSA to identify the remaining issues. The identified issues as well as further information made available by the applicant upon request were evaluated in a series of scientific meetings with Member State experts in May – June 2008.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in July – August 2008 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative uses as a herbicide in barley and wheat for the control of wild oat, black-grass and meadow-grass as proposed by the applicant. Full details of the GAP can be found in the attached endpoints.

The representative formulated product for the evaluation was 'Avadex 15G' ('Mon 7966'), a granule (GR) containing 150 g/kg tri-allate.

[1] OJ No L 224, 21.08.2002, p. 25, as amended by Regulation (EC) No 1095/2007 (OJ L 246, 21.9.2007, p. 19)

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that at least some quality control measurements of the plant protection product are possible. Adequate methods are available to monitor residues given in the respective residue definition in food/feed of plant origin and in environmental matrices, however a data gap was set for a monitoring method for residues in food of animal origin.

In the mammalian metabolism studies, tri-allate was rapidly but incompletely absorbed after oral administration. It was evenly distributed and extensively metabolised, showing no potential for accumulation. According to the precautionary principle, classification of tri-allate as **Xn**, **R22** "**Harmful if swallowed**" was proposed, however acute dermal and inhalation toxicity were low. Tri-allate was not a skin or eye irritant; classification with risk phrase **R43** "**May cause sensitisation by skin contact**" was proposed according to the results of a Magnusson & Kligman test.

Decreased body weight and clinical signs of neurotoxicity were the most common effects found in rats, dogs and hamsters upon short-term administration. Reversible anaemia and liver toxicity were also found in these species, while the liver was the main target organ in mice. Upon long-term exposure, reduced body weight and liver toxicity were still evident, but no potential for carcinogenicity was observed in rat, mouse or hamster.

Although some *in vitro* tests (mainly Ames tests and a Sister Chromatid Exchange Assay) gave positive results, based on the weight of evidence, tri-allate was considered to have no genotoxic potential *in vivo*.

Reproduction toxicity studies reflected the same kind of effects in parents, as in short-term studies. In the two generation study, reduced pregnancy rate was associated with parental toxicity and in the developmental study in rat; decreased foetal weight and retarded ossification were linked to maternal toxicity. In rabbit an apparent increase in the incidence of fused sternebrae was observed without maternal toxicity, this finding gave rise to an intense debate by the experts, but considering the low severity of the effect, the meeting agreed not to propose a classification related to developmental toxicity for tri-allate.

No sign indicative of delayed neurotoxicity was found in acute and short-term neurotoxicity studies in hen. Clear signs of neurobehavioural toxicity were seen in an acute and a short-term neurotoxicity studies in rat. No inhibition of cholinesterase activity was detected, but a special investigation showed a strong correlation between the presence of axonal degeneration in the brain and CNS-like behavioural effects caused by tri-allate leading to a proposal for classification with **Xn**, **R48/22** "**Harmful: danger of serious damage to health by prolonged exposure if swallowed**".

A data package of studies was provided on the metabolite TCPSA[2], a major metabolite in plant and the environment, leading to the conclusion that TCPSA is not relevant for groundwater and that the Acceptable Daily Intake (ADI) of tri-allate covers the toxicity of the metabolite.

The **ADI of tri-allate was 0.025 mg/kg bw/day** based on the 2-year rat study and applying a safety factor of 100; the **Acceptable Operator Exposure Level (AOEL) was 0.032 mg/kg bw/day** based on the 90-day neurotoxicity study in rat, a safety factor of 100 and a correction factor for low oral absorption of 50 %; and the **Acute Reference Dose (ARfD) was 0.6 mg/kg bw** based on the acute neurotoxicity study in rat and applying a safety factor of 100. Dermal absorption was 12 % for the concentrate and in-use spray dilution, based on an *in vivo* study in monkeys. The level of operator exposure calculated for the representative formulation 'Avadex 15G', at a maximum dose rate of 2.25 kg tri-allate/ha was below the AOEL according to selected data from the Pesticide Handler's Exposure Database (PHED), considering the use of gloves during loading and application of the granules. Worker exposure was not considered relevant for the representative use of tri-allate. Estimated bystander and residential exposure resulting from the use of 'Avadex 15G' was below the AOEL.

Metabolism studies of tri-allate labelled in the allyl position were considered in the DAR which showed that residues consisted primarily of metabolites TCPSA, M14[3] and M15[4]. A provisional residue definition for risk assessment of tri-allate, TCPSA and the glycoside conjugates (M14 and M15) expressed as tri-allate was proposed by the residues expert meeting. The residue definition proposed in the DAR did not include the glycoside conjugates. In addition, the expert meeting concluded the metabolism could not be finalised because there is a data gap for a wheat study of tri-allate labelled in the diisopropylamine moiety. The meeting identified this data gap to address a concern about the potential formation of nitrosamines from the diisopropylamine moiety in plants. It should be noted that in wheat grain, total metabolites were 0.008 mg/kg (5.10 % of TRR).

In radio-labelled rotational crop studies the residue was made up of tri-allate and TCPSA but it was questioned why M14 and M15 were not looked for. In addition, it was considered that, on the basis of the residue levels in radish roots (at 30 days after application) in these studies, a data gap should be identified for field studies. The primary crop residue trials data in wheat and barley presented analysis for tri-allate and TCPSA. No accurate conversion factor is available to enable levels of glycoside conjugates to be accounted for.

Residues were seen to be stable in frozen storage for up to 56 months. The need for processing studies is not currently triggered. Intakes by livestock triggered the need for animal metabolism data

[2] TCPSA: 2,3,3-trichloroprop-2-ene-sulfonic acid
[3] M14: 6-*O*-(carboxycarbonyl)-1-deoxy-1-[(2,3,3-trichloro-2-propenyl)-sulfinyl]-D-glucopyranoside
[4] M15: 6-*O*-(carboxycarbonyl)-1-deoxy-1-[(2,3,3-trichloro-2-propenyl)-sulfonyl]-D-glucopyranoside

for ruminants. A goat metabolism study showed the majority of radioactivity was incorporated into natural compounds. The only possible compounds of significance were tri-allate and TCPSA, and the feeding studies confirmed this.

The risk assessment could not be finalised because of the inclusion of 'glycoside conjugates' in the residue definition. Additionally, the theoretical concern over the formation of nitrosamines has resulted in a data gap for a wheat metabolism study. On this basis no maximum residue levels (MRL) were proposed by the expert meeting.

The risk assessment can not be finalised because of the rotational crop issue amongst others.

Only studies with tri-allate labelled in the allylic position are available in the fate and behaviour section. The need for addressing the metabolites that may result from the diisopropylamine moiety was identified during the peer review and discussed in the PRAPeR meeting. The applicant provided a position paper to clarify this issue. This position paper made use of public scientific literature to select the input parameters for modelling and as part of the consideration for estimating the formation of nitrosamines potentially produced by water treatment. These scientific papers had not been previously submitted in the dossier. In view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to the EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, the new studies could not be considered in the peer review. However the meeting considered that the issue needs to be addressed and therefore identified a data gap to address the potential formation of diisopropylamine[5] in soil and contamination of ground water.

Tri-allate exhibited moderate to medium persistence in soil under dark aerobic conditions at 20 °C ($DissT_{50}$ = 35 – 61 d); however these rates may only be considered as dissipation rates since volatilization contributed to a great extent to the losses observed. Data were reanalyzed by the applicant with ModelMaker (V.4.0.) to separate the degradation and volatilization processes. The calculated degradation rates were in the range of DT_{50} = 38.4 – 75.2 d.

Of the six or seven minor metabolites identified, only TCPSA (max. 3.74 % AR by HPLC and max. 7.38 % AR by TLC) was fully characterized and further addressed for environmental risk assessment. TCPSA exhibited low to moderate persistence under dark aerobic conditions at 20 °C in soil.

Volatiles collected in the organic traps (max. 16.17 % AR after 120 d) of the aerobic degradation experiments were not characterized but were assumed to be tri-allate. Unextractable radioactivity amounted to max. 25.3 % AR at the end of the study (120 days after treatment). Radioactivity found in the ethanolamine trap (max. 21.2 % AR after 120 d) was assumed to be CO_2. The need for further

[5] Diisopropylamine: *N*-(propan-2-yl)propan-2-amine

identification of potentially volatile tri-allate soil metabolites and the characterization of soil metabolites found in the available study had been identified during the peer review. The majority of experts agreed with the rapporteur Member State that it is reasonable to assume that the non-characterised radioactivity in the volatile traps is the active substance. The EU risk assessment of the representative use proposed could therefore be acceptably concluded without further regard to the characterisation of the volatiles. However some experts considered that it is necessary to confirm the complete route of degradation for national risk assessments and therefore a data gap was identified for a study to investigate the aerobic degradation in soil including identification of residues in volatile organic traps and adequate identification of soil metabolites.

Tri-allate was very highly persistent in soil under anaerobic conditions at 20 °C. Photolysis in soil of tri-allate is almost negligible when compared with aerobic degradation. A field dissipation study with trials at four different United Kingdom sites is available. Tri-allate exhibited low to high persistence in these trials. The rapporteur Member State assessed the studies as scientifically valid and representative of Northern European conditions. However they proposed using data obtained from laboratory degradation studies for environmental modelling for EU risk assessment due to the potential effect of volatilization on the results of these trials. The DT_{90}'s observed in some of the field dissipation studies were above 1 yr and triggered the need to assess potential of accumulation of tri-allate in soil. PEC in soil and accumulation of tri-allate in soil were estimated on the basis of the worst case field half-life of 205 d. For TCPSA the PEC in soil was estimated on basis of the maximum observed in the laboratory studies determined by TLC. Tri-allate may be considered immobile to slightly mobile in soil according the available study. Metabolite TCPSA may be considered very highly mobile in soil according to the available study.

Tri-allate was stable to hydrolysis at pH 4 and 7 at 50 °C, however it hydrolyses under alkaline conditions. The half-life at 25 °C in the aqueous pH 9 solution was 52 d. Aqueous photolysis is not expected to contribute to the environmental degradation of tri-allate on basis of the lack of UV absorption at wavelengths above 290 nm. Biodegradability studies available show that tri-allate is not readily biodegradable.

In the water sediment systems, tri-allate dissipated relatively rapidly from water by partition to the sediment and volatilization. Half-lives of tri-allate in the whole system are 52.8 – 62.0 d. No major metabolites were identified either in the water or in the sediment phases. Mineralization and unextractable residues in the sediment are practically negligible (CO_2 = 1.51 – 4.35 % AR; unextractable in sediment = 2.77 – 3.26 % AR).

$PEC_{SW/SED}$ were calculated for tri-allate and its soil metabolite TCPSA on the basis of the FOCUS SW scheme and models for the scenarios relevant to cereals in Northern EU (D1-D5, R1). Since the product is a granular formulation, the applicant proposed spray drift values for the granules based on

a specific study. The approach was considered acceptable by the rapporteur Member State and reported as Step 3 calculations. Additional FOCUS Step 4 calculations included spray drift mitigation by buffer zones and run off mitigation by vegetative buffer strips. The method used to implement runoff mitigation is not agreed in the latest FOCUS Landscape and mitigation guidance document and therefore the rapporteur Member State recalculated the Step 4 FOCUS SW without run off mitigation.

Potential ground water contamination by tri-allate and its soil metabolite TCPSA was addressed by modelling calculations with FOCUS PELMO 3.3.2. The rapporteur Member State calculations resulted in 80th percentile annual average concentrations in the leachate at 1 m depth below 0.001 µg/L for tri-allate and in the range of 0.76 – 15.42 µg/L for metabolite TCPSA. The metabolite TCPSA has a clear potential to exceed the trigger of 0.1 µg/L in ground water and requires assessment of its toxicological and ecotoxicological relevance including consumers risk assessment. Relevance of TCPSA was assessed during the peer review following the step-wise procedure set out in the guidance document for relevance of metabolites in ground water (see sections 2.8, 3.3 and 5.2). Tri-allate is a volatile organic compound and studies available indicate that tri-allate displays significant volatilisation from soil surfaces. However on the basis of the atmospheric half-life calculated (DT_{50} = 3.8 h), it is considered unlikely that tri-allate may be subjected to long-range transport.

The first tier risk assessment for direct consumption of granules results in values above the trigger values, indicating low acute, short-term and long-term risk for small seed-eating birds and mammals. The risk to grazing birds and mammals from consumption of residues of tri-allate in the young cereal shoots was estimated using the residues data presented in the DAR. The acute, short-term and long-term TER estimated for birds and the acute and long-term TER values estimated for mammals were above the Annex VI trigger values, indicating a low risk for birds and mammals.

Potential for bioaccumulation was considered since tri-allate has a log P_{ow} of 4.06. The first tier TER values estimated for earthworm-eating birds was above the Annex VI trigger value, however the TER value for earthworm-eating mammals was below the Annex VI trigger value. After a refinement process the risk to earthworm-eating mammals was considered as low. The first tier TER values for fish-eating birds and mammals were 7 and 1.9, respectively, indicating a low risk for fish-eating birds. A potential high risk for fish-eating mammals was identified. A data gap was identified by the EFSA after the PRAPeR 48 meeting to ask to the applicant to submit a new refinement of the potential high risk for fish-eating mammals.

Based on the available studies, tri-allate was considered very toxic to aquatic organisms. The acute and chronic TER values based on the used of PEC_{SW} from FOCUS step 4 with a 10 m non spray buffer zone were above the Annex VI trigger values. Risk mitigation measures similar to 10 m non spray buffer zone are needed in Member States. The risk of the TCPSA metabolite for aquatic

organisms is low.

Since tri-allate has a log P_{ow} of 4.06 the potential for bioconcentration should be considered. The BCF = 1400 was derived from a study with *Lepomis macrochirus.* The EFSA noted after the meeting that tri-allate has a BCF >1000 and a field soil DT_{90} >100 days. For these reasons the EFSA identified a data gap to assess the potential for biomagnification of tri-allate through aquatic food chains.

A low acute risk was identified for earthworms. The long-term risk to earthworms needs further refinement. It is proposed by the rapporteur Member State in the DAR that further information is required on the long-term risk to earthworms. Further information is required to fully address the potential risk of tri-allate to other non-target macro-organisms. A data gap was proposed for the submission of a litter bag study.

Risk mitigation such as an in-field no spray buffer zone of 10 m was considered necessary for the non-target plants.

The risk was considered to be low to bees, non-target arthropods, soil non-target micro-organisms and biological methods of sewage treatment.

Key words: tri-allate, peer review, risk assessment, pesticide, herbicide

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BACKGROUND

Commission Regulation (EC) No 1490/2002 laying down the detailed rules for the implementation of the third stage of the work program referred to in Article 8(2) of Council Directive 91/414/EEC and amending Regulation (EC) No 451/2000 as amended by Commission Regulation (EC) No 1095/2007, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Tri-allate is one of the 84 substances of the third stage, part B, covered by the Regulation (EC) No 1490/2002 designating the United Kingdom as rapporteur Member State.

In accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, the United Kingdom submitted the report of its initial evaluation of the dossier on tri-allate, hereafter referred to as the draft assessment report, received by the EFSA on 6 August 2007. Following an administrative evaluation, the draft assessment report was distributed for consultation in accordance with Article 11(2) of the Regulation (EC) No 1490/2002 on 19 November 2007 to the Member States and on 4 October 2007 to the main applicant Gowan Comércio Internacional e Servicos as identified by the rapporteur Member State.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, the EFSA identified and agreed on lacking information to be addressed by the applicant as well as issues for further detailed discussion at expert level.

Taking into account the requested information received from the applicant, a scientific discussion took place in expert meetings in May – June 2008. The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in July – August 2008 leading to the conclusions as laid down in this report.

During the peer review of the draft assessment report and the consultation of technical experts no critical issues were identified for consultation of the Scientific Panel on Plant Protection Products and their Residues (PPR).

In accordance with Article 11c(1) of the amended Regulation (EC) No 1490/2002, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period provided for by the same Article. A list of the relevant endpoints for the active substance as well as the formulation is provided in appendix 1.

The documentation developed during the peer review was compiled as a **peer review report** comprising of the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State's draft assessment report:

- the comments received,
- the resulting reporting table (revision 1-1, 6 March 2008)

as well as the documents summarising the follow-up of the issues identified as finalised at the end of the commenting period:

- the reports of the scientific expert consultation,
- the evaluation table (revision 2-1, 16 September 2008).

Given the importance of the draft assessment report including its addendum (compiled version of July 2008 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

By the time of the presentation of this conclusion to the EU-Commission, the rapporteur Member State has made available amended parts of the draft assessment report which take into account mostly editorial changes. Since these revised documents still contain confidential information, the documents cannot be made publicly available. However, the information given can be found in the original draft assessment report together with the peer review report, both of which are publicly available.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Tri-allate is the ISO common name for *S*-2,3,3-trichloroallyl di-isopropyl(thiocarbamate) (IUPAC).

Tri-allate belongs to the class of thiocarbamate herbicides. Tri-allate is a selective herbicide, it acts through inhibition of the fatty acid and lipid biosynthesis and also the isoprenoid (i.e. gibberellic acid), flavenoid and kaurene biosynthesis (i.e. anthocyanins). Tri-allate is used for the control of wild oats, black-grass and meadow-grass in summer/winter barley and summer/winter wheat.

The representative formulated product for the evaluation was 'Avadex 15G' ('Mon 7966'), a granule (GR) containing 150 g/kg tri-allate, registered under different trade names in Europe.

The representative uses evaluated comprise post sowing and pre-emerge applications with tractor mounted ground applicator to control wild oats, black-grass and meadow-grass in summer and winter barley and wheat, in Northern Europe at a single application at a maximum rate of 2.25 kg a.s./ha.

SPECIFIC CONCLUSIONS OF THE EVALUATION

1. Identity, physical/chemical/technical properties and methods of analysis

The minimum purity of tri-allate is 940 g/kg. There are no FAO specifications.

The data initially submitted by the applicant were not supportive of the technical specification. An updated technical specification was provided with the impurities well below 0.1% deleted from the specification. The updated specification has been evaluated in an addendum to vol. 4 (April 2008) and accepted by the experts at PRAPeR Meeting 46 (May 2008).

As the formation of the potentially highly toxic NDIPA[6] during the manufacturing process is unlikely, but not excluded, it was considered a relevant impurity by the experts at PRAPeR Meeting 49 (June 2008). However, NDIPA was not found in the five batches for the source under consideration, but was specified at a level of 1 mg/kg, and considering that no toxicological information is available on this compound, the experts at PRAPeR Meeting 49 (June 2008) proposed to set a maximum value for this impurity at the level of 0.02 mg/kg. The analytical method (GC-NPD) submitted in the dossier for the determination of NDIPA was not evaluated by the rapporteur Member State and not peer reviewed, however it was considered acceptable by the EFSA and has an LOQ of 0.015 mg/kg.

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of tri-allate or the respective formulation, however the following data gaps were identified:
- information on the purity of one of the starting materials for the production of the technical material
- information on the level of ethoxylation for the stabilizer
- Spectra for NDIPA
- Possible increase of impurity NDIPA during storage and/or the formulation of the PPP to be addressed
- Analytical method for NDIPA in the formulation.

The main data regarding the identity of tri-allate and its physical and chemical properties are given in appendix 1.

Adequate analytical methods are available for the determination of tri-allate in the technical material and in the representative formulation (GC-FID), as well as for the determination of the respective impurities in the technical material (GC-MS, GC-NPD), however a data gap has been identified for an

[6] NDIPA: *N*-nitroso-*N*-(propan-2-yl)propan-2-amine

analytical method for the determination of the additive in the technical material (PRAPeR Meeting 46; May 2008).

Adequate methods are available to monitor all compounds in the respective residue definitions in food/feed of plant origin and environmental matrices. An analytical method for food of animal origin is required as experts at PRAPeR meeting 50 set the residue definition for monitoring for food of animal origin as tri-allate and TCPSA expressed as tri-allate.

Residues of tri-allate in plant matrices can be monitored with an analytical method based on the multi-method DFG S19, by GC-MS with LOQ of 0.01 mg/kg (cereal grain) and LOQ of 0.02 mg/kg (barley and wheat straw).

An adequate GC-MS method is available to monitor residues of tri-allate in soil with LOQ of 0.01 mg/kg. It should be mentioned that an HPLC-MS/MS method is also available for the monitoring of the metabolite TCPSA[7] in plant matrices with LOQ of 0.01 mg/kg (cereal grain) and in soil with LOQ of 0.005 mg/kg.

Tri-allate residues in water can be monitored with GC-MS with LOQ of 0.05 µg/L and TCPSA residues with HPLC-MS/MS with LOQ of 0.1 µg/L.

Adequate GC-MS method is available to monitor residues of tri-allate in air with LOQ of 1.83 µg/m³.

Tri-allate is not classified as toxic or highly toxic and therefore analytical methods for the determination of residues in human and animal tissues and fluids are not required

2. Mammalian toxicology

Tri-allate was discussed at the PRAPeR Experts' Meeting on mammalian toxicology (PRAPeR 49) in June 2008.

No analysis of the impurity profile of the batches used in the toxicological studies is available. The meeting agreed to set a data gap for this information. The meeting also agreed that NDIPA is a relevant impurity and its maximum level should be 0.02 mg/kg in the technical specification.

2.1. Absorption, Distribution, Excretion and Metabolism (Toxicokinetics)

Absorption, distribution, metabolism and excretion of tri-allate were investigated in rat (single and multiple oral doses) and in monkey (dermal and intramuscular administration); further experiments

[7] TCPSA: 2,3,3-trichloroprop-2-ene-sulfonic acid

with tri-allate metabolites were conducted *in vitro* and *in vivo* in rat to confirm the proposed metabolic pathway.

Tri-allate was rapidly absorbed after oral dosing; as a biliary cannulation study was not performed, 50 % oral absorption was considered based on urine excretion, expired air, carcass and cage wash observed in rat after 10 days. Once absorbed, tri-allate was evenly distributed and extensively metabolised with no tri-allate being recovered from urine and only up to 8 % of the administered dose in faeces. Oxidation of the sulphur group was the major pathway, leading to the major and most common metabolite M1[8], which was further oxidized to TCPSA; TCPSA accounted for about 6 % of the applied dose in urine and faeces of rats and up to 17.6 % in monkey urine.

Two metabolites, M14[9] and M15[10] were identified in plants, but not in rat metabolism studies. These metabolites resulted from further conjugation with carbohydrates such as oxalic acid. The fate of plant glycosides in mammals consists of hydrolysis which may already take place in the gastrointestinal tract, resulting in the generation of M1 and TCPSA respectively. Therefore the toxicity of these metabolites was addressed by the studies conducted with tri-allate and TCPSA respectively.

Tri-allate was rapidly and almost completely eliminated after 10 days; the remaining (2 %) of the radioactivity was bound to haemoglobin in the cellular fraction of the blood and in the highly perfused organs, indicating no potential for bioaccumulation.

2.2. ACUTE TOXICITY

Two acute oral toxicity studies were submitted with the same strain of rat, resulting in conflicting outcomes: the LD_{50} of the older study was 1100 mg/kg bw while the LD_{50} of the more recent study was 3455 mg/kg bw. Additional information was considered from preliminary studies for genotoxicity studies and following a precautionary principle, classification as **Xn** "**Harmful**", and risk phrase **R22** "**Harmful if swallowed**" was proposed. Low toxicity was observed upon dermal and inhalation administrations; tri-allate was not irritant to skin and eyes. Although no sensitization reactions were found in a Buehler test with 9 induction treatment, a 95 % sensitization rate was found in a Magnusson & Kligman test, therefore classification with **R43** "**May cause sensitisation by skin contact**" was also proposed.

[8] M1: 2,3,3-trichloroprop-2-ene-sulfinic acid
[9] M14 : 6-*O*-(carboxycarbonyl)-1-deoxy-1-[(2,3,3-trichloro-2-propenyl)-sulfinyl]-D-glucopyranoside
[10] M15 : 6-*O*-(carboxycarbonyl)-1-deoxy-1-[(2,3,3-trichloro-2-propenyl)-sulfonyl]-D-glucopyranoside

2.3. SHORT-TERM TOXICITY

The oral short-term effects of tri-allate were investigated in a 1-month feeding study in rat and hamster, in an 8-week study in mouse (liver cell proliferation study) and dog (by capsule), a 90-day feeding study in rat, mouse and hamster and a 1-year capsule study in dog; additionally, two older studies on dogs (2-year and 90-day) were only used as corroborative evidence of validated studies. Other routes were tested in two 21-day dermal toxicity studies with rats and rabbits and one 7-week inhalation toxicity study in rat.

The most sensitive finding upon short-term administration of tri-allate was reduction in body weight and body weight gain in rats, mice dogs and hamster. Clinical signs of neurotoxicity were noted in dog at 72 mg/kg bw/day, rat at 130 mg/kg bw/day and hamster at higher doses, but not in mouse.

Tri-allate caused reversible anaemia in dog at 15 mg/kg bw/day, in rat at higher doses and in hamster, mostly accompanied by increased reticulocytes count and sometimes by haematopoiesis in the spleen. In male rats, tri-allate caused alpha$_{2u}$-globulin deposition which resulted in increased nephropathy of the kidneys; this finding was considered to be specific to male rat and consequently not relevant for humans. Liver toxicity was found in all species; induction of peroxisome proliferation was shown in mouse hepatocytes from the dose of 46 mg/kg bw/day, as well as induction of CYP 450 enzyme activity (≥100 mg/kg bw/day) but without increased liver cell proliferation.

The relevant oral NOAELs were the dose levels of 2.5 mg/kg bw/day in dog from the 1-year study, 11.5 mg/kg bw/day in mouse, 12 mg/kg bw/day from the 8-week dog study and 43.2 mg/kg bw/day in hamster. In the 90-day feeding study in rat, the NOAEL was 6.71 mg/kg bw/day but this was superseded by the 90-day neurotoxicity study in rat (see point 2.7). When applied dermally to rabbits, tri-allate caused mortality and increased reticulocytes count at 1500 mg/kg bw/day; the systemic NOAEL was the dose level of 300 mg/kg bw/day; as expected from a sensitising substance, local skin irritation was noted at all dose levels (from 60 mg/kg bw/day and above). The NOAEL in the 7-week inhalation study was 0.03 mg/L air equivalent to approximately 10.4 mg/kg bw/day based on reduced body weight at the next dose level of 0.1 mg/L air (34.6 mg/kg bw/day), considering that the increased incidence of nephropathy in the kidney of male rats was due to alpha$_{2u}$-globulin deposition and therefore not relevant for humans.

2.4. GENOTOXICITY

Tri-allate was found to be mutagenic in three Ames tests. A positive response was also obtained in a Sister Chromatid Exchange assay on Chinese Hamster Ovary (CHO) cells in the presence and absence of metabolic activation. In the other four *in vitro* studies: gene mutation assay on HPRT locus in CHO cells; mouse lymphoma assay in L5178Y cells; and unscheduled DNA synthesis (UDS) in both mouse and in rat hepatocytes, no mutagenic, genotoxic or clastogenic effects were observed.

Tri-allate was assessed *in vivo* for the induction of cytogenetic effects in bone marrow of rat and mouse and DNA-damage in a UDS test using mouse hepatocytes. No chromosome aberration, chromosomal damage, damage to the mitotic apparatus in the erythroblasts or DNA damage in mouse liver cells was observed. This was supported by a cytogenetic test in bone marrow cells of the Syrian golden hamster after application of tri-allate for up to 13 weeks via the diet.

Based on the weight of evidence, it was agreed that tri-allate has no genotoxic potential *in vivo*.

2.5. LONG-TERM TOXICITY

Long-term toxicity of tri-allate was examined in a two-year study in rat and mouse, and a 75-95 weeks study in hamster. An older 2-year rat study was not accepted by the rapporteur Member State due to lack of validation and limited haematological and clinical parameters investigated.

In the rat study, the NOAEL was the dose level of 2.5 mg/kg bw/day based on decreased body weight, increased mortality, increased incidence of testicular atrophy and increased severity in chronic progressive nephropathy in males at the dose level of 13 mg/kg bw/day; the latter observation was considered to be most likely due to alpha$_{2u}$-globulin accumulation. Testicular atrophy and aspermatogenesis were consistently observed in debilitated or dying animals and were not reproduced in the reproduction toxicity studies, therefore the experts agreed that the finding was derived from systemic toxicity and not treatment related.

In mouse, the NOAEL was the dose level of 12.4 mg/kg bw/day based on clinical chemistry changes suggestive of liver toxicity, increased liver weight, eosinophilic foci in the liver, mineralisation in brain and cornea of the eyes, and degeneration of the spinal cord at the top dose of 37.5 mg/kg bw/day.

The NOAEL in the chronic toxicity and carcinogenicity study in hamster was 16.2 mg/kg bw/day, based on reduction in body weight gain and food consumption, clinical chemistry changes suggestive of liver toxicity, reduction in spleen weight, extramedullary haematopoiesis, and flaking/scaly skin observed at the top dose of 110 mg/kg bw/day.

No evidence of treatment-related oncogenicity was found in either rats, mice or hamsters.

2.6. REPRODUCTIVE TOXICITY

Reproductive toxicity of tri-allate was tested in a two-generation reproduction toxicity study in rat and a developmental toxicity study in rat and in rabbit.

Reproduction toxicity

Main effects observed in the two-generation study were reduced body weight during lactation in F_0 and F_1 dams, and reduced pup birth weight and pre-weaning weights at the top dose of 30.7 mg/kg bw/day; this high dose was associated with reduced pregnancy rate – at a clearly toxic dose to male and female animals. Additionally, clinical signs indicative of neurotoxicity (circling movements and head bobbing) were evident at the top dose in a few females from F_0 and F_1 generations; males from the F_1 generation presented increased kidney weight and increased incidence of chronic nephritis. The NOAEL for parental, reproduction and offspring toxicity was the dose level of 7.7 mg/kg bw/day.

Developmental toxicity

In the developmental toxicity study in rats, maternal toxicity was shown by mortality, clinical signs of neurotoxicity, and impaired food consumption and reduced body weight gain at the high dose level of 90 mg/kg bw/day; this toxicity was associated with reduced foetal birth weight, retarded ossification of the skull and an increased incidence of sternebrae anomalies. Both maternal and foetal NOAELs were the dose level of 30 mg/kg bw/day.

In rabbits, the maternal NOAEL was the mid-dose level of 15 mg/kg bw/day, based on decreased maternal body weight during gestation at 45 mg/kg bw/day. Increased fused sternebrae was observed in foetuses at the two highest doses (slightly/well above the historical control range) and reduced body weight at the top dose only. New historical control data presented by the applicant were found to be irrelevant for the study due to the difference between the period they were covering and the date at which the study had been performed. Although no maternal toxicity was found at the mid-dose, the effect itself was not considered severe enough to merit classification; therefore no classification was proposed by the meeting. The NOAEL for developmental toxicity was the lowest dose tested of 5 mg/kg bw/day.

2.7. NEUROTOXICITY

Delayed neurotoxicity

The potential for tri-allate to cause delayed neurotoxicity was investigated in an acute and short-term (90-day) study in hens. A further 42-day neurotoxicity study in chickens was not accepted by the rapporteur Member State due to missing key information and the limited quality of the study.

During the 42-day observation period of the acute study, dose-related decrease in body weight and clinical signs (diarrhoea, salivation, uncontrolled neck movement and transient leg weakness) were found; no histopathological lesion was observed up to the highest dose of 2500 mg/kg bw.

In the 90-day study, the NOAEL was the dose level of 100 mg/kg bw/day based on clinical signs and body weight loss seen at 200 mg/kg bw/day; the NOAEL for delayed neurotoxicity was the highest

dose tested of 300 mg/kg bw/day. No sign indicative of delayed neurotoxicity was observed in either the acute or short-term studies in hen.

Neurotoxicity

Neurotoxicity was investigated in three acute studies, including an investigation on cholinesterase inhibition, a 13-week dietary study, an assessment of brain pathology upon 5-week dietary exposure and a developmental neurotoxicity study, all performed with rats and considered acceptable by the rapporteur Member State.

In the acute studies, clear signs of neurobehavioural toxicity (on neuromuscular, central nervous system (CNS) activity and CNS excitability, as shown by the increased incidence of abnormal gait, circling, unusual behaviour, head shaking, abnormal righting reflex, decreased forelimb grip strength, ataxia, tremors, tendency to move backward and spontaneous somersaults) were observed at doses of 400 mg/kg bw and above. Doses of 200-300 mg/kg bw already showed some clinical signs of neurotoxicity (flat footed appearance/decreased motor activity). However no neuropathological changes were evident and no inhibition of plasma, red blood cell or brain cholinesterase activity was observed up to the highest dose. The acute NOAEL was the dose level of 60 mg/kg bw.

In the short-term study, the NOAEL was the dose level of 6.4 mg/kg bw/day based on reduced body weight and microscopic lesions which occurred in all three sections of the spinal cord and in sciatic, tibial and sural nerves, characterised by myelin degeneration with evidence of axonal fragmentation at the higher doses of 32.9 mg/kg bw/day and up. At 128.8 mg/kg bw/day, neurobehavioural changes were also noted, including circling behaviour, retropulsion, impaired righting reflex, and increased alertness and motor activity, impairment of gait, increased foot splay, and decreased grip strength, most of which were still present at the end of the recovery period. Based on the findings observed at 32.9 mg/kg bw/day already, a classification of tri-allate with **Xn**, **R48/22** "**Harmful: danger of serious damage to health by prolonged exposure if swallowed**" was proposed.

In the 5-week special investigation study, using a more up-to-date stain technique, a strong correlation was shown between the presence of axonal degeneration in the brain – degenerating axons in specific areas in brainstem levels and in the cerebellum (central white matter and/or deep nuclei) – and the CNS-like behavioural effects caused by tri-allate.

The developmental neurotoxicity study showed reduced maternal body weights and food consumption during gestation, slight increases in motor activity of offspring and reduced pup body weights and weight of young adult offspring at 60 mg/kg bw/day. Maternal, developmental toxicity and developmental neurotoxicity NOAELs were the dose level of 30 mg/kg bw/day.

2.8. FURTHER STUDIES

Metabolites

TCPSA was found to be a major metabolite in plants and in the environment – estimated to occur in groundwater according to fate and behaviour environmental models at levels up to 32 µg/L, thus requiring further toxicological assessment. TCPSA was also a metabolite found in rat studies (see point 2.1) and its toxicity was considered to be addressed to some extent by the toxicity studies performed in rats and other species. Toxicological studies performed with this metabolite included an acute oral toxicity study in rat, an Ames test, an *in vitro* chromosome aberration test in Chinese hamster V79 cells, a cell mutation assay at the thymidine kinase locus in mouse lymphoma L5178Y cells and a 14-day dietary range finding study in rat[11].

The acute oral LD_{50} of TCPSA was determined to be higher than 2000 mg/kg bw in female rat. No genotoxic potential was found in the three *in vitro* genotoxicity studies performed with TCPSA. The sodium salt of TCPSA did not provide any toxicity under the conditions of the study up to the dose level of 1413 mg/kg bw/day when administered to rats for 14 days; clinical chemistry, haematology or microscopic examination of organs and tissues were not performed.

An assessment (using the step-wise procedure in the Guidance Document on relevance of metabolites in groundwater) was presented in Addendum 5 and considered at the mammalian toxicology expert meeting (PRAPeR 49). In the absence of any specific indication of toxicity it was concluded that TCPSA is of equivalent toxicity or most likely of lower toxicity compared to tri-allate. Not enough data were available to set specific reference values for the metabolite, therefore the reference values of tri-allate apply to TCPSA.

TCPSA was found to have no toxicological relevance for groundwater according to the guidance document on groundwater metabolites[12].

2.9. MEDICAL DATA

Medical surveillance data including a detailed neurological assessment of exposed factory workers with relatively high exposures of tri-allate did not suggest any adverse effects in the workers.

[11] The subsequent 28-day study was presented to the rapporteur Member State after completion of the Draft Assessment Report. In view of the restrictions concerning the acceptance of new (including newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, the new studies could not be considered in the peer review.

[12] Sanco/221/2000 – rev.10 (25 February 2003): Guidance document on the assessment of the relevance of metabolites in groundwater of substances regulated under Council Directive 91/414/EEC.

2.10. ACCEPTABLE DAILY INTAKE (ADI), ACCEPTABLE OPERATOR EXPOSURE LEVEL (AOEL) AND ACUTE REFERENCE DOSE (ARFD)

ADI

Initially in the draft assessment report, the rapporteur Member State proposed an ADI of 0.03 mg/kg bw/day based on the long-term rat study presenting a NOAEL of 2.5 mg/kg bw/day, a safety factor of 100 and rounding-up 0.025 to 0.03 mg/kg bw/day. This approach was agreed by the experts at the meeting, which is supported by the 1-year dog study with the same NOAEL. However no rounding-up was considered. The **ADI for tri-allate was established at 0.025 mg/kg bw/day**.

AOEL

Considering the critical effects of tri-allate as potentially neurotoxic, the rapporteur Member State proposed an AOEL of 0.032 mg/kg bw/day based on rat 90-day neurotoxicity study with a NOAEL of 6.4 mg/kg bw/day, a correction factor for the limited oral absorption of 50 % and a safety factor of 100. The approach was agreed by the meeting. The **AOEL was set at 0.032 mg/kg bw/day**.

ARfD

The rapporteur Member State proposed in the draft assessment report an ARfD based on the acute neurotoxicity study in rat, considering a NOAEL of 300 mg/kg bw. The NOAEL of this study was changed to 60 mg/kg bw during the written procedure, considering the decreased motor activity observed at the highest dose level. The meeting agreed to set the **ARfD at 0.6 mg/kg bw** based on the acute neurotoxicity study and a safety factor of 100.

2.11. DERMAL ABSORPTION

Three *in vitro* studies on human skin and one *in vivo* study in monkeys were conducted using an emulsifiable concentrate formulation (EC), rather than the granule (GR) representative formulation. As dermal absorption is expected to be greater from an EC formulation than from a GR formulation, and penetration through monkey skin is expected to be greater than through human skin, a reasonable worst case was considered from the *in vivo* study resulting in a dermal penetration of 12 % for both the concentrate and the in-use spray dilution.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product 'Avadex 15G' is a granule (GR) formulation containing 150 g tri-allate/kg. It is a post-sowing/pre-emergence herbicide used on winter and spring barley, and winter and spring wheat. Applications of 'Avadex 15G' will be performed via tractor mounted or trailed granule placement equipment (surface application without incorporation) at a maximum dose rate of 2.25 kg tri-allate/ha, corresponding to 15 kg product/ha.

Operator exposure

As neither the German nor the UK POEM models contain any data relating to the loading and application of granular pesticides, the Pesticide Handler's Exposure Database (PHED) was used to estimate the level of operator exposure to tri-allate. From the distribution of exposures between individual replicates, 75th percentile exposure values from these data were considered representative surrogate values; a revised 25 ha/day work rate was considered appropriate as well as a 60 kg body weight for operators. It was assumed that operators are wearing gloves with normal work wear when loading and applying the product.

The resulting systemic exposure for operators assuming a dermal absorption of 12 % and inhalation absorption of 100 % is below the AOEL if personal protective equipment (PPE), as gloves, is worn during loading and applying the product.

Estimated operator exposure presented as % of AOEL (0.032 mg/kg bw/day) with PPE* - application rate of 2.25 kg tri-allate/ha

Representative use	Application method	Model/data	% of AOEL
Cereals	Tractor-mounted / trailed granule placement equipment	Selected data from the PHED	72 %

*PPE: gloves during loading and application

Worker exposure

Tri-allate is a pre-emergence herbicide applied directly to the soil. Thus, the scenario of re-entry of workers is not applicable and a worker re-entry risk assessment was not considered necessary

Bystander exposure

The representative use of 'Avadex 15G' may result in the possible exposure of bystanders and neighbouring residents to tri-allate vapour or drifting particles as tri-allate is considered as moderately volatile (vapour pressure of 1.2 x 10^{-2} Pa at 20 ºC).

Bystander exposure to vapour was calculated from field measurements in published data on residues of tri-allate in air adjacent to treated crops, assuming a body weight of 60 kg for an adult, a body weight of 15 kg for a small child, a respired volume of 15.2 m^3/day for adults and of 8.3 m^3/day for children. The highest exposure obtained by this calculation (which comes from the children exposure) represented 0.6 % of the AOEL.

Total systemic bystander exposure has been calculated based on field measurements of drift fallout, assuming an exposed body area of 2 m^2 and the same level of inhalation exposure for a bystander as that estimated for an operator during application from selected PHED data.

The EFSA notes that bystander exposure was recalculated by the rapporteur Member State in the reporting table, taking into consideration the dermal absorption value of 12 % (instead of 100%) and this was accepted by the experts.

Estimated bystander/residential exposure presented as % of AOEL (0.032 mg/kg bw/day) - application rate of 2.25 kg tri-allate/ha

Representative use	Application method	Model/data	% of AOEL
Cereals	Tractor-mounted / trailed granule placement equipment	Vapour exposure calculations (published field study data)	0.6 %
		Total bystander exposure to vapour and drift	7 %
		Children's exposure to drift fallout (US EPA)	20 %

It is also possible that drift fallout may be deposited in gardens adjacent to the treated area and that users of these gardens may become exposed through contact with deposits. The drift fallout values referred to above and the US EPA values for residential exposure resulting from contact with treated lawns were used to estimate this type of exposure for small children playing on a lawn contaminated with fallout from drifting particles of 'Avadex 15G'.

It was concluded that unprotected bystander and residential exposure resulting from 'Avadex 15G' according to its representative use was below the AOEL.

3. Residues

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

Uses of tri-allate on barley and wheat were supported by two metabolism studies in wheat and one in peas. In a 1982 study tri-allate was applied at 0.37N rate to wheat crop grown in a glasshouse, and in a second 2004 GLP study wheat crop was grown outdoors in screened enclosures after treatment with tri-allate at N rate. A metabolism study in peas (0.68N with respect to cereal GAP; N rate with respect to peas) was supplied to provide supporting information on non-extracted residues. The rapporteur Member State noted that peas and cereals represent different plant metabolism groups and the applicant supplied justification for making the extrapolation between the two groups in this particular case based on the close similarity of the metabolism data itself (radioactivity distribution, chromatographic profiles, identified major metabolites). Three significant metabolites were found:

TCPSA by oxidation of the sulfur and M14 and M15 by conjugation. In wheat grain, total metabolites were 0.008 mg/kg (5.10 % of TRR). The amounts of total metabolites in the inedible parts of wheat were 0.07 mg/kg (43.66 % of TRR) for forage, 0.30 mg/kg (40.33 % of TRR) for hay, and 0.77 mg/kg (51.92 % of TRR) for straw.

The meeting of experts noted that all the plant metabolism studies used tri-allate in which the radiolabeled carbon was incorporated in the allylic position. The meeting of experts considered that this was not acceptable as the fate of the other side of the molecule was not elucidated. This is an important issue because it is possible that nitrosamines could be formed. The meeting of experts concluded that a cereal metabolism study with labelling on the diisopropylamine moiety is a data gap.

A provisional residue definition for risk assessment of tri-allate, TCPSA and their glycoside conjugates expressed as tri-allate was proposed by the meeting of experts. For monitoring it was agreed that the residue definition is tri-allate. Following the meeting the rapporteur was asked to derive a conversion factor between the risk assessment and monitoring residue definition. The rapporteur in the non-peer reviewed addendum 7 concluded that this is not possible because it would be very unreliable to do this from the metabolism study, and in the residue trials the conjugates were not analysed. Therefore this issue has to remain as a data gap. It may be that new residues data will be needed to produce a robust conversion factor.

Sufficient residues trials were supplied for wheat and barley in northern Europe. It was demonstrated that in freezer storage residues are stable for up to 56 months. Given the low residues in food items processing studies are currently not supplied or required

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

The metabolism of tri-allate in rotational crops was investigated where application of radiolabelled tri-allate was applied at a rate of circa 1N. As for the primary crop metabolism the label was only in the allylic moiety and not the diisopropylamine moiety. Therefore pending the outcome of the primary wheat metabolism study an additional rotational crop study may be required. Lettuce, radish and wheat were planted at plant back intervals of 30, 120 and 365 days. On investigation of the residue the only significant compounds identified were tri-allate and TCPSA. Unlike in the primary crops, where significant levels of the two conjugates M14 and M15 were found, these were not analysed for in the rotational crop study. The meeting of experts considered that these need to be addressed as it is expected that these compounds should be present in rotational crops and therefore a data gap was set.

The applicant's statement in the evaluation table mentioned that the residue levels of tri-allate and of TCPSA in rotational crops were below 0.05 mg/kg in all edible parts of the rotated crops at all plant

back intervals; this was however not the case for radish roots at 30 days after application (DAA; tri-allate 0.08 mg/kg) nor for the sum of relevant residues (tri-allate and TCPSA). Significant residues were also detected in wheat straw (0.84 mg/kg) at 193 DAA.

The meeting proposed to refer to the OECD guidance document for the trigger values since the Lundehn document is not clear.

The meeting discussed the possibility to propose restrictions on rotational crops and to leave the final decision to Member States to require further cold rotational crop field trials that comply with the relevant national practice in case of authorising this use. Therefore a data gap was identified to address the potential for residues to occur in rotational crops and the necessity to set MRLs for rotational crops. The risk assessment can not be finalised due to this issue.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

One goat was dosed orally once daily for five consecutive days with gelatine capsules containing ^{14}C-tri-allate (radio-chemical purity 100%) at a dose level corresponding to 14 mg as/kg in feed (or approx. 75N). The N rate is only provisional as the rotational crop residues are not as yet defined. It was clearly demonstrated that tri-allate is rapidly and extensively eliminated in the goat. The radiolabel was widely distributed among goat tissues and at a wide range of levels: omental fat (0.017 mg/kg), round muscle tissues (0.033 mg/kg), milk (0.177 mg/kg), liver (1.084 mg/kg) and kidney (2.462 mg/kg). Tri-allate was extensively metabolised. The incorporation of ^{14}C-tri-allate into natural constituents such as sugars, vitamins, proteins, amino acids, and lipids has been demonstrated. The most abundant radiolabel in milk was lactose into which the radiolabel from tri-allate was incorporated. Incorporation into triglycerides was also proved for milk. In goat liver, kidney, and round muscle, incorporation of ^{14}C-tri-allate into amino acids and proteins as well as sugars and vitamins was demonstrated. After treatment of lactating goats with tri-allate, very low concentrations of tri-allate were found in omental fat (0.002 mg/kg). Also very low concentrations of the metabolite M16[13] were found in milk (0.004 mg/kg). The applicant stated that M16 may arise from tri-allate by treatment with KOH/methanol as an artefact of the extraction procedure in the method of analysis and the rapporteur Member State considered this to be plausible. In the mammalian toxicology section of the DAR, this metabolite was considered as an artefact of the analytical method and the meeting of experts decided to rely on this conclusion. In goat liver, kidney, and round muscle neither tri-allate nor metabolite M16 were found. The applicant suggested that either radiolabelled $^{14}CO_2$ or two-carbon products are formed via metabolism of tri-allate, which can undergo additional metabolic transformations to be incorporated into natural products.

[13] M16: *S*-[(2*E*)-2,3-dichloro-1-methoxyprop-2-en-1-yl] dipropan-2-ylcarbamothioate

In a second 1983 non-GLP study the combined metabolism of tri-allate and metabolite TCPSA were investigated using test compounds labelled at the allylic carbon atom. After a seven day acclimatisation period, three lactating goats (Nubian breed) were orally dosed for 5 days with a mixture of radiolabelled tri-allate at a level of 8.5 mg/kg diet and radiolabelled TCPSA at a level of 8.1 mg/kg diet. This corresponded to a 1:1 mole ratio of the two compounds and represents approximately 130N and 70N, respectively, in relation to total highest residue intakes of tri-allate and metabolite TCPSA for the goat. The great majority of recovered radioactivity was present in the urine and faeces (98%). No significant metabolites of TCPSA or tri-allate were detected in any of the edible matrices. There was over 100% recovery of the TCPSA in the urine and faeces.

The need for a hen metabolism study was not triggered by the current intakes. This should be reviewed when the rotational crop residue levels are resolved.

In a livestock feeding study, dairy cattle were dosed at a reported dose level of 1, 3 and 10 mg/kg diet of both tri-allate and TCPSA. All residues in the low dose group were <0.01 mg/kg. Residues in the middle dose group were <0.01 mg/kg for all matrices apart from kidney (0.1 mg/kg TCPSA) and perirenal fat (0.01 mg/kg tri-allate and 0.05 mg/kg TCPSA). Residues in the high dose group were <0.01 mg/kg except in kidney (0.05 mg/kg TCPSA), perirenal fat (0.03 mg/kg tri-allate and 0.15 mg/kg TCPSA) and omental fat (0.01 mg/kg for both tri-allate and TCPSA).

A hen feeding study was also presented with the same dosing regime as the cattle study. Residues above 0.01 mg/kg were only found in the high dose birds. Residues of TCPSA were found in eggs at a max level of 0.03 mg/kg. At sacrifice residues were only found in fat (0.04 mg tri-allate/kg).

On the available data the meeting of experts concluded that the residue definition for monitoring and risk assessment is tri-allate and TCPSA expressed as tri-allate. The meeting also questioned the dose rates in the feeding and metabolism study if it was on a dry weight (dw) basis. A response on this was received from the applicant with a calculation to demonstrate that it must have been on a dw basis. This case was rejected by the rapporteur so this issue remains as a data gap. Some anomalies with the studies have been noticed by the EFSA. Residues occur in the feeding study when from the metabolism study no residues would be expected. In addition, the residues in fat of TCPSA are strange because TCPSA from its structure and calculated log K_{ow} should not be present in fat, and certainly not at levels higher than tri-allate. During the written procedure the rapporteur was given the opportunity to address these anomalies but they did not do so.

3.3. CONSUMER RISK ASSESSMENT

Currently the consumer risk assessment can not be finalised for the following reasons:

- Residues in rotational crops are not finalised.

- There is no conversion factor to take into account the conjugated metabolites M14 and M15.
- A wheat metabolism study is required.
- No full risk assessment is available for TCPSA in ground water. One was done for adults, which gave intakes resulting in 4 % of the ADI being used up.

3.4. PROPOSED MRLS

No MRLs can be proposed at this time as the risk assessment can not be finalised.

4. Environmental fate and behaviour

Tri-allate fate and behaviour in the environment was discussed in PRAPeR 47 (Subgroup 2) Experts' meeting (May 2008) on basis of the DAR (July 2007) and Addendum 6 (May 2008). The ^{14}C-labelled tri-allate used was labelled only in the allylic position of the trichloropropene moiety. The need for addressing the metabolites that may result from the diisopropylamine moiety was identified during the peer review and discussed in the PRAPeR meeting.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

Route of degradation of ^{14}C-labelled tri-allate in soil under dark aerobic conditions was investigated in one study with four soils (pH 6.6 – 7.1; OC 1.3 – 2.5 %; clay 8.4 – 30.7 %) at 20 °C and 10 °C (one soil, Niven: pH 6.6; OC 1.8 %; clay 12.1 %) maintained at 40 % MWHC. Full mass balance was only obtained for one soil (Niven) since the other three soils were not combusted to measure unextracted residue. The narrow soil pH range tested was noted by the rapporteur Member State. However since hydrolysis is enhanced at alkaline pH, the range tested was considered to be a worst case with respect to tri-allate. The meeting of experts considered that a higher fraction of metabolites could have been formed in soils with higher pH. However this was not apparent in the data available. Six or seven metabolites were identified in the different experiments, none of them exceeding the 5 % AR in any of the soils when quantified by HPLC. Of these, only TCPSA (max. 3.74 % AR increasing at the end of the study 120 days after treatment (DAT) in two of the soils) was fully characterized and further addressed for environmental risk assessment. Analysis by TLC resulted in the quantification of higher amounts for this metabolite (up to 7.38 % AR). Since the isopropyl moieties of the molecule were not labelled, it is not possible to determine which metabolites may be formed from it and to what extent. However the break down pattern that results in the formation of TCPSA is likely to be associated with the concomitant formation of diisopropylamine or related compounds. Diisopropylamine is a known precursor of the nitrosamine NDIPA that is considered to be of concern with respect to human health (see for example: *Opinion concerning dialkyl- and dialkanolamines and*

their salts in cosmetic products adopted by the SCCNFP during the 17th plenary meeting of 12 June 2001[14]).

A clarification to address the potential ground water contamination by diisopropylamine arising from the use of tri-allate and the potential formation of nitrosamines was required from the applicant during the peer review. The applicant provided a position paper in which it was confirmed that the formation of diisopropylamine in soil cannot be excluded. The applicant modelled leaching of the diisopropylamine to groundwater using FOCUS PELMO and FOCUS PEARL models and then estimated the *N*-nitrosodiisopropylamine concentrations that could be produced by water treatment with an oxidiser (chlorination, ozonisation). The position paper intended to clarify this issue made use of public scientific literature to select the input parameters for modelling and as part of the consideration for estimating the formation of nitrosamines potentially produced by water treatment. These scientific papers had not been previously submitted in the dossier. In view of the restrictions concerning the acceptance of new (including newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, the new studies could not be considered in the peer review. However the meeting considered that the issue needs to be addressed and therefore identified a data gap to address the potential formation of diisopropylamine in soil and contamination of ground water. Unextractable radioactivity amounted to max. 25.3 % AR at the end of the study (120 DAT). Radioactivity found in the ethanolamine trap (max. 21.2 % AR after 120 d) was assumed to be CO_2. However it may not be completely excluded that other volatile acidic metabolites derived from tri-allate contribute to this residue fraction. The amount of volatiles collected in the organic traps was significant (max. 16.17 % AR after 120 d) and this was not characterized but assumed to be tri-allate. The meeting of experts considered the lack of characterisation of volatiles as a serious deficiency of the study, considering the structure and physical and chemical properties of tri-allate. The meeting considered that the actual amounts of soil metabolites identified in the study could have been underestimated due to volatilization. The need for further identification of potentially volatile tri-allate soil metabolites and the characterization of soil metabolites found in the available study had been identified during the peer review. A clarification was required from the applicant, who presented an argumentation based on the volatile fractions for the water sediment study indicating that the vast majority of the volatile fraction is expected to be tri-allate. The majority of experts agreed with the rapporteur Member State that it is reasonable to assume that the non-characterised radioactivity in the volatile traps is the active substance. This assumption is further supported by the relatively high vapour pressure of 0.012 Pa at 20 °C for tri-allate. The EU risk assessment of the representative use proposed could therefore be acceptably concluded without further regard to the characterisation of the volatiles. However some experts considered that it is necessary to confirm the complete route of degradation for national risk assessment and therefore a data gap was identified for a study to investigate the aerobic degradation

[14] http://ec.europa.eu/health/ph_risk/committees/sccp/docshtml/sccp_out144_en.htm

in soil including identification of residues in volatile organic traps and adequate identification of soil metabolites.

Degradation under anaerobic conditions at 20 °C was investigated in one soil (pH 6.1; OC 1.08 %; clay 19.3 %). Four different metabolites were found, none of them were characterized since they did not exceed 5 % AR. However comparison with TCPSA standard show that this metabolite is not formed under anaerobic conditions.

A photolysis in soil study under natural sunlight (January-February) in Kentucky USA (37 °N) and a non guideline photolysis in soil study under artificial light (Xe arc lamp) are available in the dossier. Photolysis in soil of tri-allate is almost negligible when compared with aerobic degradation. No photolysis metabolites were formed at sufficiently significant amounts to require further identification.

4.1.2. PERSISTENCE OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

Rate of degradation in soil under aerobic conditions at 20 and 10 °C was investigated in the same study reported in the route section. Tri-allate exhibited moderate to medium persistence in soil in this study ($DissT_{50}$ = 35 – 61 d), however these rates may only be considered as dissipation rates since volatilization contributed to a great extent to the losses observed. Data were reanalyzed by the applicant with ModelMaker (V.4.0.) to separate the degradation and volatilization processes. The calculated degradation rates were in the range of DT_{50} = 38.4 – 75.2 d.

Degradation of the metabolite TCPSA under dark aerobic conditions at 20 °C was investigated in one study on three soils (pH 5.3 – 7.3; OC 0.96 – 2.67; clay 1.5 – 9.9) maintained at 45 % MWHC. TCPSA exhibits low to moderate persistence (DT_{50} = 9.0 – 40.1 d) under these conditions in soil. Under dark anaerobic conditions at 20 °C tri-allate was very highly persistent in soil (DT_{50} = 394 d).

A field dissipation study is available with trials at four different United Kingdom sites (pH 6.6 – 7.5; OC 1.32 – 3.81 %, clay 0.8 – 12.6 %). Both bare soil and cultivated plots were investigated. Tri-allate exhibited low to high persistence in these trials ($DT_{50\ bare\ soil}$ = 10 – 158 d; $DT_{50\ cultivated}$ = 8 – 205 d). The rapporteur Member State assessed the studies as scientifically valid and representative of Northern European conditions. However, according to the rapporteur Member State's assessment of field studies, volatilization could have contributed to the observed dissipation of tri-allate in field. Therefore the rapporteur Member State proposed to use data obtained from laboratory degradation studies for environmental modelling. Hence kinetic results from field studies had not been used for modelling in the risk assessment of the EU representative uses. Member States may need to consider effect of volatilization on the results of these studies before using the results in the risk assessment of

products containing tri-allate. The DT_{90}'s observed in some of the field dissipation studies were above 1 yr and triggered the need to assess potential of accumulation of tri-allate in soil.

During the peer review a clarification on the influence that the formulation may have over the persistence of tri-allate in soil was requested to the applicant. The applicant did not provide adequate information regarding this potential influence of the formulation on the fate and behaviour of tri-allate. However since the half-life used to asses fate and behaviour in soil was determined in a field study with a granular formulation comparable to the product supported for the representative uses evaluated at EU level, the meeting considered that no further information is needed.

PEC in soil and accumulation of tri-allate in soil were estimated on the basis of the worst case field half-life of 205 d. For TCPSA, the PEC soil was estimated on the basis of the maximum observed in the laboratory studies determined by TLC (7.4 % AR, worst case).

4.1.3. MOBILITY IN SOIL OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

A soil batch adsorption / desorption study with five soils (pH 5.0 – 7.5; OC 0.21 – 2.63 %; clay 5.2 – 46.3 %) is available for tri-allate. Tri-allate may be considered immobile to slightly mobile in soil according to this study (K_{foc} = 2982 – 13768 mL/g). A soil batch adsorption / desorption study with three soils (pH 5.4 – 7.6; OC 1.28 – 2.98 %; clay 17.4 – 34.15 %) is available for the soil metabolite TCPSA. TCPSA may be considered very highly mobile in soil according to this study (K_{foc} = 0.5 – 4.4 mL/g).

An aged residue column leaching study is available in the dossier. Only one polar peak that does not correspond to tri-allate or TCPSA was detected in the leachate. Low mobility of tri-allate was confirmed by this study.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Hydrolysis of tri-allate was preliminary investigated in buffered aqueous solutions (pH 4, 7 and 9) at 50 °C. Hydrolysis occurred only at pH 9. A second test was conducted at pH 9 at 40 °C and 25°C. In the experiment performed at 25 °C, four unidentified metabolites were formed, one of them reaching an increasing level of 9.8 % AR at the end of the study. Further attempts of identification were unsuccessful. The half-life at 25 °C in the aqueous pH 9 solution was 52 d.

Aqueous photolysis is not expected to contribute to the environmental degradation of tri-allate on basis of the lack of UV absorption at wavelengths above 290 nm.

Biodegradability studies available show that tri-allate is not readily biodegradable.

Fate of tri-allate in aquatic systems was investigated in a study with two water / sediment systems (pH_{water} 7.5 – 8.8 ; pH_{sed} not reported; OC_{sed} 2.1 – 2.9 %; $clay_{sed}$ 12.5 – 27.8 %). Tri-allate dissipated relatively rapidly from water by partition to the sediment (max. 49.9 – 51.0 % AR as tri-allate in the sediment after 7 d) and by volatilization. Half-lives of tri-allate in the whole system were 52.8 – 62.0 d. No major metabolites were identified either in the water or in the sediment phases. Mineralization and unextractable residues in the sediment were practically negligible (CO_2 = 1.51 – 4.35 % AR; unextractable in sediment = 2.77 – 3.26 % AR).

$PEC_{SW/SED}$ were calculated for tri-allate and the soil metabolite TCPSA on basis of the FOCUS SW scheme and models for the scenarios relevant to cereals in Northern EU (D1-D5, R1). FOCUS SW Step 4 calculations are available for tri-allate. For metabolite TCPSA only calculations up to Step 2 are available. Since the formulation is granular, the applicant proposed spray drift values for the granules based on a specific study. The approach was considered acceptable by the rapporteur Member State and reported as Step 3 calculations. However since it constitutes a deviation from standard Step 3 modelling, it should be regarded as a FOCUS Step 4 approach. Additional FOCUS Step 4 calculations included spray drift mitigation by buffer zones and run off mitigation by vegetative buffer strips. The method used to implement runoff mitigation is not agreed in the latest FOCUS Landscape and mitigation guidance document and therefore the rapporteur Member State recalculated the Step 4 FOCUS SW without run off mitigation. Results are presented considering two mitigation options (10 m buffer zone or a 5 m buffer zone with deflector plates) that result in equivalent values.

4.2.2. POTENTIAL FOR GROUND WATER CONTAMINATION OF THE ACTIVE SUBSTANCE THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

Potential ground water contamination by tri-allate and its soil metabolite TCPSA was addressed by the applicant in the dossier by FOCUS PELMO 3.3.2. The calculations were not considered reliable for the metabolite since the maximum observed in laboratory experiments (3.74 %; HPLC determination) was used as a surrogate of the kinetic formation fraction in the modelling. The data from the degradation studies do not allow an accurate determination of the formation fraction of TCPSA. However the rapporteur Member State estimated a formation fraction of 30 % as a reasonable worst case. Using the same model as the applicant, the rapporteur Member State calculations resulted in 80th percentile annual average concentrations in the leachate at 1 m depth below 0.001 µg/L for tri-allate and in the range of 0.76 – 15.42 µg/L for metabolite TCPSA. The metabolite TCPSA has a clear potential to exceed the trigger of 0.1 µg/L in ground water and requires assessment of its toxicological and ecotoxicological relevance including consumer risk assessment. During the peer review it was noted that results with only one of the FOCUS GW models were

available in the dossier. The applicant provided additional calculations with FOCUS PEARL. The results indicate that FOCUS PEARL may result in higher calculated concentrations for metabolite TCPSA (2.56 – 31.29 µg/L) than the calculations available from FOCUS PELMO modelling. Relevance of TCPSA was assessed following the step-wise procedure set out in the guidance document for relevance of metabolites in ground water (see sections 2.8, 3.3 and 5.2).[15]

4.3. FATE AND BEHAVIOUR IN AIR

Tri-allate is a volatile organic compound (Henry's law constant = 0.89 Pa m^3 mol^{-1} at 20°C) and studies available indicate that tri-allate displays significant volatilisation from soil surfaces. This may need further consideration when reassessing fate and behaviour of tri-allate at field-scale for the formulated product.

The meeting of experts noted that there was no consideration to address global warming potential or ozone depletion in the dossier of tri-allate. Although not considered a formal data requirement, this information would be expected for a volatile compound containing halogen atoms. The rapporteur Member State considered that this was probably not necessary in view of short active substance half-life in air. On the basis of the atmospheric half-life calculated (DT_{50} = 3.8 h) it is considered unlikely that tri-allate may be subjected to long-range transport.

5. Ecotoxicology

The risk assessment was conducted according to the following guidance documents: SANCO/4145/2000 (birds and mammals), SANCO/3268/2001 (aquatic environment), SANCO/10329/2002 (terrestrial environment), ESCORT 2 (non-target arthropods). In view of the restrictions concerning the acceptance of new (including newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, the new studies could not be considered in the peer review.

5.1. RISK TO TERRESTRIAL VERTEBRATES

To estimate the TER, values were estimated by the rapporteur Member State according to the EPPO 2003 guidance. The EPPO 2003 guidance suggest estimating the risk of the granule ingested intentionally through the calculation of the reasonable worst case daily grit (or granule) dose (DGD_{rwc}). The first tier risk assessment resulted in TER values for direct consumption of granules as food items above the trigger values, indicating a low acute, short-term and long-term risk for small seed-eating birds and mammals.

[15] Guidance document on the assessment of the relevance of metabolites in ground water of substances regulated under council directive 91/414/EEC, Sanco/221/2000-rev.10-final.

The risk to grazing birds and mammals from consumption of residues of tri-allate in the young cereal shoots were estimated using the residues data presented in the DAR. The TERs estimated for birds and mammals were above the Annex VI trigger values, suggesting a low risk for the intended uses.

Tri-allate has a log P_{ow} of 4.06, indicating a potential for bioaccumulation, and therefore the risk from secondary poisoning was assessed. The first tier TER values for earthworm-eating birds and mammals were 12.7 and 1.71, indicating a low risk to earthworm-eating birds, but a high risk to earthworm-eating mammals. To refine the risk assessment the rapporteur Member State proposed that common shrew (*Sorx araneus*) be considered an indicator species for earthworm-eating mammals according to the guidance SANCO/4145/2002. The rapporteur Member State submitted a few literature articles: Gurney *et al*. (1998)[16]; Johnson *et al*. (1992)[17], Tew *et al*. (1994)[18]; Harrington and Macdonald (2002).[19] Given that tri-allate is applied to autumn/winter and early spring crops pre-emergence, the overall conclusion proposed by the rapporteur Member State was that it is unlikely earthworm-eating species such as shrews will be feeding in open cereal fields sufficiently for them to consume enough tri-allate contaminated worms to lead to any long-term risk. The rapporteur Member State concluded that under more realistic use conditions the risk was considered as low.

The first tier TER values for fish-eating birds and mammals were 7 and 1.9 respectively. The experts at the PRAPeR 48 meeting discussed the risk to fish-eating birds and mammals, and which BCF this should be based upon (BCF from a standard exposure situation BCF= 1400 versus BCF observed in a test system with sediment BCF = 574). The experts considered that in the sediment study the test substance was applied to the sediment 30 days before the water and the fish were added to the system. It was discussed if binding to sediment is taken into account twice with this approach. The experts did not agree with use of the BCF from the sediment study, but if this approach to is used refine the BCF then it should be compared to the total load PEC to avoid double-counting of binding to sediment.

The EFSA noted a misunderstanding in the open point 5.1 of the discussion table of tri-allate, in the phrase "In case the BCF = 1400 was used giving TER_{lt} 7 for fish-eating-birds and 130 for mammals." The correct TER_{lt} (when BCF of 1400 was used) for fish-eating mammals was 1.9 instead of 130. This TER_{lt} = 130 was estimated by the rapporteur Member State based on the BCF of 574 obtained from the sediment test using the catfish. As noted above, the experts did not agree with the use of this study for the refinement of the risk assessment. The correct TER_{lt} value was below the Annex VI

[16] Gurney J.E., Perrett J, Crocker D.R. and Pascual A.L. (1998) "Mammals and farming: information for risk assessment", Report No PN0919 Milestone Report CSL project No M37. Unpublished.
[17] Johnson I.P., Flowerdew J.R. and Hare R. (1992) "Populations and diet of small mammals rodents and shrews in relation to the pesticide usage", Pesticides, Cereals farming and Environment, The Boxworth project (144-15), HMSO London.
[18] Tew T. E., Todd I.A., and Macdonnald (1994) "Field margins and small mammals", BCPC Monograph 58.
[19] Harrington, L.A. and Macdonald, D.W. (2002) "A Review of the Effects of Pesticides on Wild Terrestrial Mammals in Britain", WildCRU, Oxford: Royal Society for Protection of birds.

trigger value and therefore a new refinement of the risk assessment was considered necessary. In consequence, the EFSA has identified a data gap after the peer review for further refinement of the risk assessment to fish-eating mammals.

5.2. RISK TO AQUATIC ORGANISMS

Based the available studies, tri-allate was considered as very toxic to aquatic organisms. Algae were the most sensitive species (96 h E_bC_{50} = 0.024 mg/L). It was agreed at the meeting of experts the toxicity was higher at the 96 hours than 72 hours.

The first tier risk assessment indicated that the acute and chronic TER values based on PEC_{SW} from FOCUS Step 3 were below the Annex VI trigger values for all the aquatic organism except for aquatic plants and sediment-dwelling organisms. An essential risk for the aquatic organism was observed in most of the FOCUS scenarios. A higher tier risk assessment was done considering the PEC_{SW} from FOCUS Step 4 with a 10 m buffer zone. All the acute and chronic TER values for drainage as well as for run off scenarios were above the Annex VI trigger values.

A low risk could be identified for aquatic organisms based on the use of mitigation measures in an example buffer zone of 10 m.

The first tier risk assessment for the relevant metabolite TCPSA gave acute TER values above the Annex VI trigger value. Consequently the risk of the TCPSA metabolite for aquatic organisms is low. The TCPSA metabolite was identified in the fate and behaviour section as a ground water metabolite (the concentration of the TCPSA for ground water was estimated as 31.29 µg/L, which was higher than the PEC_{SW} of 9.6 µg/L). This did not change the outcome of the aquatic risk assessment of TCPSA.

Since tri-allate has a log P_{ow} of 4.06 the potential for bioconcentration should be considered. Two different bioconcentration studies have been submitted. A BCF of 1400 was derived from a standard study with *Lepomis macrochirus* with a clearance time of 2.7 days and BCFs in the range of 210 to 574 derived from a test sediment system with catfish (*Icatalurus punctatus*). The experts discussed at the meeting the risk to fish-eating birds and mammals and on which BCF value it should be based. The experts during the meeting noted that in the sediment study, the test substance was applied to the sediment 30 days before the water and the fish were added to the system. It was discussed that binding to sediment is taken into account twice with this approach. The experts did not agree with use of the BCF from the sediment study, but if this type of approach is used to refine the BCF then it should be compared to the total load PEC to avoid double-counting of the binding to sediment.

The EFSA noted after the meeting that tri-allate has a BCF >1000 and a field soil DT_{90} of >100 days. The EFSA has identified a data gap after the peer review for submission of information for the potential for biomagnification of tri-allate in aquatic food chains.

5.3. RISK TO BEES

Tri-allate is of low toxicity to bees. The LD_{50} values for oral and contact exposure were >111.5 and >100 µg a.s./L, respectively. The oral and contact Hazard Quotients (HQ) values were <22.5 and <20 which were below the Annex VI trigger value, indicating that the risk to bee is considered as low.

5.4. RISK TO OTHER ARTHROPOD SPECIES

The applicant submitted studies with ground dwelling species only that it is in agreement with the ESCORT 2 guidance. Two standard laboratory tests were conducted with the preparation 'Avadex 15G' and with *Poecilus cupreus* and with *Pardosa spp*. Two additional Tier 2 extended laboratory studies were conducted with the spider *Pardosa spp.* and with *Aleochara bilineata*.

The first tier laboratory studies showed effects lower than the ESCORT 2 trigger of 50 % for *P. cupreus* and *Pardosa spp*. The second tier extended laboratory study with *A. bilineata* showed an effect of 12.9 % reduction in reproduction, and the study with *Pardosa spp.* showed a statistically significant increase in mortality (14.7 %) compared to the controls within the first two weeks.

It was agreed at the meeting of expert that studies with soil dwelling arthropods should not be required as the intended uses of tri-allate are on the surface and not in the soil.

The results of the studies (below the ESCORT 2 trigger value of 50 %) indicated a low risk within the in-field areas.

The applicant proposed that 13.43 % of the applied rate is deposited at 1 m distance, to estimate the exposure that reaches off-field areas. When compared to the highest level of effects of *Pardosa* at 21 days (20.6 %) with the estimated exposure, then it could be concluded that the off-field risk to non-target arthropods from the use of tri-allate is low.

In conclusion, a low risk is expected to the non-target arthropods inhabiting the in-field as well as off-field areas for the representative uses of tri-allate.

5.5. RISK TO EARTHWORMS

Tri-allate and the relevant soil metabolite TCPSA showed an acute toxicity to earthworms of $LC_{50\ corr.}$= 274 mg a.s./kg soil and LC_{50} >1000 mg TCPSA/kg soil. The acute TER values based on maximum initial PEC_{soil} were above the Annex VI trigger values.

Since the DT_{90} in field soil was 682 days for tri-allate, a reproductive study for earthworms using the formulation was provided. $NOEC_{corr.}$ = 13.62 mg a.s./kg soil was obtained from the study, and the chronic TER value estimated with this $NOEC_{corr.}$ gave a value of 3.22, which was below the Annex VI trigger value.

Further information is required in the DAR to address the potential and unclear adverse effects seen in the earthworm chronic toxicity study. A new earthworm field study was available but not taken into account by the rapporteur Member State. In view of the restrictions concerning the acceptance of new (including newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, the new studies could not be considered in the peer review.

A data gap has been identified for an earthworm field study.

5.6. RISK TO OTHER SOIL NON-TARGET MACRO-ORGANISMS

Tri-allate is potentially persistent in soil, having a DT_{90} of 682 days in field soil. The potential risk to soil litter degradation process from tri-allate should be addressed according to the SANCO guidance 10329/2002.

The applicant recently submitted a new litter bag study, but this new study was not evaluated by the rapporteur Member State. A data gap has been identified for the submission of a new litter bag study.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

Effect on soil nitrification and respiration were < 25 % at concentrations up to 11.25 kg a.s./ha, up to 5 times the PEC_{soil} (4.232 mg a.s./kg soil). It was concluded that the risk to soil micro-organisms was low for the evaluated uses.

5.8. RISK TO OTHER NON-TARGET-ORGANISMS (FLORA AND FAUNA)

Effects of tri-allate on seedling emergence and vegetative vigour were investigated in 4 monocotyledons and 6 dicotyledonous plant species. The lowest endpoint (ER_{50} = 0.021 kg a.s./ha) was observed for the oat. The TERs values for oat were below the Annex VI trigger value of 5 at a distance of 1 m. The TERs values were above the Annex VI trigger with a non-spray buffer zone of 10 m. Therefore risk mitigation such as an in-field no spray buffer zone of 10 m was considered necessary for the evaluated uses.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

Respiration of active sludge was not affected up to the highest tested concentration of 1000 mg/L. It was concluded that the risk to biological methods of sewage treatment was considered to be low for the intended uses.

6. Residue definitions

Soil

Definition for risk assessment: tri-allate, data gap identified for the investigation on the potential formation of diisopropylamine.

Definition for monitoring: tri-allate, data gap identified for the investigation on the potential formation of diisopropylamine.

Water

Ground water

Definition for exposure assessment: tri-allate, TCPSA, data gap identified for the investigation on the potential formation and leaching of diisopropylamine.

Definition for monitoring: tri-allate, TCPSA, data gap identified for the investigation on the potential formation and leaching of diisopropylamine.

Surface water

Definition for risk assessment: tri-allate, data gap identified for the investigation on the potential formation of diisopropylamine.

Definition for monitoring: tri-allate, data gap identified for the investigation on the potential formation of diisopropylamine.

Air

Definition for risk assessment: tri-allate

Definitions for monitoring: tri-allate

Food of plant origin

Definition for risk assessment: tri-allate, TCPSA and their glycoside conjugates expressed as tri-allate (provisional).

Definition for monitoring: tri-allate

Food of animal origin

Definition for risk assessment: tri-allate and TCPSA expressed as tri-allate.

Definition for monitoring: tri-allate and TCPSA expressed as tri-allate.

Overview of the risk assessment of compounds listed in residue definitions for the environmental compartments

Soil

Compound (name and/or code)	Persistence	Ecotoxicology
Tri-allate	Moderate to medium persistence ($DT_{50\ lab}$ = 38.4 – 75.2 d); however it may be highly persistent in Northern EU field conditions ($DT_{50\ bare\ soil}$ = 10 – 158 d; $DT_{50\ cultivated}$ = 8 – 255 d).	The chronic risk to earthworms is high Data gap (a new reproduction study)
Data gap identified for the investigation on the potential formation of diisopropylamine	No data available Data gap	No data available

Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg/L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
Tri-allate	Immobile to slightly mobile	FOCUS PELMO 3.3.2: no scenarios exceed 0.1 µg/L		Yes	Yes

Compound (name and/or code)	**Mobility in soil**	**> 0.1 µg/L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)**	**Pesticidal activity**	**Toxicological relevance**	**Ecotoxicological activity**
	(K_{foc} = 2982 – 13768 mL/g)	FOCUS PEARL 3.3.3: no scenarios exceed 0.1 µg/L			
TCPSA	Very highly mobile (K_{foc} = 0.5 – 4.4 mL/g)	FOCUS PELMO 3.3.2: all scenarios exceeded 0.75 µg/L, one scenario exceeded 10 µg/L FOCUS PEARL 3.3.3: all scenarios exceeded 0.75 µg/L, four scenarios exceeded 10 µg/L		No, however the ADI of tri-allate applies to TCPSA in order to perform a full risk assessment	No
Data gap identified for the investigation on the potential formation and leaching of diisopropylamine (precursor of NDIPA: *N*-nitroso-diisopropanolamine)	No data available Data gap	No data available Data required		No data available, no conclusion is possible on its relevance	No data available, no conclusion is possible on its relevance

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Tri-allate	High risk to aquatic organisms
Data gap identified for the investigation on the potential formation of diisopropylamine	No data available

Air

Compound (name and/or code)	Toxicology
Tri-allate	Rat LC_{50} inhalation > 5.3 mg/L air/4 hour, whole body as aerosol atmosphere – no classification is proposed

LIST OF STUDIES TO BE GENERATED, STILL ONGOING OR AVAILABLE BUT NOT PEER REVIEWED

- Information on the purity of one of the starting materials for the production of the technical material (relevant for all representative uses evaluated, date of submission unknown, data gap identified by experts of PRAPeR 46 meeting, May 2008; refer to chapter 1).
- Information on the level of ethoxylation for the stabilizer as well as a method of analysis for it in the technical material (relevant for all representative uses evaluated, date of submission unknown, data gap identified by experts of PRAPeR 46 meeting, May 2008; refer to chapter 1).
- Spectra for NDIPA (relevant for all representative uses evaluated, date of submission unknown, data gap identified by experts of PRAPeR 46 meeting, May 2008; refer to chapter 1).
- Possible increase of impurity NDIPA during storage and/or the formulation of the PPP as well as an analytical method for this impurity in the formulation to be addressed (relevant for all representative uses evaluated, date of submission unknown, data gap identified by experts of PRAPeR 46 meeting, May 2008; refer to chapter 1).
- An analytical method for the determination of tri-allate and TCPSA residues in food of animal origin (relevant for all representative uses evaluated, date of submission unknown, data gap identified by the EFSA as a consequence of the decision of the experts of PRAPeR 50 meeting, June 2008; refer to chapters 1 and 6).
- Information on the impurity profile of the batches used in key toxicological studies (relevant for all representative uses evaluated; date of submission unknown, data gap identified by experts of PRAPeR 49 meeting, June 2008; refer to point 2).
- 28-Day oral toxicity study conducted with the metabolite TCPSA (relevant for all representative uses evaluated; study submitted and evaluated by the rapporteur Member State but not peer-reviewed, as laid down in Commission Regulation (EC) No. 1095/2007; refer to point 2.8).
- Wheat metabolism study labelled on the diisopropylamine moiety (relevant for all uses evaluated, data gap identified by meeting of experts May 2008, proposed submission date unknown; a case for none submission of data was made in addendum 7, refer to chapter 1).
- It should be clarified what the dose rate was in the animal feeding studies (relevant for all uses evaluated, data gap identified by meeting of experts May 2008, proposed submission date unknown, refer to chapter 1).
- A robust conversion factor needs to be derived to take into account the conjugated metabolites M14 and M15 in the risk assessment (relevant for all uses evaluated, data gap identified by meeting of experts May 2008, some information is given in column 3 of the evaluation table but it is not peer reviewed, refer to chapter 1).
- Levels of M14 and M15 metabolites should be addressed for rotational crops (relevant for all uses evaluated, data gap identified by meeting of experts May 2008, proposed submission date unknown, refer to chapter 1).

- In the stability study it should be confirmed that the recovery samples were handled in the same way as the analytical method sample and that a significant degradation did not occur in the recovery samples (relevant for all uses evaluated, data gap identified by meeting of experts May 2008, some information was given in addendum 7 but it was not peer reviewed, refer to chapter 1).
- The potential for rotational crop residues and the need for MRLs must be addressed (relevant for all uses evaluated, data gap identified by meeting of experts May 2008, proposed submission date unknown, refer to chapter 1).
- The potential formation of diisopropylamine in soil and contamination of ground water needs to be addressed (this potential metabolite is a known precursor of *N*-nitrosodiisopropilamine (NDIPA) (relevant for all representative uses evaluated; submission date proposed by the applicant: position paper based on public scientific literature already available to the rapporteur Member State, not considered during the peer review on basis of Commission Regulation 1095/2007; refer to chapters 4 and 6).
- A data gap was identified for a study to investigate the aerobic degradation in soil including identification of residues in volatile traps and adequate identification of soil metabolite (this data gap was not considered by the experts' meeting essential to finalise the EU risk assessment of the representative uses proposed; no submission date proposed by the applicant; refer to point 4.1).
- A refinement of the risk for fish-eating mammals is required (this data gap was considered relevant for all representative uses evaluated) submission date proposed by the applicant: unknown refer to point 5.1.
- Information of the potential for biomagnification in aquatic food chains (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; data gap identified by the EFSA after the meeting; refer to point 5.2.
- Further refinement of the long-term risk to earthworms is required (relevant for all representative uses evaluated; submission date proposed by the applicant: the study (Moser, 2006) was submitted in December 2006 but in line with the new Commission Regulation (EC) 1095/2007, new studies could not been considered in the peer review; data gap indentified in the DAR refer to point 5.5).
- To address the potential risk to the soil litter degradation process a new litter bag study is required (This is relevant for all representative uses evaluated. Submission date proposed by the applicant: the rapporteur Member State informed the experts that this study is already completed (Foster 2006), but in line with Commission Regulation (EC) 1095/2007 new studies could not been considered in the peer review; data gap identified in the DAR, refer to point 5.6).

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as proposed by the applicant, which comprise 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, in Northern Europe at a single application at a maximum rate of 2.25 kg a.s./ha.

The representative formulated product for the evaluation was 'Avadex 15G' ('Mon 7966'), a granule (GR) containing 150 g/kg tri-allate, registered under different trade names in Europe.

Adequate analytical methods are available for the determination of tri-allate residues in food of plant origin and in the environmental matrices; however a data gap was set for a monitoring method for residues in food of animal origin.

Sufficient analytical methods as well as methods relating to physical, chemical and technical properties are available to ensure that at least some quality control measurements of the plant protection products are possible.

From the mammalian toxicity studies, classification of tri-allate as **Xn, R22** "**Harmful if swallowed**" was proposed, however acute dermal and inhalation toxicity were low. Tri-allate was not a skin or eye irritant; classification with risk phrase **R43** "**May cause sensitisation by skin contact**" was proposed according to the results of a Magnusson & Kligman test.

Decreased body weight and clinical signs of neurotoxicity were the most common effects found in rats, dogs and hamsters upon short-term administration. Reversible anaemia and liver toxicity were also found in these species, while the liver was the main target organ in mice. Upon long-term exposure, reduced body weight and liver toxicity were still evident, but no potential for carcinogenicity was observed in rat, mouse or hamster. Tri-allate was considered to have no genotoxic potential *in vivo*.

Reproduction toxicity studies reflected the same kind of effects in parents, as in short-term studies. In the 2-generation study, reduced pregnancy rate was associated with parental toxicity and in the developmental study in rat; decreased foetal weight and retarded ossification were linked to maternal toxicity. In the rabbit apparent increase in the incidence of fused sternebrae was observed without maternal toxicity, but considering the low severity of the effect, the meeting agreed not to propose a classification related to developmental toxicity for tri-allate.

No sign indicative of delayed neurotoxicity was found in acute and short-term neurotoxicity studies in hen. Clear signs of neurobehavioural toxicity were seen in an acute and a short-term neurotoxicity studies in rat. No inhibition of cholinesterase activity was detected, but a special investigation showed a strong correlation between the presence of axonal degeneration in the brain and CNS-like behavioural effects caused by tri-allate leading to a proposal for classification with **Xn**, **R48/22** "**Harmful: danger of serious damage to health by prolonged exposure if swallowed**".

The **Acceptable Daily Intake (ADI) of tri-allate was 0.025 mg/kg bw/day**, the **Acceptable Operator Exposure Level (AOEL) was 0.032 mg/kg bw/day** and the **Acute Reference Dose (ARfD) was 0.6 mg/kg bw**.

The estimated level of operator exposure was below the AOEL according to selected data from the Pesticide Handler's Exposure Database (PHED), considering the use of gloves during loading and application of the granules. Worker exposure was not considered relevant for the representative use of tri-allate. Estimated bystander and residential exposure resulting from the use of 'Avadex 15G' was below the AOEL.

Metabolism studies (labelled in the allyl position) were considered in the DAR which showed the residues consisted primarily of tri-allate, TCPSA and metabolites M14 and M15. A provisional residue definition for risk assessment of tri-allate, TCPSA and the glycoside conjugates (M14 and M15) expressed as tri-allate was proposed by the residues expert meeting. The residue definition proposed in the DAR did not include the glycoside conjugates.

In addition, the expert meeting concluded the metabolism could not be finalised because there is a data gap for a wheat study labelled in the diisopropylamine moiety. The meeting identified this data gap to address a concern about the potential formation of nitrosamines from the diisopropylamine moiety in plants. It should be noted that in wheat grain, total metabolites were 0.008 mg/kg (5.10 % of TRR).

In radio-labelled rotational crop studies the residue was made up of tri-allate and TCPSA but it was questioned why M14 and M15 were not looked for. In addition, it was considered that, on the basis of the residue levels in radish roots (at 30 DAA) in these studies, a data gap should be identified for field studies. The primary crop residue trials data in wheat and barley analysed for tri-allate and TCPSA. No accurate conversion factor is available to enable levels of glycoside conjugates to be accounted for.

Residues were seen to be stable in frozen storage for up to 56 months. The need for processing studies is not currently triggered. Intakes by livestock triggered the need for animal metabolism data for ruminants. A goat metabolism study showed the majority of radioactivity was incorporated into

natural compounds. The only possible compounds of significance were tri-allate and TCPSA, and the feeding studies confirmed this.

The risk assessment could not be finalised because of the inclusion of 'glycoside conjugates' in the residue definition. Additionally, the theoretical concern over the formation of nitrosamines has resulted in a data gap for a wheat metabolism study. On this basis no MRLs were proposed by the expert meeting. The risk assessment can not be finalised because of the rotational crop issue amongst others.

Only studies with tri-allate labelled in the allylic position are available in the fate and behaviour section. The need for addressing the metabolites that may result from the diisopropylamine moiety was identified during the peer review and discussed in the PRAPeR meeting. The applicant provided a position paper to clarify this issue. This position paper made use of public scientific literature to select the input parameters for modelling and as part of the consideration for estimating the formation of nitrosamines potentially produced by water treatment. These scientific papers had not been previously submitted in the dossier. In view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to the EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, the new studies could not be considered in the peer review. However the meeting considered that the issue needs to be addressed and therefore identified a data gap to address the potential formation of diisopropylamine in soil and contamination of ground water.

Tri-allate exhibited moderate to medium persistence in soil under dark aerobic conditions at 20 °C ($DissT_{50}$ = 35 – 61 d), however these rates may only be considered as dissipation rates since volatilization contributed to a great extent to the losses observed. Data were reanalyzed by the applicant with ModelMaker (V.4.0.) to separate the degradation and volatilization processes. The calculated degradation rates were in the range of DT_{50} = 38.4 – 75.2 d.

Of the six or seven minor metabolites identified, only TCPSA (max. 3.74 % AR by HPLC and max. 7.38 % AR by TLC) was fully characterized and further addressed for environmental risk assessment. TCPSA exhibited low to moderate persistence under dark aerobic conditions at 20 °C in soil.

Volatiles collected in the organic traps (max. 16.17 % AR after 120 d) of the aerobic degradation experiments were not characterized but were assumed to be tri-allate. Unextractable radioactivity amounted to max. 25.3 % AR at the end of the study (120 DAT). Radioactivity found in the ethanolamine trap (max. 21.2 % AR after 120 d) was assumed to be CO_2. The need for further identification of potentially volatile tri-allate soil metabolites and the characterization of soil metabolites found in the available study had been identified during the peer review. The majority of experts agreed with the rapporteur Member State that it is reasonable to assume that the non-characterised radioactivity in the volatile traps is the active substance. The EU risk assessment of the

representative use proposed could therefore be acceptably concluded without further regard to the characterisation of the volatiles. However some experts considered that it is necessary to confirm the complete route of degradation for national risk assessment and therefore a data gap was identified for a study to investigate the aerobic degradation in soil including identification of residues in volatile organic traps and adequate identification of soil metabolites.

Tri-allate was very highly persistent in soil under anaerobic conditions at 20 °C. Photolysis in soil of tri-allate is almost negligible when compared with aerobic degradation.

A field dissipation study with trials at four different United Kingdom sites is available. Tri-allate exhibited low to high persistence in these trials. The rapporteur Member State assessed the studies as scientifically valid and representative of Northern European conditions. However they proposed using data obtained from laboratory degradation studies for environmental modelling for EU risk assessment due to the potential effect of volatilization on the results of these trials. The DT_{90}'s observed in some of the field dissipation studies were above 1 yr and triggered the need to assess potential of accumulation of tri-allate in soil.

PEC in soil and accumulation of tri-allate in soil were estimated on basis of the worst case field half-life of 205 d. For TCPSA the PEC_{soil} was estimated on basis of the maximum observed in the laboratory studies determined by TLC.

Tri-allate may be considered immobile to slightly mobile in soil according the available study. Metabolite TCPSA may be considered very highly mobile in soil according to the available study.

Tri-allate was stable with regard to hydrolysis at pH 4 and 7 at 50 °C, however it hydrolyses under alkaline conditions. The half-life at 25 °C in the aqueous pH 9 solution was 52 d.

Aqueous photolysis is not expected to contribute to the environmental degradation of tri-allate on basis of the lack of UV absorption at wavelengths above 290 nm.

Biodegradability studies available show that tri-allate is not readily biodegradable.

In the water sediment systems, tri-allate dissipated relatively rapidly from water by partition to the sediment and volatilization. Half-lives of tri-allate in the whole system are 52.8 – 62.0 d. No major metabolites were identified either in the water or in the sediment phases. Mineralization and unextractable residues in the sediment are practically negligible (CO_2 = 1.51 – 4.35 % AR; unextractable in sediment = 2.77 – 3.26 % AR).

$PEC_{SW/SED}$ were calculated for tri-allate and its soil metabolite TCPSA on basis of the FOCUS SW scheme and models for the scenarios relevant to cereals in Northern EU (D1-D5, R1). Since the product is a granular formulation, the applicant proposed spray drift values for the granules based on a specific study. The approach was considered acceptable by the rapporteur Member State and reported as Step 3 calculations. Additional FOCUS Step 4 calculations included spray drift mitigation by buffer zones and run off mitigation by vegetative buffer strips. The method used to implement runoff mitigation is not agreed in the latest FOCUS Landscape and mitigation guidance document and therefore the rapporteur Member State recalculated the Step 4 FOCUS SW without run off mitigation.

Potential ground water contamination by tri-allate and its soil metabolite TCPSA was addressed by modelling calculations with FOCUS PELMO 3.3.2. The rapporteur Member State calculations resulted in 80th percentile annual average concentrations in the leachate at 1 m depth below 0.001 µg/L for tri-allate and in the range of 0.76 – 15.42 µg/L for metabolite TCPSA. The metabolite TCPSA has a clear potential to exceed the trigger of 0.1 µg/L in ground water and requires assessment of its toxicological and ecotoxicological relevance including consumers risk assessment. Relevance of TCPSA was assessed during the peer review following the step-wise procedure set out in the guidance document for relevance of metabolites in ground water (see sections 2.8, 3.3 and 5.2). Tri-allate is a volatile organic compound and studies available indicate that tri-allate displays significant volatilisation from soil surfaces. However on the basis of the atmospheric half-life calculated (DT_{50} = 3.8 h), it is considered unlikely that tri-allate may be subjected to long-range transport.

The acute, short-term and long-term TER estimated for birds and mammals were above the Annex VI trigger values, indicating a low risk for birds and mammals. Tri allate has a log P_{ow} of 4.06, therefore the risk to earthworm-eating birds and mammals was assessed. After a refinement process to refine the potential risk to earthworm-eating mammals, the risk to earthworm-eating birds and mammals was considered as low. The first tier TER values for fish-eating birds and mammals were 7 and 1.9 respectively, indicating a low risk for fish-eating birds, however a potential risk for tri-allate to fish-eating mammals. A data gap has been identified by the EFSA after the PRAPeR 48 to ask to the applicant to submit a new refinement of the potential high risk for fish-eating mammals.

Based on the available studies tri-allate was considered as highly toxic to aquatic organisms. A higher tier risk assessment was conducted with the PEC_{SW} from FOCUS Step 4 with a 10 m buffer zone. All the acute and chronic TER values for drainage as well as for the run off scenarios were above the Annex VI trigger values. A low risk could be identified for aquatic organisms based on the use of mitigation measures, for example a non-spray buffer zone of 10 m. Then risk of the TCPSA metabolite for the aquatic organism is low. The BCF of 1400 was derived from a study with *Lepomis macrochirus*. The EFSA has identified a data gap after the peer review for submission of information for the potential for biomagnification of tri-allate in aquatic food chains.

The acute TER values for earthworms for tri-allate based on maximum initial PEC_{soil} were above the Annex VI trigger values. The chronic TER value was 3.22, was below the Annex VI trigger value. The rapporteur Member State proposed that further information is required on the long-term risk to earthworm. In conclusion, a low acute risk was identified for earthworms however a high chronic risk was identified.

A data gap has been identified for an earthworm field study. A data gap has identified for submission of a new litter bag study.

Risk mitigation measures such as an in-field no spray buffer zone of 10 m was considered necessary for the non-target plants.

The risks for tri-allate was considered to be low to bees, non-target arthropods, soil non-target micro-organisms and for biological methods of sewage treatment.

Particular conditions proposed to be taken into account to manage the risk(s) identified

- Operator exposure was estimated to be below the AOEL if personal protective equipment (PPE) as protective gloves during loading and application of the granules are worn, according to selected data from the Pesticide Handler's Exposure Database (PHED) (refer to point 2.12).
- Non-spray buffer zone of 10 m to aquatic organisms (refer to point 5.2).
- Non-spray buffer zone of 10 m to non-target plants (refer to point 5.8).

Critical areas of concern

- The risk assessment can not be finalised. The main issue being that the primary plant metabolism data is not complete.
- Soil metabolite TCPSA may reach levels above 10 μg/L in groundwater in vulnerable scenarios.
- Potential soil metabolite diisopropylamine, not assessed due to the lack of pertinent labelling, is known to be a precursor of nitrosamines.
- The risk to fish-eating mammals needs further refinement.
- Potential for biomagnification in aquatic food chains needs to be addressed.
- Long-term risk to earthworms needs further refinement.
- Potential risk to the soil litter degradation process needs to be addressed.

APPENDIX 1 – LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

(Abbreviations used in this list are explained in appendix 2)

Identity, Physical and Chemical Properties, Details of Uses, Further Information

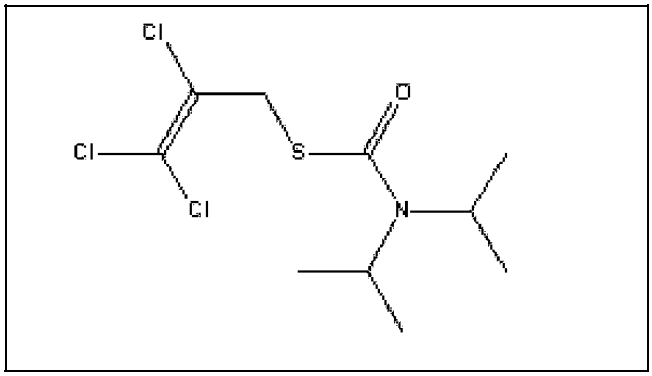
Active substance (ISO Common Name) ‡	Tri-allate
Function (*e.g.* fungicide)	Herbicide
Rapporteur Member State	UK
Co-rapporteur Member State	None

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	*S*-2,3,3-trichloroallyl di-isopropyl (thiocarbamate); *S*-2,3,3-trichloroallyl di-isopropylthiocarbamate
Chemical name (CA) ‡	*S*-(2,3,3-trichloro-2-propenyl) bis(1-methylethyl) carbamothioate
CIPAC No ‡	97
CAS No ‡	2303-17-5
EC No (EINECS or ELINCS) ‡	218-962-7
FAO Specification (including year of publication) ‡	None
Minimum purity of the active substance as manufactured ‡	940 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	NDIPA (Nitroso-diisopropylamine) max. 0.02 mg/kg
Molecular formula ‡	$C_{10}H_{16}Cl_3NOS$
Molecular mass ‡	304.7 g/mol

Appendix 1 – List of endpoints

Structural formula ‡



Appendix 1 – List of endpoints

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	33.5 - 34.1 °C (99.8% w/w)
Boiling point (state purity) ‡	279 °C (99.8% w/w) (degradation occurs before boiling)
Temperature of decomposition (state purity)	260 – 330 °C (100% w/w)
Appearance (state purity) ‡	White crystalline solid (99.8% w/w)
	Dark brown glassy solid (95.6% w/w – technical grade)
Vapour pressure (state temperature, state purity) ‡	0.012 Pa at 20 °C (100% w/w) 0.023 Pa at 25 °C (100% w/w)
Henry's law constant ‡	0.89 Pa m^3 mol^{-1} at 20°C
Solubility in water (state temperature, state purity and pH) ‡	0.0041 g/L at 20°C (pH 7) (98.5% w/w)
Solubility in organic solvents ‡ (state temperature, state purity)	Solubility at 20°C in g/L (99.8% w/w): acetone >500 1,2-dichloroethane: >500 ethanol: >500 ethyl acetate: > 500 heptane: > 500 methanol: 500 xylene: > 500
Surface tension ‡ (state concentration and temperature, state purity)	49.0 mN/m at 20°C (90% saturated solution) (98.5% w/w)
Partition co-efficient ‡ (state temperature, pH and purity)	log $P_{O/W}$ = 4.06 ±0.78 at 21°C (pH 7.03 (98.5% w/w) log $P_{O/W}$ = 4.57 (calculated using EPI-suite 3.2)
Dissociation constant (state purity) ‡	No dissociation could be observed (titration method or UV-spectrophotometric method) (99.9% w/w)
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	No absorption maxima between 210 nm and 900 nm were recorded under alkaline (90/10 (v/v) methanol/water; [NaOH]=0.1 N), neutral (methanol), and acidic (90/10 (v/v) methanol/water; [HCl]=0.1 N) conditions (99.8% w/w)
Flammability ‡ (state purity)	Not highly flammable (95.6% w/w) Auto-flammable (auto-ignition temperature of 360 °C) (95.6% w/w)
Explosive properties ‡ (state purity)	Not explosive (95.6% w/w)
Oxidising properties ‡ (state purity)	Not oxidizing (Statement)

Appendix 1 – List of endpoints

Summary of representative uses evaluated (Tri-allate)*

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	g as/hL min – max (l)	water L/ha min – max	kg as/ha min – max (l)		
Cereals (barley and wheat)	Northern Europe	Avadex 15G Mon 7966	F	weeds	GR	150 g/kg	broad-cast applica-tion	post-sowing, pre-emergence of crop	1	nr	nr	nr	2.25	nr	Commercial harvest [1]

[1} Consumer risk assessment can not be finalised.

* For uses where the column "Remarks" is marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s).
(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 suckling 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. fluoroxypyr). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-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 pre-harvest interval

Appendix 1 – List of endpoints

Methods of Analysis

Analytical methods for the active substance (Annex IIA, point 4.1)

Technical as (analytical technique)	GC-FID
Impurities in technical as (analytical technique)	GC-MS, GC-NPD
Plant protection product (analytical technique)	GC-FID

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Tri-allate
Food of animal origin		Tri-allate and TCPSA expressed as tri-allate
Soil		Tri-allate
Water	surface	Tri-allate
	drinking/ground	Tri-allate + TCPSA
Air		Tri-allate

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	Tri-allate: GC-MS (LOQ = 0.01 mg/kg) cereal grain) or (LOQ = 0.02 mg/kg (barley and wheat straw). TCPSA: HPLC-MS/MS – 0.01 mg/kg cereal grain)
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Open
Soil (analytical technique and LOQ)	Tri-allate: GC-MS (LOQ 0.01 mg/kg) TCPSA: HPLC with MS/MS (LOQ 0.005 mg/kg)
Water (analytical technique and LOQ)	Tri-allate: GC-MS (LOQ 0.05 µg/L) TCPSA: HPLC-MS/MS (LOQ = 0.1 µg/L)
Air (analytical technique and LOQ)	Tri-allate: GC-MS (LOQ 1.83 µg/m3)
Body fluids and tissues (analytical technique and LOQ)	Not required as the active is not classified as toxic or highly toxic.

Appendix 1 – List of endpoints

Classification and proposed labelling with regard to physical and chemical data (Annex IIA, point 10)

	RMS/peer review proposal
Active substance	None

Appendix 1 – List of endpoints

Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism (toxicokinetics) (Annex IIA, point 5.1)

Rate and extent of oral absorption ‡	Rapidly absorbed after an oral dose. Urinary radiolabel mostly eliminated within 6 h after a low dose. Evidence for complete absorption considered to be inconclusive and hence estimate of 50% based on rat data.
Distribution ‡	Rapidly and widely distributed into organs and tissues. Highest concentrations in blood cells followed by spleen.
Potential for accumulation ‡	Limited potential. Very low retention, however, evidence of covalent binding to blood cells considered responsible for prolonged beta phase of elimination.
Rate and extent of excretion ‡	Rapidly and almost completely eliminated except for blood cells (2% of applied dose after 10 days) In the rat, up to 80% of the major metabolite were eliminated in faeces or urine within 6 h after oral dose of 5 mg/kg bw.
Metabolism in animals ‡	Extensively metabolised. No parent found in urine and <10% in faeces after a low dose in rats.
Toxicologically relevant compounds ‡ (animals and plants)	Parent and TCPSA
Toxicologically relevant compounds ‡ (environment)	Parent (TCPSA is not relevant in ground water)

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	1100 mg/kg bw	**R22**
Rat LD_{50} dermal ‡	> 5000 mg/kg bw	
Rat LC_{50} inhalation ‡	> 5.3 mg/L air (4 hours, whole body, as aerosol atmosphere)	
Skin irritation ‡	Not irritating	
Eye irritation ‡	Not irritating	
Skin sensitisation ‡	Sensitising in Magnusson & Kligman study, but not sensitising in 9-induction Buehler method study	**R43**

Appendix 1 – List of endpoints

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Neurotoxicity in rats, dogs and hamsters; slight to moderate anaemia in rats, hamsters, mice and dogs	
Relevant oral NOAEL ‡	6.4 mg/kg bw/day in rats (90-day neurotoxicity study) 12 mg/kg bw/day in dogs (8-week capsule study) 2.5 mg/kg bw/day in dogs (1-year capsule study) 11.5 mg/kg bw/day in mice (8-week feeding study) 43.2 mg/kg bw/day in hamster (90-day feeding study)	
Relevant dermal NOAEL ‡	Systemic NOAEL: 300 mg/kg bw/day Local LOAEL: 60 mg/kg bw/day based on 21-day dermal study in rabbit	
Relevant inhalation NOAEL ‡	0.03 mg/L air (equivalent to 10.4 mg/kg bw/day) based on 7-week inhalation study in rats	

Genotoxicity ‡ (Annex IIA, point 5.4)

Tri-allate is unlikely to be genotoxic	

Appendix 1 – List of endpoints

Long term toxicity and carcinogenicity (Annex IIA, point 5.5)

Target/critical effect ‡	Rat: Reduced mean body weight and reduced body weight gain in male rats but not in females; increased incidence of chronic progressive nephropathy with slightly increased severity in males, considered most likely due to alpha2µ-globulin accumulation. Mice: increased liver weight, eosinophilic foci in liver, mineralisation in brain and cornea of the eyes, degeneration in the spinal cord. Hamster: flaking/scaly skin, reduced body weight gain and food consumption, liver toxicity, reduced spleen weight.	
Relevant NOAEL ‡	2.5 mg/kg bw/day in rats (2-year, feeding study) 12.4 mg/kg bw/day in mice (2-year, feeding study) 16.2 mg/kg bw/day in hamster (79-95 weeks feeding study)	
Carcinogenicity ‡	Tri-allate is unlikely to pose carcinogenic risk to humans: Kidney tubular cell tumours in male rats with clear NOEL. Kidney toxicity in male rats considered to be mediated by alpha2µ-globulin mechanism. Apparent increased hepatocellular carcinomas and adenomas in mice within historical control	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Parents: Reduced body weight during lactation in F0 & F1 dams Reproductive: Reduced pregnancy rate in F1 females at 2nd mating. Offspring's: Reduced pup birth weights and pre-weaning weights	
Relevant parental NOAEL ‡	7.7 mg/kg bw/day	
Relevant reproductive NOAEL ‡	7.7 mg/kg bw/day	
Relevant offspring NOAEL ‡	7.7 mg/kg bw/day	

Appendix 1 – List of endpoints

Developmental toxicity

Developmental target / critical effect ‡	Rat: Maternal: reduced body weight and food consumption Foetal: reduced birth weight and retarded ossification. Rabbit: Maternal: Reduced body weight gain during gestation. Foetal: Reduced body weights and increased incidence of fused sternebrae No classification proposed	
Relevant maternal NOAEL ‡	Rat: 30 mg/kg bw/day Rabbit: 15 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 30 mg/kg bw/day Rabbit: 5 mg/kg bw/day	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	NOAEL: 60 mg/kg bw	
Repeated neurotoxicity ‡	Nerve degeneration at 33 mg/kg bw/day (in 90-day neurotoxicity study in rat) NOAEL: 6.4 mg/kg bw/day	**Xn, R 48/22**
Delayed neurotoxicity ‡	No evidence of delayed neurotoxicity	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	Tri-allate has no cholinesterase activity. Evaluation of alpha2-µglobulin in rat kidney. Developmental neurotoxicity in rat: No developmental neurotoxic effects were observed, NOAEL: 30 mg/kg bw/day, based on reduced maternal and pups body weights

Appendix 1 – List of endpoints

Studies performed on metabolites or impurities ‡	TCPSA: The acute oral LD_{50} of TCPSA in female rats was > 2000 mg/kg bw. There was no evidence of genotoxicity in the *Salmonella typhimurium* reverse mutation assay, in an *in vitro* chromosome aberration test in Chinese hamster V79 cells and in Cell mutation assay at the thymidine kinase locus in mouse lymphoma L5178Y cells. In a 14-day range-finding study, TCPSA-Na salt did not provide any toxicity up to 1413 mg/kg bw/day when administered to rats for 14-days. Clinical chemistry, haematology or microscopic examination of organs and tissues were not performed.

Medical data ‡ (Annex IIA, point 5.9)

Cross-sectional occupational study did not show any association between tri-allate exposure and the measures of neurological function.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.025 mg/kg bw/day	2-year study in rats	100
AOEL ‡	0.032 mg/kg bw/day	90-day neurotoxicity study	200* (100 + 50 %)*
ARfD ‡	0.6 mg/kg bw	acute neurotoxicity study	100

* Correction factor for low oral absorption of 50 %

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (e.g. Avadex 15G)	12% dermal absorption (concentrate and spray dilution) based on an *in vivo* monkey study using a 480 g/l EC formulation.

Appendix 1 – List of endpoints

Exposure scenarios (Annex IIIA, point 7.2)

Operator	Operator exposure estimates using selected data from the Pesticide Handlers' Exposure Database (PHED): Tractor-mounted or trailed granule-placement equipment: % of AOEL With PPE (gloves during loading and application) 72 %
Workers	As 'Avadex 15G' will be applied only as a pre-emergence treatment, there will be no foliar residues of tri-allate to which workers entering a treated crop could be exposed. Exposure is considered to be negligible.
Bystanders	Estimates of bystander exposure to tri-allate vapour following the application of 'Avadex 15G' based on published field study data and measurements in a field study (unprotected) represents 7 % of the AOEL; Based on field measurements of drift deposition and published EPA residential exposure values, exposure of children represents 20 % of the AOEL.

Classification and proposed labelling with regard to toxicological data (Annex IIA, point 10)

	RMS/peer review proposal
Substance classified (tri-allate)	Xn, R22 "Harmful if swallowed"; R43 "May cause skin sensitisation by skin contact"; Xn, R48/22 "Harmful: danger of serious damage to health by prolonged exposure if swallowed"

Appendix 1 – List of endpoints

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

Plant groups covered	Open
Rotational crops	Cereal (wheat), leafy (lettuce), root (radish). Replant intervals: 30, 150, 365 days. Open for the conjugates.
Metabolism in rotational crops similar to metabolism in primary crops?	Broadly similar: tri-allate and metabolite TCPSA found. In addition: a polar unknown characterised as polysaccharide.
Processed commodities	Open
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Not studied. Residues in consumable crop <LOQ.
Plant residue definition for monitoring	Tri-allate only.
Plant residue definition for risk assessment	Total of tri-allate + TCPSA + glycoside conjugates expressed as tri-allate (provisional).
Conversion factor (monitoring to risk assessment)	Open

Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

Animals covered	Goat only
Time needed to reach a plateau concentration in milk and eggs	3 days (goat milk)
Animal residue definition for monitoring	Tri-allate and TCPSA expressed as tri-allate
Animal residue definition for risk assessment	Tri-allate and TCPSA expressed as tri-allate
Conversion factor (monitoring to risk assessment)	Not required
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	No

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

Open

Appendix 1 – List of endpoints

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 Introduction)

Tri-allate and TCPSA (grain and straw): 18 months for 0.1mg/kg fortified residues. Up to 56 months for incurred residues ≥0.01mg/kg

Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

Intake by livestock ≥0.1mg/kg diet / day		Ruminant: yes	Poultry: no	Pig: no
		Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)		Open	no	no
Potential for accumulation (yes/no):		Tri-allate and TCPSA: no	Tri-allate and TCPSA: no	Tri-allate and TCPSA: no
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)		no	no	no
		Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) 10mg/kg diet cattle and poultry. Open for feeding rate Residue levels in matrices : Mean (max) mg/kg		
Muscle		Tri-allate (< 0.01) TCPSA (<0.01)	Tri-allate (< 0.01) TCPSA (<0.01)	Tri-allate (< 0.01) TCPSA (<0.01)
Liver		Tri-allate (< 0.01) TCPSA (<0.01)	Tri-allate (< 0.01) TCPSA (<0.01)	Tri-allate (< 0.01) TCPSA (<0.01)
Kidney		Tri-allate (< 0.01) TCPSA (0.05)	Tri-allate (< 0.01) TCPSA (<0.01)	Tri-allate (< 0.01) TCPSA (0.03)
Fat	Perirenal (Highest residues)	Tri-allate (0.03) TCPSA (0.15)	Tri-allate (0.04) TCPSA (<0.01)	Tri-allate (<0.01) TCPSA (<0.01)
Milk		Tri-allate (<0.01) TCPSA (<0.01)		
Eggs				

Appendix 1 – List of endpoints

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)			Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Wheat	NE		**Tri-allate**	**TCPSA**	Grain Straw	0.02 0.1	0.01 0.12 (Tri-allate)	0.01 0.05
		Grain	8x<0.01	8x <0.01				
		Straw	7x<0.05 0.12	7x <0.05 0.11				
Barley	NE		**Tri-allate**	**TCPSA**	Grain Straw	0.02 0.1	0.01 0.23 (TCPSA)	0.01 0.05
		Grain	4x<0.01	4x <0.01				
		Straw	0.05 0.09 0.10 0.12	3x <0.05 0.23				

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17
(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the representative use
(c) Highest residue

Appendix 1 – List of endpoints

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

ADI	0.025 mg/kg bw/day
TMDI (% ADI) according to WHO European diet	Open
TMDI (% ADI) according to national (to be specified) diets	Open
IEDI (WHO European Diet) (% ADI)	Open
NEDI (specify diet) (% ADI)	Open
Factors included in IEDI and NEDI	Open
ARfD	0.6 mg/kg bw/day
IESTI (% ARfD)	Open
NESTI (% ARfD) according to national (to be specified) large portion consumption data	Open
Factors included in IESTI and NESTI	Open

Processing factors (Annex IIA, point 6.5, Annex IIIA, point 8.4)

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
Barley grain	None	n/a	n/a	n/a
Wheat grain	None	n/a	n/a	n/a
Not determined. Not required due to low residues in grain (<0.01mg/kg)				

Appendix 1 – List of endpoints

Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6)

Wheat (grain)	Open
Barley (grain)	Open

When the MRL is proposed at the LOQ, this should be annotated by an asterisk after the figure.

Appendix 1 – List of endpoints

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

Mineralization after 100 days ‡	19.34 – 43.98 % after 120 d at 20 °C; [^{14}C-allyl]-label (n^{20}= 4) 17.36 % after 120 d at 10 °C; [^{14}C-allyl]-label (n= 1)
Non-extractable residues after 100 days ‡	25.29 – 35.92 % after 120 d at 20 °C; [^{14}C-allyl]-label (n= 4) 19.47 % after 120 d at 10 °C; [^{14}C-allyl]-label (n= 1)
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	**HPLC ANALYSIS** TCPSA – 1.56 – 3.74 % at 16 - 120 d at 20 °C (n= 4). TCPSA – 3.04 % at 64 d at 10 °C (n= 1). [^{14}C-allyl]-label **TLC ANALYSIS** TCPSA – 2.82 – 7.38 % at 4 – 120 d at 20 °C (n= 4). TCPSA – 6.54 % at 64 d at 10 °C (n= 1). [^{14}C-allyl]-label

Route of degradation in soil - Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation ‡	
Mineralization after 100 days	3.6 % after 126 d, [^{14}C-allyl]-label (n= 1)
Non-extractable residues after 100 days	12.0 % after 126 d, [^{14}C-allyl]-label (n= 1)
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	None
Soil photolysis ‡	
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	None

[20] n corresponds to the number of soils.

Appendix 1 – List of endpoints

Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

Laboratory studies ‡

Parent	Aerobic conditions					
Soil type	pH	t. °C / % MWHC	DT_{50} / **DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Niven Sandy Loam	6.6 (water) 5.4 (KCl)	20 °C / 40 % MWHC	63.2 / 209.9	63.2	0.99	SFO*
Holms 2 Clay Loam	6.9 (water) 6.7 (KCl)	20 °C / 40 % MWHC	38.4 / 127.4	35.1	0.99	SFO*
Genoch 2 Sandy Loam	6.7 (water) 5.9 (KCl)	20 °C / 40 % MWHC	69.3 / 230.1	69.3	0.88	SFO*
Dalcairnie Silt Loam	7.1 (water) 6.6 (KCl)	20 °C / 40 % MWHC	75.2 / 249.8	75.2	0.99	SFO*
Niven Sandy Loam	6.6 (water) 5.4 (KCl)	10 °C / 40 % MWHC	112.3 / 373.2	Not determined	1.00	SFO*
Geometric mean/median		20 °C / 40 % MWHC	59.6 / 198.0	58.3	N / A	N / A

*DT_{50}'s were calculated separately for volatilisation, degradation, etc. using first order degradation kinetics. The DT_{50} values quoted represent degradation only.
**DT90's were extrapolated beyond the study duration

Appendix 1 – List of endpoints

TCPSA	Aerobic conditions					
Soil type	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d) †	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
BBA 2.2 Loamy Sand	5.3 ($CaCl_2$)	20 °C / 45 % MWHC	15.6 / 51.7	15.6	0.99	SFO
BBA 2.3 Sandy Loam	5.8 ($CaCl_2$)	20 °C / 45 % MWHC	40.1 / 133.1 (ext)	34.2	0.97	SFO
BBA 3A Loam	7.3 ($CaCl_2$)	20 °C / 45 % MWHC	9.0 / 29.9	6.84*	0.93	SFO
Geometric mean/median		20 °C / 45 % MWHC	17.8 / 59.0	15.4*	N / A	N / A

* It should be noted that a value of 16.85 days for the mean DT50 for TCPSA at 20°C and pF2 was used in modelling in volume 3 and is reported elsewhere in this list of endpoints. This difference arose as originally correction was not made for the soil BBA 3A loam. The difference between the two values is not considered to significantly affect PECgw and PECsw values for TCPSA. Additionally, if an effect were to be observed from using 16.85d in place of 15.4 d, it would that PEC values for TCPSA would be increased, and its use is therefore a worse-case.

Field studies ‡

Tri-allate	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	Org. Carbon (%)	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (r^2)	DT_{50} (d) Norm.	Method of calculation
Evesham Silty Sand – Bare soil	UK	1.32	7.5	30	10	32	0.90	N/ A	SFO
Bedford Loamy Sand – Bare soil	UK	3.81	7.1	30	158	524	0.93	N / A	SFO
Stratford Loamy Sand – Bare soil	UK	1.79	7.0	30	27	91	0.72	N / A	SFO
Catthorpe Silty Sand – Bare soil	UK	2.77	6.6	30	92	307	0.76	N / A	SFO
Evesham Silty Sand – Cultivated	UK	1.32	7.5	30	56	186	0.80	N / A	SFO
Bedford Loamy Sand – Cultivated	UK	3.81	7.1	30	205	682	0.79	N / A	SFO
Stratford Loamy Sand – Cultivated	UK	1.79	7.0	30	8	27	0.72	N / A	SFO

Appendix 1 – List of endpoints

Field studies ‡

Tri-allate	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	Org. Carbon (%)	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (r^2)	DT_{50} (d) Norm.	Method of calculation
Catthorpe Silty Sand - Cultivated	UK	2.77	6.6	30	56	186	0.91	N / A	SFO
Geometric mean					46	153	N/A	N/A	N/A

pH dependence ‡ (yes / no) (if yes type of dependence)	No.
Soil accumulation and plateau concentration ‡	No study performed. Theoretical calculated values available below.

Appendix 1 – List of endpoints

Laboratory studies ‡

Tri-allate	Anaerobic conditions					
Soil type	pH ($CaCl_2$)	t. °C / % MWHC	DT_{50} / DT_{90} (d) *	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy Loam	6.07	20 °C / flooded soil	277 / 921	N/A	0.95	SFO
Geometric mean/median						

* DT50's and DT90's represent dissipation rather than true degradation rates.

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Tri-allate ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Speyer 2.2 Loamy Sand	2.17	5.7	N/A	N/A	92.4	4257	0.95
Senozan Silt Loam	1.0	5.8	N/A	N/A	38.5	3853	0.93
Itingen Clay	2.63	7.0	N/A	N/A	63.6	2416	0.93
Spra 02 Sand	0.21	7.5	N/A	N/A	15.5	7399	0.95
Lynsted Clay Loam	1.81	5.0	N/A	N/A	64.8	3582	0.94
Arithmetic mean					55.0	4301	0.94
pH dependence, Yes or No			No				

TCPSA ‡							
Soil Type	OC %	Soil pH ($CaCl_2$)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Mechtildhausen Loam	1.28	7.4	N/A	N/A	0.06	4.4	1.03
Mussig Clay Loam	2.98	7.6	N/A	N/A	0.02	0.5	0.91
Bretagne Silt Loam	2.00	5.4	N/A	N/A	0.06	2.9	1.09
Arithmetic mean/median					0.05	2.6	1.01
pH dependence (yes or no)			No				

Appendix 1 – List of endpoints

Mobility in soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

Aged residues leaching ‡	Aged for (d): 30 d Time period (d): 2 d Eluation (mm): 200 mm
	Analysis of soil residues post ageing (soil residues pre-leaching): 84.3 % tri-allate 90.9 % total radioactivity retained in top 2 cm
	Leachate: 0.86 % total radioactivity in leachate 82.9 % total radioactivity retained in top 3 cm

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	DT_{50} (d): 205 days Kinetics: SFO Field or Lab: representative worst case from field dissipation studies.
Application data	Crop: wheat Depth of soil layer: 5cm Soil bulk density: 1.5g/c**M3** % plant interception: Pre-emergence therefore no crop interception Number of applications: 1 Interval (d): N/A Application rate(s): 2250 g as/ha

Appendix 1 – List of endpoints

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average
Initial	3.000	
Short term 24h	2.990	2.995
2d	2.980	2.990
4d	2.960	2.980
Long term 7d	2.930	2.965
28d	2.729	2.862
50d	2.533	2.760
100d	2.139	2.545
Plateau concentration	1.232 mg/kg after 7 yr	

Route and rate of degradation in water (Annex IIA, point 7.2.1)

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	pH 4: No significant degradation at 50 °C after 5 days
	pH 7: No significant degradation at 50 °C after 5 days
	pH 9: DT50 = 52 d at 25 °C (1st order) M1: 9.8 % AR (30 d)
Photolytic degradation of active substance and metabolites above 10 % ‡	Tri-allate does not exhibit absorption above 290 nm and therefore an aqueous photolysis study was not required.
Quantum yield of direct phototransformation in water at Σ > 290 nm	No value reported
Readily biodegradable ‡ (yes/no)	No.

Appendix 1 – List of endpoints

Degradation in water / sediment

Tri-allate	Distribution (max in water 91.3 % after 1 d. Max. in sed 51.0 % after 7d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.**	St. (r^2)	DT_{50}-DT_{90} water*	St. (r^2)	DT_{50}-DT_{90} sed*	St. (r^2)	Method of calculation
Sandy Loam	8.3†	N/R	20	62.0 / 206	0.95	76.6 / 255	0.95	207 / 687	0.95	SFO
Clay Loam	8.8†	N/R	20	52.8 / 175	0.90	131 / 427	0.90	215 / 714	0.90	SFO
Arithmetic Mean			20	57.4 / 191		104 / 341		211 / 701		N/A

†pH values for the beginning of the study, pH's at the end of the study were 7.5 and 8.4 for the sandy loam and clay loam respectively.
N/R = Not reported
*DT_{50}'s were calculated separately using first order degradation kinetics for volatilisation, degradation, etc. and are therefore relevant DT_{50} values.
**DT_{50} and DT_{90} values quoted for the whole system represent dissipation rather than true degradation due to losses by volatilisation. Whole system degradation values are between those for water and sediment individually.

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization x % after 100 d. (end of the study).	Non-extractable residues in sed. max x % after n d	Non-extractable residues in sed. max x % after 100 d (end of the study)
Sandy Loam	8.3†	N/R	4.35	3.26 (100 d)	3.26
Clay Loam	8.8†	N/R	1.51	2.77 (100 d)	2.77

N/R = Not reported
†pH values for the beginning of the study, pH's at the end of the study were 7.5 and 8.4 for the sandy loam and clay loam respectively

Appendix 1 – List of endpoints

PEC (surface water) and PEC sediment (Annex IIIA, point 9.2.3)

Parent: tri-allate Parameters used in FOCUSsw step 1 and 2	Version control no. of FOCUS calculator: FOCUS STEPS 1-2 Vers. 1.1 Molecular weight (g/mol): 304.7 Water solubility (mg/L): 4.1 at 20 °C K_{OC} (L/kg): 4301.4 DT_{50} soil (d): 58.2 days (geomean from lab studies. NB 56 days from median field data was proposed by the notifier and accepted by the RMS for step 2 calculation only) DT_{50} water/sediment system (d): 68.2 days (mean proposed by notifier from sediment/water studies and accepted by RMS as a conservative value) DT_{50} water (d): 103.8 (mean from sediment water studies - degradation) DT_{50} sediment (d): 210.9 (mean from sediment water studies - degradation) Crop interception (%): 0
Parameters used in FOCUSsw step 3	Version control no. of FOCUS software: FOCUS SWASH 1.1 FOCUS MACRO 4.4.2 FOCUS PRZM SW 1.1.1 FOCUS TOXSWA 1.1.1 Vapour pressure: 0.012 Pa. Koc: 4301.4 mL/g 1/n: 0.94 (Freundlich exponent general) Amendments to account for granular formulation: Drift to ditch (1.5 m) – 12.62 mg / m^3 Drift to stream (2.0 m) – 6.264 mg / m^3 Drift to pond – 0.492 mg / m^3 (standard drift value) CAM = 6 DEPI = 1
Parameters used in FOCUSsw step 4	Mitigation by use of either a 10 m grassed buffer strip (for granular application without deflector plates) or a 5 m grassed buffer strip (for granular application with deflector plates) for ditch and stream scenarios, to mitigate run-off and drift. Amendments: Drift to ditch – 0.225 mg / m^3 Drift to stream – 0.270 mg / m^3 *Run-off 5 m buffer – 50 % input reduction *Run-off 10 m buffer – 90 % input reduction

Appendix 1 – List of endpoints

Application rate	Crop: Winter Cereals** Crop interception: 0 % Number of applications: 1 Interval (d): N/A Application rate(s): 2250 g as/ha Application window: Earliest application 3 weeks prior to emergence; 30 day window.

*Reductions based on Winkler, R (2001)
** NB. For Steps 1 and 2 the Crop type selected was 'pome / stone fruit, late appl.' because the drift input 15.7 % is nearer to that shown for granular formulations in the study of Bailey, 2002. 15.7 % cf. 13.43 % at 1 m.

FOCUS STEP 3 Scenario	Water body	Maximum PEC_{SW} (µg/L)	Maximum PEC_{SED} (µg/kg)
D1 (Lanna)	Ditch	41.837	86.136
D1 (Lanna)	Stream	20.391	11.773
D2 (Brimstone)	Ditch	41.883	88.831
D2 (Brimstone)	Stream	20.765	44.619
D3 (Vreedepeel)	Ditch	41.177	19.079
D4 (Skousbo)	Pond	0.489	2.112
D4 (Skousbo)	Stream	19.927	4.158
D5 (La Jailliere)	Pond	0.489	2.234
D5 (La Jailliere)	Stream	21.498	5.777
R1 (Weiherbach)	Pond	0.858	7.497
R1 (Weiherbach)	Stream	15.148	14.495

Appendix 1 – List of endpoints

FOCUS STEP 4 Scenario	Water body	Maximum PEC_{SW} (µg/L)		Maximum PEC_{SED} (µg/kg)	
D1 (Lanna)	Ditch	0.746		2.199	
D1 (Lanna)	Stream	0.878		1.234	
D2 (Brimstone)	Ditch	0.752		2.072	
D2 (Brimstone)	Stream	0.896		2.175	
D3 (Vreedepeel)	Ditch	0.733		0.347	
D4 (Skousbo)	Pond	See Step 3		See Step 3	
D4 (Skousbo)	Stream	0.858		0.181	
D5 (La Jailliere)	Pond	See Step 3		See Step 3	
D5 (La Jailliere)	Stream	0.926		0.252	
		5 m Buffer	10 m Buffer	5 m Buffer	10 m Buffer
R1 (Weiherbach)	Pond	See Step 3	See Step 3	See Step 3	See Step 3
R1 (Weiherbach)	Stream	2.638r	0.833d	11.138	11.138

d: main input via drift
r: main input via runoff

Appendix 1 – List of endpoints

FOCUS STEP 4 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
D2 (Brimstone)	Ditch	0 h	0.752		2.072	
		24 h	0.621	0.683	2.015	2.070
		2 d	0.519	0.625	1.954	2.065
		4 d	0.375	0.533	1.829	2.049
		7 d	0.249	0.436	1.674	2.013
		14 d	0.045	0.284	1.455	1.895
		21d	0.026	0.201	1.316	1.777
		28 d	0.026	0.159	1.320	1.679
		42 d	0.191	0.121	1.275	1.560
		50 d	0.020	0.110	1.205	1.524
		100 d	0.014	0.069	1.070	1.362

Appendix 1 – List of endpoints

Metabolite - TCPSA Parameters used in FOCUSsw step 1 and 2	Version control no. of FOCUS calculator: FOCUS STEPS 1-2 Vers. 1.1 Molecular weight (g/mol): 247.46 Maximum observed: 3.74 % (soil aerobic degradation) Water solubility (mg/L): 1000 (assumed as a worst-case) K_{OC} (L/kg): 2.6 DT_{50} soil (d): 16.85 days (Geomean from soil aerobic degradation studies – corrected for moisture content) DT_{50} water/sediment system (d): 1000 days (assumed as a worst-case) DT_{50} water (d): 1000 (assumed as a worst-case) DT_{50} sediment (d): 1000 (assumed as a worst case)
Application rate	Application / crop type: no drift (incorporation or seed treatment)* Crop interception: 0 % Number of applications: 1 Interval (d): N/A Application rate(s): 2250 g as/ha Region and Season of application: Northern Europe; Oct – Feb**

* incorporation or seed treatment scenario was chosen because it represent worst-case as no drift, i.e. no loss of tri-allate prior to TCPSA formation is assumed
** Only autumn/winter scenario was chosen because this represents worst-case scenario with regard to run-off/drainage inputs

Appendix 1 – List of endpoints

Time after maximum concentration [days]	PECsw TCPSA [µg/L]		PECsed TCPSA [µg/kg]	
	Actual	TWA	Actual	TWA
0	9.63	-	0.25	-
1	9.62	9.63	0.25	0.25
2	9.62	9.62	0.25	0.25
4	9.60	9.62	0.25	0.25
7	9.58	9.61	0.25	0.25
14	9.54	9.58	0.25	0.25
21	9.49	9.56	0.25	0.25
28	9.44	9.54	0.25	0.25
42	9.35	9.49	0.24	0.25
50	9.30	9.46	0.24	0.25
100	8.98	9.30	0.23	0.24

TWA: time-weighted average

PEC (ground water) (Annex IIIA, point 9.2.1)

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	For FOCUS gw 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 DT_{50lab}: 58.2 d (normalised to 10kPa or pF2, 20 °C with Q10 of 2.2). Tri-allate K_{OC}: arithmetic mean = 4301 (Kom = 2495), $^1/_n$= 0.94. Geometric mean TCPSA DT_{50lab}: 16.9 d* (normalised to 10kPa or pF2, 20 °C with Q10 of 2.2). TCPSA K_{OC}: arithmetic mean = 2.6 (Kom = 1.51), $^1/_n$= 1.01. TCPSA formation fraction: 30 %.

Appendix 1 – List of endpoints

Application rate	Application rate: 2250 g tri-allate/ha. No. of applications: 1 Time of application (month or season): 1 week prior to emergence (winter)

**The correct value should be 15.4 d but 16.9 d was used in modelling with FOCUS PELMO. The RMS considers that this small difference is not significant. The correct value of 15.4 d was used in modelling with FOCUS PEARL.*

PEC(gw) - FOCUS modelling results (80th percentile annual average concentration at 1m)

	Scenario	Tri-allate (µg/L)	Metabolite (µg/L)		
			TCPSA		
PELMO 3.3.2 / Winter Cereals	Chateaudun	< 0.001	1.679		
	Hamburg	< 0.001	6.840		
	Jokioinen	< 0.001	15.417		
	Kremsmunster	< 0.001	2.344		
	Okehampton	< 0.001	6.956		
	Piacenza	< 0.001	2.364		
	Porto	< 0.001	5.787		
	Sevilla	< 0.001	0.765		
	Thiva	< 0.001	0.915		

	Scenario	Tri-allate (µg/L)	Metabolite (µg/L)		
			TCPSA		
PEARL 3.3.3 / Winter Cereals	Chateaudun	< 0.001	6.535		
	Hamburg	< 0.001	20.242		
	Jokioinen	< 0.001	31.292		
	Kremsmunster	< 0.001	10.371		
	Okehampton	< 0.001	14.873		
	Piacenza	< 0.001	6.818		
	Porto	< 0.001	5.795		
	Sevilla	< 0.001	2.562		
	Thiva	< 0.001	3.325		

Appendix 1 – List of endpoints

Fate and behaviour in air (Annex IIA, point 7.2.2, Annex III, point 9.3)

Direct photolysis in air ‡	Not studied - no data requested
Quantum yield of direct phototransformation	Not studied - no data requested
Photochemical oxidative degradation in air ‡	DT_{50} of 3.851 hours derived by the Atkinson Calculation. OH (12 h) concentration assumed = 1.5 x 10^6 cm^{-3}
Volatilisation ‡	Not studied - no data requested
	from soil surfaces (BBA guideline): ≤ 29.7 % after 24 hours at 20 °C. ≤ 16.2 % after 24 hours at 10 °C. NB. Tri-allate applied as the granular formulation 'Avadex 15G'
Metabolites	None

PEC (air)

Method of calculation	There is currently no guidance on determining the predicted environmental concentrations of pesticides in air.

$PEC_{(a)}$

Maximum concentration	N/A

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: Tri-allate, data gap identified for the investigation of the potential formation of diisopropylamine. Surface Water: Tri-allate, data gap identified for the investigation of the potential formation of diisopropylamine. Sediment: Tri-allate, data gap identified for the investigation of the potential formation of diisopropylamine. Ground water: Tri-allate, TCPSA, data gap identified for the investigation of the potential formation and leaching of diisopropylamine. Air: Tri-allate

Appendix 1 – List of endpoints

Monitoring data, if available (Annex IIA, point 7.4)

Soil (indicate location and type of study)	N/A
Surface water (indicate location and type of study)	N/A
Ground water (indicate location and type of study)	Full sample details not provided. 430 sample data primarily from the Anglian and Southern Regions of the UK for the occurrence of tri-allate in groundwater. Max observed concentration of 81 ng/L. Only one other sample displayed detectable concentrations of tri-allate. TCPSA not analysed for.
Air (indicate location and type of study)	N/A

Points pertinent to the classification and proposed labelling with regard to fate and behaviour data

Candidate for R53

Appendix 1 – List of endpoints

Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Species	Test substance	Time scale	Endpoint (mg/kg bw/day)	Endpoint (mg/kg feed)
Birds ‡				
Bobwhite quail	Technical tri-allate	Acute	1560	-
Mallard duck	Technical tri-allate	Short-term	> 1208	> 5620
Bobwhite quail	Technical tri-allate	Long-term	54	500
Mammals ‡				
Rat	Technical tri-allate	Acute	1100* mg a.s./kg bw	
Rat	Technical tri-allate	Long-term	9.0 (males)	150

* The acute rat toxicity endpoint was changed during the meeting of toxicology experts, and consequently updated in the ecotoxicology section by EFSA after the peer-review.

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

Pre-emergence application to cereals at 1 x 2.25 kg a.s./ha in both Northern and Southern Europe

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
Small seed-eating bird	Acute	direct consumption of granules	455	10
Small seed-eating bird	Short-term	direct consumption of granules	> 354	10
Small seed-eating bird	Long-term	direct consumption of granules	18	5
Large herbivorous bird consuming early cereals	Acute	0.11	14182	10
Large herbivorous bird consuming early cereals	Short-term	0.11	>10982	10
Large herbivorous bird consuming early cereals	Long-term	0.09	600	5
Fish-eating bird	Long-term	7.71	7	5
Earthworm-eating bird	Long-term	4.27	12.7	5

Appendix 1 – List of endpoints

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Mammals)				
Small seed-eating mammal	Acute	direct consumption of granules	4331*	10
Small seed-eating mammal	Long-term	direct consumption of granules	200	5
Medium herbivorous mammal consuming early cereals	Acute	0.33	3333*	10
Medium herbivorous mammal consuming early cereals	Long-term	0.29	31	5
Fish-eating mammal	Long-term	0.069	1.9	5
Earthworm-eating mammal	Long-term	5.24	1.71**	5
Higher tier refinement (fish-eating birds and mammals)				
Although acceptable TERs for fish-eating birds and mammals are given for the proposed GAP, PRAPeR 48 did not accepted the proposal to use the BCF for catfish exposed via water and sediment under more realistic conditions, if required. It was felt more precautionary however to initially use a maximum total load PEC (at FOCUS Step 3) to reflect exposure via both phases.				
Higher tier refinement (earthworm-eating mammals)				
* The acute TERs for mammals were recalculated by EFSA after the peer-review, based on the revised acute rat toxicity endpoint (see footnote to the toxicity data above). ** Risk to earthworm-eating mammals considered low over long term due to low probability of expected focal species (e.g. shrews) occurring in open cereal fields.				

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Group	Test substance	Time-scale (Test type)	Endpoint	Toxicity[1] (mg/L)
Laboratory tests ‡				
Fish				
Rainbow trout (*Oncorhynchus mykiss*)	Technical tri-allate	96 hr (semi-static)	Mortality, EC_{50}	0.95 mm
Rainbow trout (*Oncorhynchus mykiss*)	Technical tri-allate	88 d (flow-through ELS)	Growth NOEC	0.038 mm
Rainbow trout (*Oncorhynchus mykiss*)	Preparation (10% w/w granules)	96 hr (static)	Mortality, EC_{50}	19 nom [1.9 a.s. ≡]

Appendix 1 – List of endpoints

Group	Test substance	Time-scale (Test type)	Endpoint	Toxicity[1] (mg/L)
Rainbow trout (*Oncorhynchus mykiss*)	TCPSA metabolite	96 hr (flow-through)	Mortality, EC_{50}	> 122 mm
Aquatic invertebrate				
Daphnia magna	Technical tri-allate	48 h (static)	Immobility, EC_{50}	0.091 mm
Daphnia magna	Technical tri-allate	21 d (flow-through)	Reproduction, NOEC	0.013 mm
Daphnia magna	TCPSA metabolite	48 h (static)	Immobility, EC_{50}	> 114 mm
Sediment dwelling organisms				
Chironomus riparius	Technical tri-allate	28 d (static, spiked water)	Emergence, NOEC	0.583 mm
Algae				
Pseudokirchneriella subcapitata [syn. *Selenastrum capricornutum*]	Technical tri-allate	96 h (static)[2]	Biomass: E_bC_{50}: Growth rate: E_rC_{50}:	72h 0.032 initial m 72h **0.022** mean m 96h 0.024 initial m 96h **0.013** mean m 72h 0.070 initial m 72h 0.046 mean m 96h 0.065 initial m 96h 0.036 mean m
Pseudokirchneriella subcapitata	TCPSA metabolite	72 h (static)	Biomass: E_bC_{50}: Growth rate: E_rC_{50}:	> 121 mm
Higher plant				
Lemna gibba	Technical tri-allate	7 d (semi-static)	Frond count, EC_{50}	2.3 mm
Microcosm or mesocosm tests: None submitted				

[1] Endpoints based on either nominal (nom) or mean measured concentrations (mm).

Appendix 1 – List of endpoints

[2] At PRAPeR 48 there was a difference of opinion whether 96h figures should be used for algae if lower than standard 72h figures. The meeting felt they should but both sets of endpoints are included here and in the following TER tables.

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2)

FOCUS Step 2

Pre-emergence application to cereals at 1 x 2.25 kg a.s./ha in both Northern and Southern Europe

Test substance	Organism[2]	Toxicity endpoint (mg/L)	Time scale	PECsw[1]	TER[2]	Annex VI Trigger
Technical tri-allate	Fish	0.95	Acute	0.118	**8.05**	100
Technical tri-allate	Fish	0.038	Chronic	0.118	**0.32**	10
Technical tri-allate	Aquatic invertebrates	0.091	Acute	0.118	**0.77**	100
Technical tri-allate	Aquatic invertebrates	0.013	Chronic	0.118	**0.11**	10
Technical tri-allate	Algae	0.022 72h 0.013 96h	Chronic	0.118	**0.19** 72h **0.11** 96h	10
Technical tri-allate	Higher plants[5]	2.3	Chronic	0.118	19.5	10
Technical tri-allate	Sediment-dwelling organisms[6]	0.583	Chronic	0.118	**4.9**	10
TCPSA metabolite	Fish	> 122	Acute	0.0096	> 12708	100
TCPSA metabolite	Aquatic invertebrates	> 114	Acute	0.0096	> 11875	100
TCPSA metabolite	Algae	> 121	Acute	0.0096	> 12604	10

[1] Maximum rounded PECsw taken from Vol. 3, Table B.8.55 and EnvFate endpoints.
[2] TERs in **bold** fail the Annex VI triggers

Appendix 1 – List of endpoints

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Pre-emergence application to cereals at 1 x 2.25 kg a.s./ha in both Northern and Southern Europe

Test substance	Organism[2]	Toxicity endpoint (mg/L)	Time scale	PECsw[1]	TER[2]	Annex VI Trigger
Technical tri-allate	Fish	0.95	Acute	0.042	**22.7**	100
Technical tri-allate	Fish	0.038	Chronic	0.042	**0.91**	10
Technical tri-allate	Aquatic invertebrates	0.091	Acute	0.042	**2.17**	100
Technical tri-allate	Aquatic invertebrates	0.013	Chronic	0.042	**0.31**	10
Technical tri-allate	Algae	0.022 72h 0.013 96h	Chronic	0.042	**0.53** 72h **0.31** 96h	10
Technical tri-allate	Sediment-dwelling organisms[6]	0.583	Chronic	0.042	13.9	10

[1] Maximum PECsw taken from D2-ditch (rounded up, see Vol. 3, Table B.8.60 and EnvFate endpoints for actual calculated figure).

[2] TERs in **bold** fail the Annex VI triggers. TERs at Step 3 have also been calculated for other scenarios/water bodies relevant to the proposed use and only 3 pond scenarios (D4, D5 and R1) passed Annex VI triggers for all organisms and timescales (see Table B.9.2.50).

Appendix 1 – List of endpoints

FOCUS Step 4
Pre-emergence application to cereals at 1 x 2.25 kg a.s./ha in both Northern and Southern Europe

Scenario	Water body type	Test organism	Time scale	Toxicity endpoint	Buffer zone distance[2]	PEC[2]	TER[3]	Annex VI trigger[5]
D5	Stream	Fish	Acute	0.95	Deflector + 5 m buffer, or 10 m buffer	0.000926	1026	100
D5	Stream	Fish	Chronic	0.038	Deflector + 5 m buffer, or 10 m buffer	0.000926	41	10
R1	Stream	Fish	Acute	0.95	5 m grass buffer	0.00264	360	100
R1	Stream	Fish	Chronic	0.038	5 m grass buffer	0.00264	14.4	10
D5	Stream	Aquatic invertebrates	Acute	0.091	Deflector + 5 m buffer, or 10 m buffer	0.000926	98.3[1]	100
D5	Stream	Aquatic invertebrates	Chronic	0.013	Deflector + 5 m buffer, or 10 m buffer	0.000926	14	10
R1	Stream	Aquatic invertebrates	Acute	0.091	5 m grass buffer	0.00264	**34.5**	100
R1	Stream	Aquatic invertebrates	Acute	0.091	10 m grass buffer	0.000833	109	100
R1	Stream	Aquatic invertebrates	Chronic	0.013	5 m grass buffer	0.00264	**4.9**	10
R1	Stream	Aquatic invertebrates	Chronic	0.013	10 m grass buffer	0.000833	15.6	10
D5	Stream	Algae	'Chronic'	0.022 72h 0.013 96h	Deflector + 5 m buffer or 10 m buffer	0.000926	23.8 72h 14.0 96h	10
R1	Stream	Algae	'Chronic'	0.022 72h 0.013 96h	5 m grass buffer	0.00264	**8.3** 72h **4.9** 96h	10
R1	Stream	Algae	'Chronic'	0.022 72h 0.013 96h	10 m grass buffer	0.000833	26.4 72h 15.6 96h	10

Appendix 1 – List of endpoints

[1] TER slightly below trigger but considered 'acceptable' due to worst case nature of calculations and because the potentially more sensitive chronic TER for daphnids is above the trigger of 10 for the same scenario.
[2] FOCUS Step 4 PECsw values determined in Section B.8.5.1 (Table B.8.62). See this Section and Section B.9.2.4.2 for discussion of why these worst case scenarios were chosen and risk mitigation options were determined.
[3] TERs in **bold** fail the Annex VI triggers and so further risk mitigation is required (increased buffer distance then used).

Bioconcentration			
Substance	Tri-allate		TCPSA metabolite
$logP_{ow}$	4.06		- 0.1938
Bioconcentration factor (BCF)[1]	1400 in 35d flow-through system using bluegill sunfish	574 in 30d water/ sediment-system with aged residues and using channel catfish	-
Annex VI Trigger for the bioconcentration factor	100 (not readily biodegradable)	100 (not readily biodegradable)	-
Level and nature of residues (%) in organisms after the 14 day depuration phase	95%	97%	-

* based on ^{14}C-tri-allate in whole fish.
BCF values are greater than Annex VI triggers, however risks to fish-eating birds and mammals are considered to be low in Vol. 3, Sections B.9.1.7.3 and B.9.3.2.3. Based on the lower BCF with channel catfish under more realistic conditions (accepted in principle at PRAPeR 48) and the elimination of 95-97% radioactivity during the depuration period, it is also concluded that the biomagnification of tri-allate in aquatic food chains is low.

Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

Test substance	Acute oral toxicity (LD_{50} µg/bee)	Acute contact toxicity (LD_{50} µg/bee)
Technical tri-allate	> 111.5	> 100
Field or semi-field tests: None submitted or required		

Appendix 1 – List of endpoints

Hazard quotients for honey bees (Annex IIIA, point 10.4)

Pre-emergence application to cereals at 1 x 2250 g a.s./ha in both Northern and Southern Europe

Test substance	Route	Hazard quotient	Annex VI trigger
Technical tri-allate	Contact	< 20	50
Technical tri-allate	Oral	< 22.5	50

Hazard Quotients and the Annex VI trigger only validated for sprayed products rather than granules, therefore above calculations are only indicative. Exposure for bees during application is minimal and tri-allate is non-systemic, therefore risk will be low.

Appendix 1 – List of endpoints

Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

Laboratory tests with the standard sensitive species *Typhlodromus pyri* and *Aphidius rhopalosiphi* have not been submitted. As the product is applied as a granule directly to bare soil, laboratory and extended laboratory studies on soil dwelling species have been provided:

Species	Life stage	Test substance, substrate and duration	Initial dose (kg a.s./ha)	Mortality	Sublethal effects	Trigger value
Poecilus cupreus	Adult	15% w/w granule, 14 days on quartz sand	2.28	3.3% not stat. sig.	None compared with -ve control	50%
Pardosa spp.	Adult	15% w/w granule, 14 days on quartz sand	2.28	32.4% stat. sig.	Transient, none compared with -ve control by day 14	50%
Aleochara bilineata	Adult + juvenile	15% w/w granule, 28 days on natural soil	2.28	Assessment of mortality not required by guideline	12.9% reduction in reproduction compared with -ve control	50%
Pardosa spp.	Adult	15% w/w granule, 21 days on natural soil	2.28	at day 14: 14.7% at day 21: 20.6% both stat. sig.	'Behavioural abnormalities' in 17.9% at day 7 compared with -ve control, this reduced to 2.9% by day 14 and none by day 21; no effect on food consumption	50%
Field or semi-field tests: None submitted or required						

Appendix 1 – List of endpoints

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7)

Test organism	Test substance	Time scale	Endpoint (all in terms of a.s.)
Earthworms			
Eisenia fetida	Technical tri-allate	Acute 14-day	LC_{50corr}[1]: 274.5 mg a.s./kg soil
Eisenia fetida	TCPSA metabolite	Acute14-day	LC_{50} > 1000 mg TCPSA/kg soil
Eisenia fetida	15% w/w granule	Chronic 56-day	$NOEC_{corr}$[1] (biomass and repro): 13.62 mg a.s./kg soil[2]
Field tests: An earthworm field study has recently been submitted but has not been evaluated by the RMS.			
Other soil macro-organisms and organic matter (OM) breakdown			
The maximum soil DT_{90f} for tri-allate is 682 days (ref. Section B.8.1.4), this is > 365 days and triggers an assessment of OM breakdown under field conditions. A litter bag field study has recently been submitted but has not been evaluated by the RMS.			

[1] Endpoint corrected for f_{oc} due to log Pow >2.0

[2] Only the endpoint from the repeat chronic worm study (by Moser & Scheffczyk, 2005) is retained in LOEP as the former study (Hayward, 2001) may not be valid. Concerns remain about the most relevant NOEC from these studies but higher tier testing is trigger in any case (see TER table below).

Soil micro-organisms				
Functional process	Test substance	Time scale (days)	Effect relative to control (%)[1]	
			2.25 kg a.s./ha or 3 mg a.s./kg soil	11.25 kg a.s./ha or 15 mg a.s./kg soil
Nitrogen mineralisation	15% w/w tri-allate granule	28	-4.77	-4.51
		56	+3.21	+2.29
		100	+2.06	-9.72
Carbon mineralisation	15% w/w tri-allate granule	28	-10.3	-6.1
		56	-14.1	+2.5
		100	-20.6	-17.2
TCPSA metabolite: No data submitted but risk considered to be covered by studies on parent compound				
Field studies: None submitted or required				

[1] -ve effect is decrease relative to control, +ve effect is increase relative to control. All effects < 25% Annex VI trigger.

Appendix 1 – List of endpoints

Toxicity/exposure ratios for soil organisms

Pre-emergence application to cereals at 1 x 2250 g a.s./ha in both Northern and Southern Europe

Test organism	Test substance	Time scale	Soil PEC[1]	TER	Trigger
Earthworms					
Eisenia fetida	Technical tri-allate	Acute	4.232	64.9_{corr}[2]	10
Eisenia fetida	TCPSA metabolite	Acute	0.2536	> 3943	10
Eisenia fetida	15% w/w tri-allate granule	Chronic	4.232	**3.22**$_{corr}$[2, 3]	5
Other soil macro-organisms					
Litter bag field study requested due to tri-allate DT_{90f} > 365 days (max. 682 days according to Vol. 3, Section B.8.1.4). Study submitted but not evaluated - it may be considered at MS level.					

[1] peak plateau PEC soil used from Vol. 3, Section B.8.3 and EnvFate endpoints
[2] endpoints corrected for f_{oc} due to log Pow >2.0
[3] long term TER is below Annex VI trigger, so earthworm field study requested. Study submitted but not evaluated - it may be considered at MS level.

Effects on non-target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)

Laboratory dose response tests:

Seedling emergence and survival:

Endpoints [kg a.s./ha]	Seed germination	Seedling emergence	Seedling survival	Phyto-toxicity	Plant height	Dry weight
Most sensitive crop spp	Ryegrass	Oat	Oat	Oat	Oat	Oat
NOEC	0.560	0.063	0.063	0.021	0.021	0.011
EC_{25}	nd	0.280	0.134	nd	0.030	0.022
EC_{50}	> 1.681	0.639	0.347	nd	0.066	0.037

Vegetative vigour and survival:

Endpoints [kg a.s./ha]	Plant survival	Phytotoxicity	Plant height	Dry weight
Most sensitive crop spp	All crops	Cucumber	Oat, Cucumber	Oat
NOEC	1.681	0.063	0.063	0.011
EC_{25}	nd	nd	0.16, 0.24	0.037
EC_{50}	> 1.681	nd	0.40, -	0.135

Appendix 1 – List of endpoints

Toxicity/exposure ratios for non-target plants

Pre-emergence application to cereals at 1 x 2250 g a.s./ha in both Northern and Southern Europe

Parameter	Most sensitive species	Endpoint [kg a.s./ha]	Drift rate (PEC) [kg a.s./ha]		TER		Trigger value
			1 m[1]	5/10 m[2]	1 m[1]	5/10 m[2]	
Seedling emergence							
Dry weight (EC_{50})	Oat	0.037	0.036	0.003	**1.0**	12.3	5
Plant height (EC_{50})	Oat	0.066			**1.8**	22	5
Phytotoxicity (NOEC)	Oat	0.021			**0.6**	7	-
Survival (EC_{50})	Oat	0.347			9.6	116	5
Emergence (EC_{50})	Oat	0.639			17.8	213	5
Germination (EC_{50})	All plants	> 1.681			46.7	560	-
Vegetative vigour							
Dry weight (EC_{50})	Oat	0.135	0.036	0.003	**3.75**	45	5
Plant height (EC_{50})	Oat	0.404			11.2	135	5
Phytotoxicity (NOEC)	Cucumber	0.063			**1.75**	21	-
Survival (EC_{50})	All plants	>1.681			46.7	560	5

[1] based on a drift value of 1.62 % (1 m distance with deflector plate) see Vol., 3 Section B.8.5.1 for discussion of granular 'drift' study

[2] based on a drift value of 0.15 % (corresponding to worst case drift scenario with deflector plate at 5 m distance **or** a 10 m buffer with no deflector plate)

values in **bold** letters represent TERs below the trigger value of 5 proposed in SANCO/10329/2002

Effects on biological methods for sewage treatment (Annex IIA 8.7)

Test type/organism	endpoint
Activated sludge	EC_{50}: > 1000 mg a.s./L: no risk envisaged

Appendix 1 – List of endpoints

Ecotoxicologically relevant compounds

Compartment	
soil	Parent (tri-allate), TCPSA metabolite
water	Parent (tri-allate)
sediment	Parent (tri-allate)
groundwater	Parent (tri-allate),

Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal
Technical tri-allate	N, R50/R53

	RMS/peer review proposal
Preparation (15% w/w clay granule)	N, R50/R53

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

(only entries marked yellow will be kept in final conclusion)

ADI	acceptable daily intake
AOEL	acceptable operator exposure level
ARfD	acute reference dose
a.s.	active substance
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DGD_{rwc}	reasonable worst case daily grit dose
DM	dry matter
DNA	deoxyribonucleic acid
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
dw	dry weight
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER50	emergence rate, median
EU	European Union
F_0	parental generation
F_1	filial generation, first
FAO	Food and Agriculture Organisation of the United Nations
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GS	growth stage
h	hour(s)

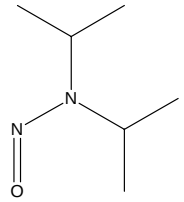
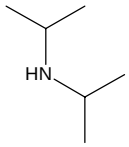
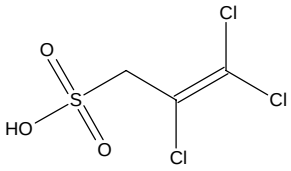
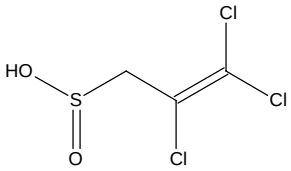
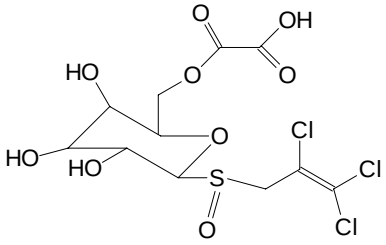
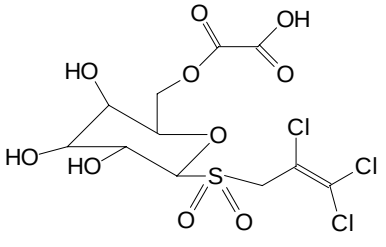
Appendix 2 – abbreviations used in the list of endpoints

ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
K_{oc}	organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LC_{50}	lethal concentration, median
LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
µg	microgram
mN	milli-Newton
MRL	maximum residue limit or level
MS	mass spectrometry
MWHC	maximum water holding capacity
NESTI	national estimated short-term intake
NIR	near-infrared-(spectroscopy)
nm	nanometer
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
OM	organic matter
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
PPE	personal protective equipment
ppm	parts per million (10^{-6})

Appendix 2 – abbreviations used in the list of endpoints

ppp	plant protection product
r^2	coefficient of determination
RPE	respiratory protective equipment
STMR	supervised trials median residue
TER	toxicity exposure ratio
TMDI	theoretical maximum daily intake
TRR	total radioactive residues
UDS	unscheduled DNA synthesis
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
yr	year

APPENDIX 3 – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
NDIPA *N*-nitrosodiisopropylamine	*N*-nitroso-*N*-(propan-2-yl)propan-2-amine	
diisopropylamine	*N*-(propan-2-yl)propan-2-amine	
TCPSA	2,3,3-trichloroprop-2-ene-sulfonic acid	
M1	2,3,3-trichloroprop-2-ene-sulfinic acid	
M14	6-*O*-(carboxycarbonyl)-1-deoxy-1-[(2,3,3-trichloro-2-propenyl)-sulfinyl]-D-glucopyranoside	
M15	6-*O*-(carboxycarbonyl)-1-deoxy-1-[(2,3,3-trichloro-2-propenyl)-sulfonyl]-D-glucopyranoside	

Appendix 3 – used compound code(s)

M16	*S*-[(2*E*)-2,3-dichloro-1-methoxyprop-2-en-1-yl] dipropan-2-ylcarbamothioate