CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance acibenzolar-S-methyl[1]

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ABSTRACT

The conclusions of the European Food Safety Authority (EFSA) following the peer review of the initial risk assessments carried out by the competent authority of the rapporteur Member State France and the co-rapporteur Member State Spain, for the pesticide active substance acibenzolar-S-methyl are reported. The context of the peer review was that required by Commission Regulation (EU) No 1141/2010 as amended by Commission Implementing Regulation (EU) No 380/2013. The conclusions were reached on the basis of the evaluation of the representative uses of acibenzolar-S-methyl as a plant activator on pome fruit, tomato and tobacco. The reliable endpoints concluded as being appropriate for use in regulatory risk assessment, derived from the available studies and literature in the dossier peer reviewed, are presented. Missing information identified as being required by the regulatory framework is listed.

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KEY WORDS

acibenzolar-S-methyl, peer review, risk assessment, pesticide, plant activator

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SUMMARY

Commission Regulation (EU) No 1141/2010, as amended by Commission Implementing Regulation (EU) No 380/2013, (hereinafter referred to as 'the Regulation') lays down the procedure for the renewal of the approval of a second group of active substances and establishes the list of those substances. Acibenzolar-S-methyl is one of the of active substances listed in the Regulation.

The RMS provided its initial evaluation of the dossier on acibenzolar-S-methyl in the Renewal Assessment Report (RAR), which was received by the EFSA on 01 March 2013. The peer review was initiated on 05 March 2013 by dispatching the RAR for consultation of the Member States and the applicant Syngenta.

Following consideration of the comments received on the RAR, it was concluded that EFSA should conduct an expert consultation in the area of mammalian toxicology and EFSA should adopt a conclusion on whether acibenzolar-S-methyl can be expected to meet the conditions provided for in Article 4 of Regulation (EC) No 1107/2009 of the European Parliament and the Council.

The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of acibenzolar-S-methyl as a plant activator on pome fruit, tomato and tobacco as proposed by the applicant. Full details of the representative uses can be found in Appendix A to this report.

Data gaps were identified in the section analytical methods for confirmatory methods for the determination of the metabolite SYN546642 in soil and water.

As an endocrine-mediated mode of action could not be ruled out regarding the morphometric changes in the cerebellum of foetuses in the developmental neurotoxicity study, a data gap has been identified in the mammalian toxicology area for the level 2 tests currently indicated in the OECD Conceptual Framework, noting that further tests might be necessary pending on the outcome.

For residues and the consumer risk assessment there are no data gaps. However the use on protected tomatoes results in an exceedence of the ARfD.

No data gaps have been identified in relation to the fate and behaviour of acibenzolar-S-methyl in the environment. Contamination of ground water above the regulatory trigger of 0.1 µg/L is not expected to occur as result of the use of acibenzolar-S-methy for the representative uses proposed.

No critical area of concern has been identified in the area of ecotoxicology. However, risk mitigation measures for aquatic organisms were proposed for the pome fruit use. Data gaps were identified.

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BACKGROUND

Commission Regulation (EU) No 1141/2010[3], as amended by Commission Implementing Regulation (EU) No 380/2013[4] (hereinafter referred to as 'the Regulation') lays down the detailed rules for the procedure of the renewal of the approval of a second group of active substances. This regulates for the European Food Safety Authority (EFSA) the procedure for organising the consultation of Member States and the applicant for comments on the initial evaluation in the Renewal Assessment Report (RAR) provided by the rapporteur Member State (RMS), and the organisation of an expert consultation, where appropriate.

In accordance with Article 16 of the Regulation, if mandated, EFSA is required to adopt a conclusion on whether the active substance is expected to meet the conditions provided for in Article 4 of Regulation (EC) No. 1107/2009 within 6 months from the receipt of the mandate, subject to an extension of up to 9 months where additional information is required to be submitted by the applicant(s) in accordance with Article 16(3).

In accordance with Article 4 of the Regulation France (hereinafter referred to as the 'RMS') received an application from Syngenta for the renewal of approval of the active substance acibenzolar-S-methyl. Complying with Article 11 of the Regulation, the RMS checked the completeness of the dossier and informed the applicant, the Commission and the Authority about the admissibility.

The RMS provided its initial evaluation of the dossier on acibenzolar-S-methyl in the RAR, which was received by the EFSA on 01 March 2013 (France, 2013). The peer review was initiated on 05 March 2013 by dispatching the RAR to Member States and the applicant Syngenta for consultation and comments. In addition, the EFSA conducted a public consultation on the RAR. The comments received were collated by the EFSA and forwarded to the RMS for compilation and evaluation in the format of a Reporting Table. The applicant was invited to respond to the comments in column 3 of the Reporting Table. The comments and the applicant's response were evaluated by the RMS in column 3.

The need for expert consultation and the necessity for additional information to be submitted by the applicant in accordance with Article 16(3) of the Regulation were considered in a telephone conference between the EFSA, the RMS, and the European Commission on 17 June 2013. On the basis of the comments received, the applicant's response to the comments and the RMS's evaluation thereof it was concluded that additional information should be requested from the applicant and the EFSA should organise an expert consultation in the areas of mammalian toxicology. According to Art. 16(2) of the Regulation COM decided to consult the EFSA. The mandate was received on 27 August 2013.

The outcome of the telephone conference, together with EFSA's further consideration of the comments is reflected in the conclusions set out in column 4 of the Reporting Table. All points that were identified as unresolved at the end of the comment evaluation phase and which required further consideration, including those issues to be considered in an expert consultation and the additional information to be submitted by the applicant, were compiled by the EFSA in the format of an Evaluation Table.

The conclusions arising from the consideration by the EFSA, and as appropriate by the RMS, of the points identified in the Evaluation Table, together with the outcome of the expert consultation where this took place, were reported in the final column of the Evaluation Table.

[3] Commission Regulation (EU) No 1141/2010 of 7 December 2010 laying down the procedure for the renewal of the inclusion of a second group of active substances in Annex I to Council Directive 91/414/EEC and establishing the list of those substances. OJ No L 322,8.12.2011, p. 10-19.

[4] Commission Implementing Regulation (EU) No 380/2013 of 25 April 2013 amending Regulation (EU) No 1141/2010 as regards the submission of the supplementary complete dossier to the Authority, the other Member States and the Commission. OJ No L 116, 26.4.2013, p.4

A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in March/April 2014.

This conclusion report summarises the outcome of the peer review of the risk assessment on the active substance and the representative formulation evaluated on the basis of the representative uses as a plant activator on pome fruit, tomato and tobacco as proposed by the applicant. A list of the relevant end points for the active substance as well as the formulation is provided in Appendix A. In addition, a key supporting document to this conclusion is the Peer Review Report, which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the initial commenting phase to the conclusion. The Peer Review Report (EFSA, 2014) comprises the following documents, in which all views expressed during the course of the peer review, including minority views, can be found:

- the comments received on the RAR,
- the Reporting Table (17 June 2013)
- the Evaluation Table (2 May 2014),
- the report(s) of the scientific consultation with Member State experts (where relevant),
- the comments received on the assessment of the additional information (where relevant),
- the comments received on the draft EFSA conclusion.

Given the importance of the RAR including its addendum (compiled version of March 2014 containing all individually submitted addenda (France, 2014)) and the Peer Review Report, both documents are considered respectively as background documents A and B to this conclusion.

It is recommended that this conclusion report and its background documents would not be accepted to support any registration outside the EU for which the applicant has not demonstrated to have regulatory access to the information on which this conclusion report is based.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Acibenzolar-S-methyl is the ISO common name for *S*-methyl benzo[1,2,3]thiadiazole-7-carbothioate (IUPAC).

This substance is a derivative of acibenzolar.

The representative formulated product for the evaluation was 'A9180A (BION 50 WG)', a water dispersible granule (WG) containing 500 g/kg acibenzolar-S-methyl.

The evaluated representative uses as plant activator comprise applications by foliar spraying on pome fruit, tomato and tobacco. Full details of the GAPs can be found in the list of end points in Appendix A.

CONCLUSIONS OF THE EVALUATION

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

The following guidance documents were followed in the production of this conclusion: SANCO/3030/99 rev.4 (European Commission, 2000), SANCO/825/00 rev. 8.1 (European Commission, 2010) and SANCO/10597/2003 –rev. 10.1 (European Commission, 2012).

The minimum purity of acibenzolar-S-methyl technical material is 970 g/kg. No FAO specification exists.

The specification is based on batch data from industrial scale production, it should be noted however that based on the data of the renewal procedure a higher minimum specification for the a.s. could be set.

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 acibenzolar-S-methyl or the representative formulation. Toluene was considered a relevant impurity from the toxicological point of view (see section 2), although at the level found in the technical specification it is considered being of no concern. The main data regarding the identity of acibenzolar-S-methyl and its physical and chemical properties are given in Appendix A.

Adequate analytical methods are available for the determination of acibenzolar-S-methyl in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material.

The residue definition for enforcement for plant matrices was set as sum of acibenzolar-S-methyl, acibenzolar acid and its conjugates expressed as acibenzolar-S-methyl. A validated analytical method for enforcement is available for this residue definition using HPLC-MS/MS with LOQs of 0.01 mg/kg in tobacco and in plants with high water content (except for lettuce). No residue definition is necessary in food of animal origin, as a consequence an inforcement analytical method for the determination of acibenzolar-S-methyl residues in foodstuffs of animal origin is not required.

The residue definition for monitoring in soil and water was set as acibenzolar-S-methyl and acibenzolar acid (CGA210007) and the metabolite SYN546642. Appropriate HPLC-MS/MS method is available for monitoring the compounds in the residue definition in soil with LOQs of 0.01 mg/kg for all compounds, however a data gap was identified for a confirmatory method for the determination of the metabolite SYN546642 in soil. Acibenzolar-S-methyl, acibenzolar acid and the metabolite SYN546642 in surface water and drinking water can be determined by by HPLC-MS/MS with LOQs of 0.05 µg/L individually, however a data gap was identified for a confirmatory method for the determination of the metabolite SYN546642 in surface water and drinking water. Residues of acibenzolar-S-methyl in air can be monitored by HPLC-UV with a LOQ of 2 µg/m^3. Analytical

methods for the determination of acibenzolar-S-methyl residues in body fluids and tissues are not required as the active substance is is not classified as toxic or very toxic.

2. Mammalian toxicity

The following guidance documents were followed in the production of this conclusion: SANCO/221/2000 rev. 10 - final (European Commission, 2003), SANCO/222/2000 rev. 7 (European Commission, 2004), SANCO/10597/2003 – rev. 10.1 (European Commission, 2012), and EFSA, 2013.

Acibenzolar-S-methyl was discussed at the Pesticides Peer Review Experts' Meeting 109 in January 2014.

The batches used in the toxicological studies support the technical specification. Considering that acibenzolar-S-methyl is not classified in accordance with Regulation (EC) No 1272/2008[5] as developmental toxic, toluene has been identified as a relevant impurity.

Acibenzolar-S-methyl is rapidly and almost completely absorbed after oral administration. The active substance is widely distributed, the highest concentrations being found in the liver, kidney, blood and blood rich tissues. Acibenzolar-S-methyl is extensively metabolised, and rapidly excreted mainly via urine.

Low acute toxicity has been observed in guideline-compliant studies aiming to define the acute toxicity potential of acibenzolar-S-methyl administered by the oral, dermal and inhalation routes. It has however been noted that, in a newly submitted micronucleus test, 4/4 mice dosed at 2000 mg/kg bw died as well as 3/14 animals dosed at 1250 mg/kg bw, which could potentially lead to a revision of the classification. The substance was not found to be irritating to eyes and skin in guideline-compliant animal studies (in rabbits), but based on observations made on exposed workers, the active substance is classified and included in the Annex VI of Regulation (EC) No 1272/2008 as irritant to eyes, skin and respiratory tract. Acibenzolar-S-methyl is a potential skin sensitiser according to a Maximisation test of Magnusson and Kligman.

The primary target organs of acibenzolar-S-methyl upon repeated administration are the red blood cells (leading to haemolytic anaemia) in all tested species, affecting the spleen in rats and mice and the liver in rats and dogs. A mechanism of action leading to haemolytic anaemia was postulated through erythrocytes glutathione depletion, altered haemoglobin (presence of methaemoglobin and sulfhaemoglobin) and increased lipid peroxidation. The relevant short term NOAEL is 10 mg/kg bw per day derived from an overall NOAEL for the 90-day and 1-year dog studies. The relevant long term NOAEL is 7.8 mg/kg bw per day derived from the 2-year study in rats. No genotoxic or carcinogenic potential is attributed to acibenzolar-S-methyl. The reproduction and fertility parameters were not affected by acibenzolar-S-methyl administration, but malformations (defects of the abdominal wall, as umbilical hernia) were observed in rats down to the lower dose tested of 10 mg/kg bw per day in the absence of maternal toxicity. Based on these developmental effects, the experts suggested that classification regarding reproductive toxicity, Repr. Cat 2 H361d, suspected of damaging the unborn child, may be appropriate[6]. In a developmental neurotoxicity study, morphometric changes in the cerebellum of foetuses were observed in the absence of maternal toxicity, which were regarded as possibly preceding the effects observed on the acoustic startle response at the higher dose tested; the NOAEL for this effect is 8.2 mg/kg bw per day.

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

[6] It should be noted that classification is formally proposed and decided in accordance with Regulation (EC) No 1272/2008. Proposals for classification made in the context of the evaluation procedure under Regulation (EC) No 1107/2009 are not formal proposals.

Regarding the interim provisions of Regulation (EC) No. 1107/2009 for the consideration of potential endocrine disrupting properties, acibenzolar-S-methyl is proposed to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as toxic for reproduction category 2, but effects on endocrine organs have not been identified. However, specific scientific criteria for the determination of endocrine disrupting properties have not yet been adopted.

Regarding the potential endocrine activity of acibenzolar-S-methyl, the experts agreed that malformations such as umbilical hernia would typically not be considered as an endocrine-mediated mode of action, however considering the morphometric changes observed in the cerebellum of foetuses in the developmental neurotoxicity study, an endocrine-mediated effect could not be ruled out. The available data is not sufficient to clarify the potential endocrine activity; in particular the Level 2 tests currently indicated in the OECD Conceptual Framework, and analysed in the EFSA Scientific Opinion on the hazard assessment of endocrine disruptors (EFSA, 2013), though not covering all the possible endocrine effects and their adversity, are not available: these are mechanistic screens for oestrogen receptor (ER) mediated, androgen receptor (AR) mediated and steroidogenesis interference-mediated modalities. These are the ER and the AR binding assays, the ER transactivation assay (OECD TG 455), the steroidogenesis assay (OECD TG 456) and the aromatase assay. Level 2 also includes a test for ER agonists and antagonists (OECD TG 457) and assays for thyroid hormone-mediated modalities (though not yet validated). Furthermore, the Level 3 *in vivo* screening assays include two validated tests, one sensitive to oestrogen agonists/antagonists (Uterotrophic assay in rodents, OECD TG 440) and one sensitive to androgen agonists/antagonists (Hershberger assay in rodents, OECD TG 441). Therefore a data gap is set for the level 2 tests (further testing might be necessary based on the outcomes).

Studies were submitted on three plant metabolites. **Metabolite CGA 210007** is also a major rat metabolite and was shown to share the toxicity potential of the parent acibenzolar-S-methyl, therefore the reference values of the parent are applicable to this metabolite. Acute oral toxicity and bacterial gene mutation assays were provided for **metabolites CGA 323060 and CGA 324041**. This information is insufficient to conclude on their (relative) toxicity relevant for consumer exposure, however, according to the representative GAPs and respective levels in residues, no further toxicological assessment is required (see section 3).

The acceptable daily intake (**ADI**), the acceptable operator exposure level (**AOEL**) and the acute reference dose (**ARfD**) of acibenzolar-S-methyl are 0.03 mg/kg bw (per day), based on the LOAEL of 10 mg/kg bw per day from the developmental toxicity study in rat, applying an uncertainty factor (UF) of 300, 100 standard factor plus additional factor of 3 to account for the LOAEL basis. No correction regarding oral absorption is necessary to derive the AOEL.

Dermal absorption is 0.1 % when handling the concentrate formulation and 33 % when handling the in-use spray dilution down to 0.25 g/L; for higher dilutions the use of a prorata percentile should be applied with a maximum value of 75 % (default value). Personal protective equipment (PPE) such as gloves during mixing and loading operations, and gloves and coveralls during applications have to be considered to ensure that **operator** exposure does not exceed the AOEL according to the German model for high crop applications. For the other representative uses, estimated operator exposure is below the AOEL without using PPE. Estimated exposure of protected **workers** harvesting pome fruits exceeds the AOEL when the 6 applications foreseen in the GAP are considered. For this activity, exposure of protected workers is below the AOEL if one application is considered. Exposure of protected workers harvesting tomatoes (indoor) and exposure of unprotected workers performing crop inspection activities are below the AOEL. **Bystander and residential** exposures are calculated to represent at most 35 % of the AOEL.

3. Residues

The assessment in the residue section below is based on the guidance documents listed in the document 1607/VI/97 rev.2 (European Commission, 1999), and the JMPR recommendations on livestock burden calculations stated in the 2004 and 2007 JMPR reports (JMPR, 2004, 2007).

Primary crop metabolism of acibenzolar-S-methyl was investigated on three different crops using foliar application treatment. These crops are representative of cereals (wheat), fruits and fruiting vegetables (tomatoes) and leafy vegetables (tobacco, lettuce). For the representative uses it was considered that the residue definition for enforcement and risk assessment should be set as the sum of acibenzolar-S-methyl and acibenzolar-acid (free and conjugated), expressed as acibenzolar-S-methyl. For other crops depending on residue trials data and toxicological data the metabolite CGA 323060 could be considered in the residue definition. Analytical methods for enforcement of this residue definition in plants are available with a LOQ of 0.01 mg/kg in high water, dry and high oil content commodities.

For the representative crops sufficient residues data are available for outdoor and protected tomato and pome fruit. For the outdoor crops the uses were only for the south of Europe.

The nature of residues in processed commodities was considered and it was concluded that the same residue definition as for primary crops can be applied to processed commodities. Studies investigating the magnitude of residues in processed commodities of tomatoes were reported.

The fate of acibenzolar-S-methyl residues in rotational crops of lettuce, mustard, radish, winter wheat and maize was investigated. All residue levels in the crops were found to be equal or below 0.001 mg/kg. Consequently, residue levels in rotational commodities are not expected to exceed 0.01 mg/kg, provided that acibenzolar-S-methyl is applied in compliance with the GAPs reported in Appendix A.

The nature of acibenzolar-S-methyl residues in commodities of animal origin was investigated in metabolism studies including one study in lactating goat and one study in laying hen. However, a residue definition for products of animal origin is not needed because the calculated dietary burden for ruminants was the only one to slightly exceed the trigger value of 0.1 mg/kg, low absolute levels in the animal metabolism studies were observed and in the available feeding studies all residues in products of animal origin were below the LOQ, despite the exaggerated dose rate. An analytical method for enforcement of residues in food of animal origin is not necessary.

For the risk assessment chronic intakes are 12.7 % of the ADI. The acute intakes were 29.4 % for apples and 120.2 % for indoor tomatoes and 58 % for outdoor tomatoes. The ARfD is exceeded for the indoor tomato use.

4. Environmental fate and behaviour

Route and rate of degradation of acibenzolar-S-methyl in soil under dark aerobic conditions was investigated in twelve experiments: 8 were submitted in the dossier for the 1st review and evaluated in the DAR (France, 1998) and 4 were submitted and evaluated for the renewal procedure in the RAR (France, 2013). Of the eight experiments presented in the original dossier four were performed in the same soil to investigate the influence of different testing conditions (concentration, soil moisture and temperature). Despite the relatively high number of experiments available the range of pHs of the soils investigated was rather narrow (only one soil has pH < 7). However, examination of the results in the acidic soil does not indicate a different behaviour with respect to all the other experiments performed in neutral and alkaline soils. Studies of degradation in soil presented in the updated AIR II dossier together with those submitted in the original dossier were used to derive soil degradation kinetic parameters for acibenzolar-S-methyl and its major soil metabolites. Acibenzolar-S-methyl was very low persistent in these experiments and rapidly hydrolyzed to acibenzolar acid (CGA 210007; max 82.6 – 96.1 % AR) that was subsequently hydroxylated to the metabolite 6-OH acibenzolar acid (SYN546642; max. 21.8 – 39 % AR). Metabolite acibenzolar acid (CGA 210007) exhibits low to high

persistence and metabolite 6-OH acibenzolar acid (SYN 546642) high to very high persistence in soil under these conditions. Mineralization reached a maximum of 53.5 % AR after 125 d and unextractable residues accounted for a maximum of 59.8 % AR after 90 d. In an additional study, persistence of metabolite 6-OH acibenzolar acid (SYN 546642) was investigated in three soils under dark aerobic conditions. Mass balances of these experiments were not closed due to the lack of quantification of volatiles and unextractable residues. The decline was biphasic and, based on the kinetic analysis, 6-OH acibenzolar acid (SYN 546642) may be considered to exhibit medium persistence in these three soils. Degradation in soil under anaerobic conditions was also investigated in one study presented in the DAR. No information was obtained on the degradation of the parent under these conditions since it completely disappeared during the aerobic phase of the study. Therefore only the behaviour of metabolite acibenzolar acid (CGA 210007) could be investigated. No degradation of metabolite acibenzolar acid (CGA 210007) was observed during the anaerobic phase. Photolysis of acibenzolar-S-methyl in dry and wet soils was investigated in one study of the original dossier and evaluated in the DAR. Light has the potential to enhance degradation of acibenzolar-S-methyl and its hydrolysis metabolite acibenzolar acid (CGA 210007). No other metabolites were reported to reach levels above 5 % AR in this study. Bound residues reached levels up to 61 % AR in the wet irradiated samples. A number of field dissipation trials with acibenzolar-S-methyl and its metabolite acibenzolar acid (CGA 210007) were available in the original dossier. None of the studies has been re-evaluated with FOCUS kinetics. Residues of trials with parent acibenzolar-S-methyl were reported as total residues including acibenzolar-S-methy plus acibenzolar acid and the half life derived can be considered a worst case for the parent acibenzolar-S-methyl. Worst case field DissT50 from these field studies have been used by the RMS to derive the worst case pome fruit PECs soil of acibenzolar-S-methy and acibenzolar acid (CGA 210007). Pome fruit PEC soil of metabolite 6-OH acibenzolar acid (SYN 546642) has been derived using worst case laboratory DT_{50}.

Batch soil adsorption/desorption studies were performed for acibenzolar-S-methyl (six soils reported in the RAR and 4 soils reported in the DAR) and its two metabolites acibenzolar acid (CGA 210007) (three soils reported in RAR and 4 soils reported in the DAR) and 6-OH acibenzolar acid (SYN 546642) (5 soils reported in the RAR). According the results of these studies, acibenzolar-S-methyl may be considered slightly to medium mobile, acibenzolar acid may be considered medium to very high mobile and 6-OH acibenzolar acid (SYN 546642) immobile to slightly mobile.

In aqueous buffered solutions acibenzolar-S-methyl was stable to hydrolysis at pH 5 and 7 and was readily hydrolysed at pH 9. The main hydrolysis metabolite was acibenzolar acid (CGA 210007) which was stable at all pH values. Under simulated sunlight, acibenzolar-S-methyl is rapidly photodegraded in water at pH 5 (DT50 < 1d) to numerous photodegradation products (< 10 %), mostly volatiles, including CO_2. Acibenzolar-S-methyl is not readily biodegradable according to the available study in the DAR. No new dark aerobic water sediment study has been submitted in the updated dossier, but data from the study presented in the original dossier and evaluated in the DAR have been re-analyzed using FOCUS kinetic guidance (FOCUS 2006). The RMS has also extended and updated the summary of the water sediment study in the RAR. In these systems, acibenzolar-S-methyl is rapidly transformed to acibenzolar acid (CGA 210007) that exhibits high persistence under these conditions (geomean DT_{50} whole system > 1 yr) and it is found both in sediment (max 38 %) and water (max 75 %) phases.

Exposure to natural aquatic environment was assessed by calculating $PEC_{SW/sed}$ with FOCUS SW models and scenarios. $PEC_{SW/sed}$ up tot FOCUS SW Step 2 were calculated for metabolites acibenzolar acid (CGA 210007) and 6-OH acibenzolar acid (SYN 546642). $PEC_{SW/sed}$ for acibenzolar-S-methyl were calculated up to FOCUS SW Step 4 to account for buffer spray drift mitigation needed. $PEC_{SW/sed}$ presented by the applicant were completed by the RMS for the different possible application dates and to take into consideration potential accumulation of metabolite acibenzolar acid (CGA 210007) (FOCUS 2001, FOCUS 2007).

The RMS assessed the potential for ground water contamination of acibenzolar-S-methy and its metabolites for the representative uses in pome fruit, tomato and tobacco calculating 20 yrs 80th

percentile of the annual average leachate concentration at 1 m depth with FOCUS GW models PEARL 4.4.4 and PELMO 4.4.3 (FOCUS 2009). None of the compounds exceeded the regulatory trigger of 0.1 µg/L for any of the representative uses and scenarios.

5. Ecotoxicology

The following documents were considered for the risk assessments: European Commission, 2002a and 2002b, SETAC, 2001 and EFSA, 2009.

It is noted that insufficient information was available to perform an assessment of whether acibenzolar-S-methyl has endocrine disrupting properties that may cause adverse effects on non-target organisms. It should be noted that, currently, there are no agreed specific scientific criteria for such an assessment. Pending the adoption of specific scientific criteria to address Annex II Point 3.8.2 of Regulation (EC) No. 1107/2009 the scientific determination of endocrine disrupting properties could not be finalised. A data gap was therefore agreed for sufficient information to address point 3.8.2 of Annex II of Regulation (EC) No. 1107/2009. Furthermore, as discussed in section 2, an endocrine-mediated effect of acibenzolar-S-methyl could not be ruled out, and therefore a data gap was set (see section 7). This data gap is relevant also for ecotoxicology.

On the basis of the available data and assessments, a low risk to **birds and mammals** was concluded for the representative uses in tobacco and tomato. Also, a low risk to birds and mammals was concluded for the representative use in pome fruit with the exception for the long-term risk to wild mammals where some TER values were slightly below the relevant trigger. Therefore, a data gap was identified to further assess the risk for herbivorous and frugivorous mammals for long-term dietary exposure. The risk from secondary poisoning and via consumption of contaminated water was assessed as low.

The risk assessments for acibenzolar-S-methyl using FOCUS step 3 exposure estimations resulted in a low risk for **aquatic organisms** for the tobacco and the tomato uses. However, a number of FOCUS step 3 scenarios indicated a high risk for the pome fruit use. Therefore, additional risk assessments were performed for these scenarios at FOCUS step 4 level. The risk assessments using these FOCUS step 4 simulations resulted in a low risk for all the relevant FOCUS surface water scenarios when a no-spray buffer zone of 20 meters was considered. A low risk to aquatic organisms was also concluded for the pertinent metabolites (using FOCUS step 2 exposure estimations). It is noted that for the metabolite 6-OH acibenzolar acid (SYN 546642), no toxicity data were available. The risk for this metabolite was addressed by assuming ten times greater toxicity than its precursor (metabolite CGA 210007).

Considering the available laboratory studies, the risk to honey**bees** was assessed as low for the representative uses. Also, the risk assessment using the standard tier 1 test species of **non-target arthropods** indicated a low risk. This conclusion was supported by the available extended laboratory studies.

Laboratory studies on earthworms, collembolan and on soil microorganisms were available. Based on the results of these studies, the risk to **earthworms** and **non-target soil macro and microorganisms** was assessed as low for the representative uses of acibenzolar-S-methyl. A concern was raised during the peer review with regard to the persistent soil metabolite 6-OH acibenzolar acid (SYN 546642), which had not been tested on earthworms. A quantitative risk assessment using worst case assumptions (i.e. worst case PECsoil, the toxicity is ten times greater than its precursor) resulted in a TER value below the relevant trigger (long-term TER of 3.08). However, on the basis of weight-of-evidence, which considered also the available data and risk assessment on collembolan, a low risk was concluded also for this metabolite.

A low risk was concluded for **non-target terrestrial plants** and organisms involved in biological methods for **sewage treatment** on the basis of the available data and assessments.

6. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments

6.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
acibenzolar-S-methyl (CGA 245704)	very low (DT_{50} = 0.04 – 0.98 d)	The risk to soil organisms was assessed as low.
acibenzolar acid (CGA 210007)	low to high (DT_{50} = 4.09 d – 106 d)	The risk to soil organisms was assessed as low.
6-OH acibenzolar acid (SYN 546642)	medium to very high (DT_{50} = 77.6 d- > 1000 d)	The risk to soil organisms was assessed as low.

6.2. 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
acibenzolar-S-methyl (CGA 245704)	Slightly to medium mobile K_{Foc} = 492 – 3288 mL/g	FOCUS GW: no	Yes	Yes	The risk to aquatic organisms was assessed as low.
acibenzolar acid (CGA 210007)	Medium to very high mobile K_{Foc} = 40 – 312 mL/g	FOCUS GW: no	No information	Yes (shares the toxicological profile of the parent acibenzolar-S-methyl)	The risk to aquatic organisms was assessed as low.
6-OH acibenzolar acid (SYN 546642)	Immobile to slightly mobile. K_{oc} = 2303 – 5806 mL/g	FOCUS GW: no	No information	No data	The risk to aquatic organisms was assessed as low.

6.3. Surface water and sediment

Compound (name and/or code)	**Ecotoxicology**
acibenzolar-S-methyl (CGA 245704)	The risk to aquatic organisms was assessed as low.
acibenzolar acid (CGA 210007)	The risk to aquatic organisms was assessed as low.
6-OH acibenzolar acid (SYN 546642) (from soil)	The risk to aquatic organisms was assessed as low.

6.4. Air

Compound (name and/or code)	**Toxicology**
acibenzolar-S-methyl (CGA 245704)	Rat LC_{50} inhalation > 5 mg/L air/4 h (nose-only), no classification required

7. List of studies to be generated, still ongoing or available but not peer reviewed

This is a list of data gaps identified during the peer review process, including those areas where a study may have been made available during the peer review process but not considered for procedural reasons (without prejudice to the provisions of Article 56 of regulation (EC) No 1107/2009 concerning information on potentially harmful effects).

- Confirmatory method for the determination of the metabolite SYN546642 in soil (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown, see section 1)
- Confirmatory method for the determination of the metabolite SYN546642 in surface water and drinking water (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown, see section 1)
- As an endocrine-mediated mode of action could not be ruled out regarding the morphometric changes in the cerebellum of foetuses in the developmental neurotoxicity study, a data gap has been identified in the mammalian toxicology area for the level 2 tests currently indicated in the OECD Conceptual Framework, noting that further tests might be necessary pending on the outcome (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown, see section 2 and 5)
- Additional risk assessments for herbivorous and frugivorous mammals for long-term dietary exposure (relevant for use in pome fruit; submission date proposed by the applicant: unknown; see section 5)

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

- Personal protective equipment (PPE) such as gloves during mixing and loading operations, and gloves and coveralls during applications have to be considered to ensure that operator exposure does not exceed the AOEL according to the German model for high crop applications (see section 2).
- PPE has to be considered for workers harvesting pome fruits and tomatoes (indoor) to ensure that exposure is below the AOEL (see section 2).
- Risk management measures comparable with the effect of 20-metre non-sprayed buffer zone from surface waters should be considered in order to mitigate the risk to aquatic organisms for the pome fruit use (see section 5).

9. Concerns

9.1. Issues that could not be finalised

An issue is listed as an issue that could not be finalised where there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the Uniform Principles in accordance with Art 26(6) of regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011[7] and where the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

[7] Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.6.2011, p. 127-175.

1. An endocrine-mediated mode of action could not be ruled out regarding the morphometric changes in the cerebellum of foetuses in the developmental neurotoxicity study. Pending the adoption of specific scientific criteria to address Annex II Points 3.6.5 and 3.8.2 of Regulation (EC) No. 1107/2009 the scientific determination of endocrine disrupting properties could not be finalised (see sections 2 and 5).

9.2. Critical areas of concern

An issue is listed as a critical area of concern where there is enough information available to perform an assessment for the representative uses in line with the Uniform Principles in accordance with Art 26(6) of regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011[8], and where this assessment does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

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

An issue is also listed as a critical area of concern the active substance is not expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009.

- None.

9.3. Overview of the concerns identified for each representative use considered

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in section 8, has been evaluated as being effective, then 'risk identified' is not indicated in this table.)

Representative use		**Pome fruits (6 applic.)**	**tomato outdoor**	**tomato indoor**	**tabacco**
Operator risk	Risk identified				
	Assessment not finalised				
Worker risk	Risk identified	X			
	Assessment not finalised				
Bystander risk	Risk identified				
	Assessment not finalised				
Consumer risk	Risk identified			X	
	Assessment not finalised				
Risk to wild non	Risk identified	X			

[8] Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.6.2011, p. 127-175.

target terrestrial vertebrates	Assessment not finalised				
Risk to wild non target terrestrial organisms other than vertebrates	Risk identified				
	Assessment not finalised				
Risk to aquatic organisms	Risk identified				
	Assessment not finalised				
Groundwater exposure active substance	Legal parametric value breached				
	Assessment not finalised				
Groundwater exposure metabolites	Legal parametric value breached[(a)]				
	Parametric value of 10µg/L[(b)] breached				
	Assessment not finalised				
Comments/Remarks					

The superscript numbers in this table relate to the numbered points indicated in sections 9.1 and 9.2. Where there is no superscript number see sections 2 to 6 for further information.

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APPENDICES

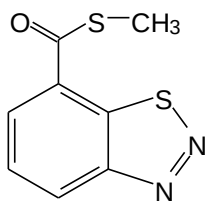
APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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

Active substance (ISO Common Name) ‡	acibenzolar-S-methyl
Function (*e.g.* fungicide)	Plant activator

Rapporteur Member State	France
Co-rapporteur Member State	Spain

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	*S*-methyl benzo[1,2,3]thiadiazole-7-carbothioate
Chemical name (CA) ‡	*S*-methyl 1,2,3-benzothiadiazole-7-carbothioate
CIPAC No ‡	597
CAS No ‡	135158-54-2
EC No (EINECS or ELINCS) ‡	Not allocated
FAO Specification (including year of publication) ‡	Not available
Minimum purity of the active substance as manufactured ‡	970 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	Toluene Max. 5 g/kg
Molecular formula ‡	$C_8H_6N_2OS_2$
Molar mass ‡	210.3 g/mol
Structural formula ‡	

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	133 °C
Boiling point (state purity) ‡	approx. 267 °C
Temperature of decomposition (state purity)	Not relevant
Appearance (state purity) ‡	White, fine cristalline powder
Vapour pressure (state temperature, state purity) ‡	4.6 x10^{-4} Pa at 25 °C
Henry's law constant ‡	1.3 x 10^{-2} Pa m^3 mol^{-1}
Solubility in water (state temperature, state purity and pH) ‡	7.7 mg/l at 25°C in pure water
Solubility in organic solvents ‡ (state temperature, state purity)	in g/L at 20 °C acetone : 28.0 toluene : 36.0 dichloromethane : 160.0 hexane 1.3 methanol 4.2 ethyl acetate 25.0 octanol 5.4
Surface tension ‡ (state concentration and temperature, state purity)	70.7 mN/m at 20.5 °C (99.8 %)
Partition co-efficient ‡ (state temperature, pH and purity)	Log Pow : 3.1 at 25°C
Dissociation constant (state purity) ‡	no dissociation constant
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	253 nm ε : 14.7 x 10^3 L mol^{-1} cm^{-1} 288 nm ε : 5.4 x 10^3 L mol^{-1} cm^{-1} 324 nm ε : 7.2 x 10^3 L mol^{-1} cm^{-1} No absorption above 290nm
Flammability ‡ (state purity)	Not flammable
Explosive properties ‡ (state purity)	Not explosive
Oxidising properties ‡ (state purity)	Not oxidising

Summary of representative uses evaluated *(acibenzolar-S-methyl)*

Crop and/or situation (a)	Member State	Product Name	F G I (b)	Pests or group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks (m)
					Type (d-f)	Conc of a.i. g/kg (i)	Method kind (f-h)	Growth stage and season (j)	Number min max (k)	Interval between applications (min)	Kg a.i./hl min max (g/hl)	Water l/ha min max	Lk a.i./ha min max (*) (g/ha)		
Pome fruit	S-EU	BION®50 WG (A9180A)	F	*Erwinia amylovora*	WG	500 g/kg	foliar spray	BBCH 59-87	6	5 days	7.7-10.0	1000-1300	100	14	i.e. 200 g/ha product
Tomato	S-EU	BION®50 WG (A9180A)	F & G	*Pseudomonas syringae pv. tomato, Xanthomonas campestris pv. vesicatoria*	WG	500 g/kg	foliar spray	BBCH 16-79	6	7 days	2.5-25.0	100-1000	25.0	3	i.e. 50 g/ha product F: 100-400 l/ha G: 200-1000 l/ha
Tobacco	S-EU	BION®50 WG (A9180A)	F	*Peronospora tabacina*	WG	500 g/kg	foliar spray	BBCH 13-89 After transplantation shock	4	7-10 days	2.5-4.2	600-1000	25.0	7	i.e. 50 g/ha product

* For uses where the column „Remarks“ in 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 classification (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 N° 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 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

Methods of Analysis

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

Technical as (analytical technique)	Determination by gas chromatography on a wide-bore capillary column using FID detection
Impurities in technical as (analytical technique)	Reversed phase HPLC determination (UV detection) or wide-bore capillary column gas chromatography (FID detection). Confirmation of the identity with MS spectra.
Plant protection product (analytical technique)	Determination by gas chromatography on a wide-bore capillary column using FID detection

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin	Acibenzolar-S-methyl, acibenzolar acid (CGA 210007) and conjugates of acibenzolar acid expressed as acibenzolar-S-methyl
Food of animal origin	No residue definition proposed.
Soil	Acibenzolar-S-methyl, acibenzolar acid CGA210007 and the metabolite SYN546642
Water surface	Acibenzolar-S-methyl, acibenzolar acid CGA210007 and the metabolite SYN546642
drinking/ground	Acibenzolar-S-methyl, acibenzolar acid CGA210007 and the metabolite SYN546642
Air	Acibenzolar-S-methyl

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	HPLC-MS/MS (2 mass transitions) for the determination of acibenzolar-S-methyl, acibenzolar acid and conjugates of acibenzolar acid with an LOQ of 0.01 mg/kg in tobacco and in plants with high water content (except for lettuce).
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Not relevant, as no residue definition was set

Soil (analytical technique and LOQ)	LC-MS/MS for the determination of acibenzolar-S-methyl, acibenzolar acid and of the metabolite SYN546642 with an LOQ of 0.01 mg/kg Data gap: confirmatory method for SYN546642
Water (analytical technique and LOQ)	LC-MS/MS for the determination of acibenzolar-S-methyl and acibenzolar acid in surface and drinking water with an LOQ of 0.05 µg/L Data gap: An analytical method and a confirmatory method fully validated for the determination of the metabolite SYN546642 in surface and drinking water**.**
Air (analytical technique and LOQ)	HPLC-UV (324 nm) with an LOQ of 2 µg/m^3
Body fluids and tissues (analytical technique and LOQ)	Not relevant as the active substance is not classified T or T+

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

	RMS/peer review proposal
Active substance	Not classified.

Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	Rapid and extensive > 90%
Distribution ‡	Widely distributed. Residues mainly found in the liver, and kidneys (low dose, single and repeated administration) Residues also found in the blood and blood rich tissues (lungs, muscles and spleen) for the high dose
Potential for accumulation ‡	No evidence for accumulation
Rate and extent of excretion ‡	Almost totally eliminated within 24 hours via urine (90 %) in form of the acid metabolite CGA 210007
Metabolism in animals ‡	> 90 % metabolised to acid, mainly in liver. Metabolism independent from sex, dose, pre-treatment Mechanistic study: Hydrolysis rates of the acibenzolar-S-methyl thioester to its corresponding acid CGA 210007 (nmol/min/mg protein): human liver (409) > rat liver (64) > rat skin (41) > human skin (11.2) > rat plasma (0.15) > human plasma (0.04)
Toxicologically relevant compounds ‡ (animals and plants)	Acibenzolar-S-methyl
Toxicologically relevant compounds ‡ (environment)	Acibenzolar-S-methyl

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	> 2000 mg/kg bw (rat) >1250 < 2000 mg/kg bw (mouse micronucleus test)	
Rat LD_{50} dermal ‡	> 2000 mg/kg bw	
Rat LC_{50} inhalation ‡	> 5 mg/L air/4h (nose-only)	
Skin irritation ‡	Non irritating	
Eye irritation ‡	Non irritating	
Skin sensitisation ‡	Sensitizing (M&K)	**H317**

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Rat: decreased RBC (haemolytic anaemia), liver and spleen (increased weight), decreased body weight Mouse: RBC (anisochromia) and spleen (increased weight and histopathological changes) Dog: decreased RBC (hypochromic aneamia), liver (increased weight), decreased body weight	
Relevant oral NOAEL ‡	28-day, rat: 100 mg/kg bw per day 90-day, rat: 25 mg/kg bw per day 90-day, mouse LOAEL: 30.6 mg/kg bw per day Overall 90-day/1-year, dog: 10 mg/kg bw per day	
Relevant dermal NOAEL ‡	28-day, rat > 1000 mg/kg bw per day (the highest dose tested)	
Relevant inhalation NOAEL ‡	No data – not required	

Genotoxicity ‡ (Annex IIA, point 5.4)

Weak evidence of clastogenicity *in vitro*, non genotoxic *in vivo*	

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

Target/critical effect ‡	Rat: Slightly depressed bw, RBC, hyperbilirubinaemia and spleen (haemosiderosis) Mouse: RBC (mild anaemia), spleen (medullary and extramedullary erythropoiesis and haemosiderosis)	
Relevant NOAEL ‡	2-year, rat: 7.8 mg/kg bw per day 18-month, mouse: 10.8 mg/kg bw per day	
Carcinogenicity ‡	Not oncogenic in rats and mice	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Parental toxicity: increased spleen and kidney weights, increased incidence and severity of splenic haemosiderosis Reproductive toxicity: No specific effects on reproduction Offspring toxicity: Reduced body weight gain -at parental toxic doses	
Relevant parental NOAEL ‡	15 mg/kg bw per day	

Relevant reproductive NOAEL ‡	306 mg/kg bw per day (the highest dose tested)	
Relevant offspring NOAEL ‡	15 mg/kg bw per day	

Developmental toxicity

Developmental target / critical effect ‡	Rat: Dams: hemorrhagic discharge. Reduced body weight gain of the 6 dams with live foetuses. Foetuses: malformations (umbilical hernia) Rabbit: Dams: death Foetuses: Slightly delayed ossification.	
Relevant maternal NOAEL ‡	Rat: 200 mg/kg bw per day Rabbit: 50 mg/kg bw per day	
Relevant developmental NOAEL ‡	Rat LOAEL: 10 mg/kg bw per day Rabbit:300 mg/kg bw per day	**H361d**

Developmental neurotoxicity

Developmental neurotoxicity critical effect ‡	Dams: No adverse effect observed Foetuses: Cerebellum, morphometric changes in males Effect on acoustic startle response in females	
Relevant maternal NOAEL ‡	326 mg/kg bw per day (the highest dose tested)	
Relevant developmental neurotoxicity NOAEL ‡	8.2 mg/kg bw per day	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No signs of acute neurotoxicity up to 2000 mg/kg bw	
Repeated neurotoxicity ‡	No evidence of neurotoxicity (FOB examinations) in rat 28-day study	
Delayed neurotoxicity ‡	Not performed – not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	Studies on possible immunotoxicity: - Anaemia not related to the formation of antibodies

	against acibenzolar-S-methyl (serum from rat). - No evidence of toxicity or of an immunosuppressant effect on the humoral immune system up to 406 mg/kg bw per day (28-day in mice; Sheep Red Blood Cells as the Antigen). *In vitro* study on the mechanism leading to haemolytic anaemia: - Acibenzolar-S-methyl and methane thiol induce erythrocytes glutathione depletion, altered haemoglobin and increased lipid peroxidation. Anaemia not related to antibodies
Studies performed on metabolites or impurities ‡	Studies on plant (and major rat) metabolite CGA 210007 **Acute toxicity** Rat oral LD_{50} > 2000 mg/kg bw Rat dermal LD_{50} > 2000 mg/kg bw Skin/eye irritation: Non irritant (rabbit). Non sensitiser (M&K) **Short term toxicity** (28-day, rat) Anaemia. Increased liver weight and decreased thymus weight. NOAEL = 100 mg/kg bw per day **Genotoxicity** Positive in reverse bacterial gene mutation assay; weakly clastogenic *in vitro*, negative *in vivo* Three other *in vitro* tests negative Overall non genotoxic, the reference values of the parent are applicable to this metabolite Studies on plant metabolite CGA 323060 **Acute toxicity** Rat oral LD_{50} > 2000 mg/kg bw **Genotoxicity** Negative in reverse gene mutation assay Studies on plant metabolite CGA 324041 **Acute toxicity** Rat oral LD_{50} > 2000 mg/kg bw **Genotoxicity** Negative in reverse gene mutation assay

Medical data ‡ (Annex IIA, point 5.9)

	Occasional irritation (skin, eyes and respiratory tract) seen in exposed workers. No adverse health effects have been associated to the handling of large quantities of acibenzolar-S-methyl

	for nearly 20 years, at a number of sites and with the use of appropriate control strategies.

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.03 mg/kg bw per day	Rat, developmental study	300 ([1])
AOEL ‡	0.03 mg/kg bw per day	Rat, developmental study	300 ([1])([2])
ARfD ‡	0.03 mg/kg bw	Rat, developmental study	300 ([1])

([1]) increased uncertainty factor by 3 as based on a LOAEL
([2]) no correction needed regarding oral absorption
Reference values applicable to metabolite CGA210007

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (A9180A (BION 50 WG) with 500 g acibenzolar-S-methyl/kg)	Concentrate:-0.1% Spray dilutions: 33% (down to 0.25 g/L) Calculated from *in vitro* study on human skin For higher dilutions : prorata data with a maximum value of 75% (default)

Exposure scenarios (Annex IIIA, point 7.2)

Operator	According to the German model, estimated exposure of the operator during mixing/loading and application of A9180A is below the established AOEL when considering the use of personal protective equipment PPE (protective gloves during mixing/loading and application and coverall) for pome fruit use and without PPE for the other intended uses. **High crops, tractor mounted equipment**, application rate 100 g acibenzolar-S-methyl/ha UK POEM — % of AOEL No PPE — 510 % PPE (gloves during M/L and application) — 360 % German model No PPE — 330 % PPE (gloves during M/L and gloves & coverall during application) — 49 %

	Low (field) crops, tractor mounted equipment, application rate 25 g acibenzolar-S-methyl/ha UK POEM (100 L/ha) — % of AOEL No PPE — 193 % PPE (gloves during M/L and application) — 33 % UK POEM (1000 L/ha) No PPE — 46 % PPE (gloves during M/L and application) — 9 % German model No PPE — 37 % PPE (gloves during M/L and gloves & coverall during application) — 2.8 % **High crops, hand-held applications**, application rate 25 g acibenzolar-S-methyl/ha German model — % of AOEL No PPE — 37 % PPE (gloves during M/L and gloves & coverall during application) — 5.9 % **Indoor applications**, application rate 25 g acibenzolar-S-methyl/ha EUROPOEM — % of AOEL No PPE — 90 % PPE (gloves & coverall) — 7 % IVA modified German model No PPE — 608 % PPE (gloves & coverall) — 70 %
Workers	For pome fruit, worker exposure is below the AOEL only with PPE (gloves) and taking into account only one application. For tomato in greenhouse, worker exposure is below the AOEL with PPE (gloves). For tomato and tobacco in field, worker exposure is below the AOEL without PPE. **Harvesting pome fruits** — % of AOEL After 1 application No PPE — 450 % PPE — 45 % Multiple applications (6 according to GAP) No PPE — 2061 % PPE — 206 % **Harvesting tomatoes (indoor)** — % of AOEL After 1 application No PPE — 64 % PPE — 6.4 %

	Multiple applications (6 according to GAP)
	No PPE 267 %
	PPE 27 %
	Crop inspections (tomato/tobacco) – field % of AOEL
	After 1 application
	No PPE 16 %
	PPE 1.6 %
	Multiple applications (6/4 according to GAP)
	No PPE 51 %
	PPE 5 %
Bystanders and residents	Bystander exposure to spray drift: % of AOEL
	standing at 5 m from spraying 35 %
	Residential exposure:
	Adults 22 %
	Children 34 %

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

Substance classified	Acibenzolar-S-methyl
Harmonised classification	As listed in Annex VI of Regulation (EC) No 1272/2008[9] (as amended): GHS07 Warning Skin Irrit. 2 H315 – Causes skin irritation* Skin Sens. 1 H317 – May cause an allergic skin reaction Eye Irrit. 2 H319 – Causes serious eye irritation* STOT SE 3 H335 – May cause respiratory irritation*
RMS/peer review proposal[10]	Considering the criteria of Regulation (EC) No 1272/2008 (as amended): GHS07 Warning Skin Irrit. 2 H315 – Causes skin irritation* Skin Sens. 1 H317 – May cause an allergic skin reaction Eye Irrit. 2 H319 – Causes serious eye irritation* STOT SE 3 H335 – May cause respiratory irritation* **Repr. 2 H361d – Suspected of damaging the unborn child**

*Based on human data

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

[10] It should be noted that proposals for classification made in the context of the evaluation procedure under Regulation (EC) No 1107/2009 are not formal proposals. Classification is formally proposed and decided in accordance with Regulation (EC) No 1272/2008.

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

Plant groups covered	Wheat (cereals), tomatoes (fruiting vegetables), tobacco and lettuce (leafy vegetable) after foliar application
Rotational crops	lettuce, radish, winter wheat, maize and mustard
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	pH 4, 90°C, 20 minutes- pH 5, 100°C, 60 minutes : stable pH 6, 120°C, 20 minutes: the parent compound is partially hydrolysed into acibenzolar acid
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes
Plant residue definition for monitoring	Sum of acibenzolar-S-methyl and acibenzolar acid and its conjugates expressed as acibenzolar-S-methyl
Plant residue definition for risk assessment	Cereals, fruits and fruiting vegetables, tobacco: Sum of acibenzolar-S-methyl and acibenzolar acid and its conjugates expressed as acibenzolar-S-methyl Other crops: depending on residue and tox data the metabolite 4OH acibenzolar acid could be considered in residue definition
Conversion factor (monitoring to risk assessment)	None

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

Animals covered	Lactating goat and hen
Time needed to reach a plateau concentration in milk and eggs	Milk : 24 hours Eggs: not reached at the end of the study (4 days)
Animal residue definition for monitoring	Not necessary due to low livestock exposure, even considering all registered uses at EU level, and low level of residues in available metabolism studies.
Animal residue definition for risk assessment	Not necessary
Conversion factor (monitoring to risk assessment)	Not relevant
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)

No residue above 0.01 mg/kg is expected in rotational crops

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

Acibenzolar-S-methyl is stable in dry commodities (wheat grain) for 24 months and in high water commodities (cabbage, squash, lettuce, tomatoes, and turnip roots) and tobacco for 21 months. Acibenzolar acid is stable in high water commodities (cabbage, squash, lettuce, tomatoes, and turnip roots) and tobacco for 21 months

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

	Ruminant	Poultry	Pig
	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)	Yes (0.15 mg/kg diet, 0.0064 mg/kg bw/day)	No	No
Potential for accumulation (yes/no)	No	No	No
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	No	No	-
	Feeding studies (feeding study on lactating cows 0.0098, 0.0512 and 0.1015 mg/kg bw/day) Residue levels in matrices : Mean (max) mg/kg		
Muscle	<0.02 mg/kg whatever the feeding dose	-	-
Liver	<0.02 mg/kg whatever the feeding dose	-	-
Kidney	<0.02 mg/kg whatever the feeding dose	-	-
Fat	<0.02 mg/kg whatever the feeding dose	-	-
Milk	<0.02 mg/kg whatever the feeding dose		

Eggs		-	

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)
Pome fruits	South EU	Apples: 7x <0.01, 0.01, 0.06, 0.08, 2x0.09	GAP: **6x100 g as/ha, PHI 14 days** Extrapolation from apples to the whole pome fruit group	0.2 mg/kg	0.09	<0.01
Tomatoes	Indoor [(d)]	Fruit: 0.06, 0.10, 0.12, 0.13, 0.18, 0.29, 0.62	GAP: **6x25 g as/ha, PHI 3 days**	1 mg/kg	0.62	0.13
	South EU	Fruit: 0.06, 0.09, 2x0.10, 0.12, 0.13, 0.14, 0.15	GAP: **6x25 g as/ha, PHI 3 days**	0.3 mg/kg	0.15	0.11

(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
(d): Use gives an exceedence of the ARfD (120.2% ARfD for BE Child)

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

ADI	0.03 mg/kg bw/day
TMDI (% ADI) according to WHO European diet	12.7% (considering all EU MRLs and new proposed ones)
TMDI (% ADI) according to French diets	N/A
IEDI (WHO European Diet) % ADI)	Not performed as TMDI is bellow ADI
NEDI (specify diet) (% ADI)	N/A
Factors included in IEDI and NEDI	N/A
ARfD	0.03 mg/kg bw/day
IESTI (%ARfD)	120.2% for indoor tomato, 58 %, for outdoor tomato, 29.4 % for apples
NESTI (% ARfD) according to national (to be specified) large portion consumption data	N/A
Factors included in IESTI and NESTI	Highest residue level for RAC STMR for apple and pear juice and quinces jelly STMRp for tomato juice and tomato preserved

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

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Tranfer factor	Yield factor	
Tomatoes, washed fruit	2	0.84	-	-
Tomatoes, peeled fruit	2	0.67	-	-
Tomatoes, juice	4	0.78	-	-
Tomato, paste/puree	4	1.88	-	-
Tomatoes, canned/preserve fruit	4	0.65	-	-
Tomatoes, Ketchup	2	1.88	-	-

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

Pome fruits:	0.2
Tomato:	0.3
Animal commodities:	Not necessary

Proposed GRL

Tobacco:	2

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

Mineralization after 100 days ‡	Phenyl label : 7.5 - 44.1 % (90 d) at 20° C (4 soils) *8.9 – 38.6 % (112 d) at 20° C (4 soils)* *43.3 –53.5 % (125 d) at 20° C (4 soils)*
Non-extractable residues after 100 days ‡	Phenyl label : 27.7 - 59.8 % (90 d) at 20° C (4 soils) *39.5 – 55.5 % (84 d) at 20° C (2 soils)* *18.5 – 25.9 % (125 d) at 20° C (4 soils)*
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	CGA 210007 : maximum 96.1% at 7 DAT % (max range 82.6 - 96.1% at 1 - 7 d) (10 soils) SYN 546642 : maximum 39.0% at 92 DAT (max range 21.8 – 39.0 % at 92 – 125 d) (4 soils)

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

Anaerobic degradation ‡	
Mineralization after 100 days	Not determined for a.s., not required (spring application, rapid aerobic degradation). CGA 210007 not degraded.
Non-extractable residues after 100 days	-
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)	Light enhances the slow degradation of acibenzolar-S-methyl on dry soil and the degradation of CGA 210007 rapidly formed on wet soil. Bound residues (irradiation, wet soil): 61 %

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

Laboratory studies

Acibenzolar-S-Methyl	Aerobic conditions						
Soil type	X^2	pH	t. °C / % MWHC	DT_{50}/DT_{90} (d)	DT_{50} (d) 20°C pF2/10kPa	r^2	Method of calculation
Silty loam	8.52	7.0	20 / 80.0	0.190/0.631	0.155	nr	SFO[a]
Loamy sand	1.58	7.4	20 / 46.7	0.204/0.679	0.157	nr	SFO[a]
Sand	0.56	8.2	20 / 23.5	0.516/1.72	0.441	nr	SFO[a]
Sandy loam	0.80	7.55	20 / 47.2	0.368/1.22	0.248	nr	SFO[a]
Silty loam [c]	1.08	7.2	20 / 60.9	0.263/0.874	0.184	nr	SFO[a]
Silty loam [c]	2.97	7.2	20 / 60.9	0.544/1.81	0.234	nr	SFO[a]
Silty loam [c]	5.11	7.2	10 / 60.9	0.981/3.26	0.266	nr	SFO[a]
Silty loam [c]	3.93	7.2	20 / 60.9	0.260/0.862	0.182	nr	SFO[a]
Silty loam [c]	1.49	7.6	20 / 41.4	0.031/0.102	0.031	0.999	SFO[b]
Geometric mean (Gartenacker, n = 5)					**0.145**		
Sandy loam	1.00	6.5	20 / 26.6	0.037/0.122	0.037	0.998	SFO[b]
Sandy loam	5.92	7.6	20 / 35.6	0.109/0.361	0.109	0.996	SFO[b]
Sandy loam	6.23	7.6	20 / 33.1	0.057/0.189	0.057	0.999	SFO[b]
Geometric mean (n=8)					**0.131**		

[a] – Kinetic evaluation from Kind, 2011
[b] – Kinetic evaluation from Mackenzie, 2012
[c] – Gartenacker soil
nr: not reported in the original report

CGA 210007	Aerobic conditions							
Soil type	X^2	pH	t. °C / % MWHC	DT_{50}/DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Silty loam	7.01	7.0	20 / 80.0	20.6/68.5	0.90	16.9	nr	SFO[a]
Loamy sand	8.94	7.4	20 / 46.7	20.3/67.3	1.0	15.6	nr	SFO[a]
Sand	1.69	8.2	20 / 23.5	106/353	0.98	90.6	nr	SFO[a]
Sandy loam	4.24	7.55	20 / 47.2	19.5/64.8	1.0	13.1	nr	SFO[a]
Silty loam [c]	7.34	7.2	20 / 60.9	24.1/80.2	0.98	16.8	nr	SFO[a]
Silty loam [c]	9.46	7.2	20 / 60.9	108/359	0.89	46.5	nr	SFO[a]
Silty loam [c]	7.57	7.2	10 / 60.9	76.3/253	0.89	20.7	nr	SFO[a]
Silty loam [c]	11.7	7.2	20 / 60.9	12.1/40.2	1.0	8.46	nr	SFO[a]
Silty loam [c]	6.78	7.6	20 / 41.4	9.4/31.3	0.96	9.43	0.995	SFO[b]
Geometric mean (Gartenacker, n = 5)					**0.94** [d]	**16.7**		
Sandy loam	4.15	6.5	20 / 26.6	4.09/13.6	0.99	4.09	0.997	SFO[b]
Sandy loam	6.11	7.6	20 / 35.6	27.2/90.5	1.0	27.2	0.989	SFO[b]
Sandy loam	7.84	7.6	20 / 33.1	29.0/96.3	1.0	29.0	0.984	SFO[b]
Geometric mean (n=8)					**0.98** [d]	**19.0**		

[a] – Kinetic evaluation from Kind, 2011
[b] – Kinetic evaluation from Mackenzie, 2012
[c] – Gartenacker soil
[d] – Arithmetic mean

SYN 546642	Aerobic conditions							
Soil type	X^2	pH	t. °C / % MWHC	DT_{50}/DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Sandy clay loam [a]	17.4	6.5	20 / 26.6	259/862	0.26	259	0.863	SFO
Sandy clay loam [b]	7.1	6.1	20 / 26.8	87/289 [b]	-	87 [b]		DFOP
Geometric mean (18 Acres, n = 2)						150		
Silty loam [a]	17.9	7.6	20 / 41.4	130/431	0.44	130	0.902	SFO
Silty loam [b]	2.1	7.5	20 / 39.0	77.6/258 [b]	-	77.6 [b]		DFOP
Geometric mean (Gartenacker, n = 2)						100.5		
Sandy loam [a]	13.0	7.6	20 / 35.6	> 1000	1.00 [e]	> 1000 [e]	0.979	SFO
Sandy loam [a]	13.1	7.6	20 / 33.1	> 1000	1.00 [e]	378	0.940	SFO
Sandy Clay loam [b]	3.0	7.9	20 / 25.1	87/288 [b]	-	86.8 [b]		DFOP
Geometric mean (n=5)					**0.68** [d]	**218**		

[a] – Kinetic evaluation from Mackenzie, 2012
[b] – From slow phase DFOP
[c] –Kinetic evaluation from Mills 2013
[d] –Arithmetic mean
[e] – No acceptable fit, default value used

Field studies

Acibenzolar-S-methyl	Aerobic conditions						
Soil type	Location	X^2	pH	DT_{50} (d) actual	St. (r^2)	Remarks	Method of calculation

Loamy sand	Les Barges, Switzerland	nr	6.6	6.5[a]	nr	DT_{50} of 6.5 days recalculated as DT_{50} = 5 days in Review Report	SFO
Silt clay	St. Aubin, Switzerland	nr	nr	0.1	nr	Radiolabelled study. Acibenzolar-S-methyl DT_{50} = 0.1 days in Review Report	SFO
Silt clay	St. Aubin, Switzerland	nr	nr	<30[a]	nr	Not presented in the Review Report	SFO
Silt clay	St. Aubin, Switzerland	nr	nr	<14[a]	nr	not presented in the Review Report	SFO
Sandy loam	Tierce, France	nr	7.3	<28[a]	nr	Recalculated as DT_{50} < 14 days in Review Report however it is not clear whether this is derived from Tierce or Aigues-Vives.	SFO
Clay loam	Aigues-Vives, France	nr	7.8	<30[a]	nr	As above	SFO
Sand	Sampson County North Carolina, USA	nr	7.2	2.0	0.52	Reported in Review Report (4 x 116 g/ha)	SFO
Loamy sand	Santa Cruz, California, USA (with Tomatoes)	nr	7.0	16.0	0.77	Reported in Review Report, plot cropped with tomatoes (4 x 114 g/ha)	SFO
Loamy sand	Santa Cruz, California, USA (bare soil)	nr	7.0	27.0	0.88	Reported in Review Report, bare soil applications (4 x 114 g/ha)	SFO
Max < 30 d.							

a - based on total residues determined as acibenzolar + CGA 210007
nr: not reported

CGA 210007	Aerobic conditions						
Soil type	Location	X[1]	pH	DT_{50} (d) actual	St. (r^2)	Remarks	Method of calculation

Clay loam	St. Aubin, Switzerland	nr	nr	5.8	nr	Radiolabelled study. DT_{50} = < 14 days in Review Report	SFO
Loamy sand	Tierce, France	nr	nr	5.5	nr	Not reported in Review Report	SFO
Loamy sand	Aigues-Vives, France	nr	7.8	19.5	nr	Not reported in Review Report	SFO
Loamy sand	Sampson County, North Carolina (USA)	nr	7.2	7.0	0.67	Reported in Review Report	SFO
Sandy clay loam	Santa Cruz, California (with Tomatoes) USA	nr	7.0	45.0	0.94	Reported in Review Report	SFO
Sandy clay loam	Santa Cruz, California (bare soil) USA	nr	7.0	59.0	0.83	Reported in Review Report	SFO
Max = 59 d.							

pH dependence ‡ (yes / no) (if yes type of dependence)	no
Soil accumulation and plateau concentration ‡	Switzerland (50 g a.s./ha for 3 years, LOD 4 µg/kg) Total residues < LOD 100 d after each treatment

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Acibenzolar-S-methyl‡					
Soil type	OC %	Soil pH	Kf (mL/g)	Kfoc (mL/g)	1/n
Loamy sand	0.8	7.3	8.3	1041	0.790
Loam	1.4	5.5	13.7	981	0.790
Sand	0.3	6.8	5.7	1885	0.780
Silt loam	4.7	7.2	58	1235	0.750
Silt loam	1.4	6.6	22.5	1618	0.847
sand	0.35	5.4	3.6	1039	0.936
Loam	1.5	7.3	49.6	3288	0.820
Loamy sand	0.46	6.2	13.2	2843	0.682
Clay loam	0.58	8	12	2076	0.891
Sandy loam	0.75	7.3	3.7	492	1.00
Arithmetic mean				**1650**	0.829
pH dependence, Yes or No			No		

CGA 210007‡					
Soil type	OC %	Soil pH	Kf (mL/g)	Kfoc (mL/g)	1/n
Silt loam	1.3	6.6	0.9	65	0.860
sand	0.3	5.4	0.6	174	0.840
Loam	1.5	7.3	2.3	150	0.820
Loamy sand	0.5	6.2	1.4	312	0.830
Clay loam	0.6	8	0.5	89	0.760
Sandy loam	0.8	7.3	0.3	40	0.870
Loamy Sand	1.3	5	0.9	72	0.910
Loamy Sand	1.1	7.5	0.7	59	0.850
Loam	4.7	7.2	2.5	52	0.960
Arithmetic mean				**113**	**0.856**
pH dependence, Yes or No			No		

SYN 546642‡					
Soil type	OC %	Soil pH	Kd (mL/g)	Kdoc (mL/g)	1/n
Sandy loam	2.38	6.1	138.1	5806	1
Silt loam	1.97	7.3	60.5	3066	1
Sandy loam	2.55	7.3	58.8	2303	1
Sandy loam	3.13	7.4	80.5	2570	1
Loamy sand	0.48	5.0	24.5	5079	1
Arithmetic mean				**3765**	**1**
pH dependence, Yes or No			No		

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

Column leaching ‡	4 soil types (sand, loamy sand, loam, silt loam ; pH 5.5 - 7.3, OC 0.4 - 4.7 %) Radioactivity in leachates < 2.7 %
Aged residues leaching ‡	2 soil types (silt loam pH 7.2 OC 2.4 %, loamy sand pH 7.6 OC 2 %). Incubation 5 h (a.s. < 22.7 %, CGA 210007 > 63.8 %). 200 mm / 2 d : 0.17 and 0.23 % RA in leachates 508 mm / 40 d. : 0.28 and 14.9 % RA in leachates (mainly CGA 210007)
Lysimeter/ field leaching studies ‡	Study not conducted as reliable adsorption coefficient values available from there adsorption/desorption studies

PEC (soil) (Annex IIIA, point 9.1.3)

PEC (soil) (OECD data point IIIA 9.4)

Parent (Acibenzolar-S-methyl) Method of calculation	DT_{50} (d): 30 days (max. field, worst case value) SFO kinetics
Application data	Crop: pome fruit Depth of soil layer: 5 cm Soil bulk density: 1.5 g/cm^3 % plant interception: 65/65/70/70/70/70 Number of application: 6 Interval (d): 5 Application rate(s): 100 g a.s./ha

PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		nc		0.191	
Short term	24h	nc	nc	0.187	0.189
	2d	nc	nc	0.183	0.187
	4d	nc	nc	0.174	0.183
Long term	7d	nc	nc	0.138	0.168
	28d	nc	nc	0.100	0.154
	50d	nc	nc	0.060	0.133
	100d	nc	nc	0.019	0.095
Plateau concentration		Not appropriate	nc:not calculated		

Parent (Acibenzolar-S-methyl) Method of calculation	DT_{50} (d): 30 days (max. field, worst case value) SFO kinetics
Application data	Crop: tomato ; tobacco Depth of soil layer: 5 cm Soil bulk density: 1.5 g/cm^3 % plant interception: 50/50/70/70/70/70 for tomato 50/50/70/70 for tobacco Number of application: 6 for tomato 4 for tobacco Interval (d): 5 Application rate(s): 25 g a.s./ha

PEC$_{(s)}$	Single application	Single application	Multiple	Multiple

(mg/kg)	Actual	Time weighted average	application Actual	application Time weighted average
Tomato or Tobacco				
Initial	nc		0.041	

CGA 210007 Method of calculation	DT_{50} = 59 d (max. field, worst case value) SFO kinetics
Application data	Crop: pome fruit Depth of soil layer: 5 cm Soil bulk density: 1.5 g/cm^3 % plant interception: 65/65/70/70/70/70 Number of application: 6 Interval (d): 5 Application rate(s): 100 g a.s./ha corrected by molar mass ratio (0.857) and occurrence (100%)

PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		nc		0.187	
Short term	24h	nc	nc	0.185	0.161
	2d	nc	nc	0.183	0.161
	4d	nc	nc	0.179	0.161
Long term	7d	nc	nc		
	28d	nc	nc	0.135	0.148
	50d	nc	nc	0.104	0.135
	100d	nc	nc	0.058	0.107
Plateau concentration		Not appropriate	nc:not calculated		

SYN 546642 Method of calculation	DT_{50} = 1000 d (max. lab.) SFO kinetics
Application data	Crop: pome fruit Depth of soil layer: 5 cm Soil bulk density: 1.5 g/cm^3 % plant interception: 65/65/70/70/70/70 Number of application: 6 Interval (d): 5 Application rate(s): 100 g a.s./ha corrected by molar mass ratio (0.933) and occurrence (40.7%)

PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		nc		0.095	
Short term	24h	nc	nc	0.0953	0.0906
	2d	nc	nc	0.0953	0.0906
	4d	nc	nc	0.0951	0.0906
Long term	7d	nc	nc	0.0949	0.0906
	28d	nc	nc	0.0936	0.0905
	50d	nc	nc	0.0922	0.0902
	100d	nc	nc	0.089	0.089
Plateau concentration		0.425 reached after 23 years	nc:not calculated		

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

Hydrolytic degradation of the active substance and metabolites > 10 %	pH 5 DT50 3.8 years (extrapolated value at 20° C) pH 7 DT50 162 d (extrapolated value at 20° C) pH 9 DT50 19 h (extrapolated value at 20° C) CGA 210007 > 10 % (stable at all pH)
Photolytic degradation of active substance and metabolites above 10 % ‡	pH 5.12, 25° C DT_{50} 0.75 h numerous metabolites, all < 10 % volatiles up to 19 % (mainly CO_2)
Quantum yield of direct phototransformation in water at Σ > 290 nm	0.036 and 0.021 at 289 and 327 nm respectively
Readily biodegradable ‡ (yes/no)	No

Degradation in water / sediment

Parent	Distribution (eg max in water 52.4% after *n* d. max. in sed 36.2 % after O DAT)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	χ^2	DT_{50}-DT_{90} water	χ^2	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Rhine River	8.6	n.d.	20	0.823	0.944	1.20	20.9	n.d.		SFO

Pond	7.1	n.d.	20	0.610	7.56	0.564	2.56	n.d.		SFO
Geometric mean/median				0.709		0.823				

n.d.: not determined

CGA 210007	Distribution (max. in water 75 % (3 d) and in sediment 38 % (59 d))									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50} whole sys. (d)	χ^2	DT_{50} Water (d)	χ^2	DT_{50}-DT_{90} Sed (d)	St. (r^2)	Method of calculation
Rhine River	8.6	n.d.	20	511	4.64	n.d.		n.d.		SFO
Pond	7.1	n.d.	20	342	1.47	n.d.		n.d.		SFO
Geometric mean/median				418						

n.d.: not determined

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization x % after n d. (end of the study)	Non-extractable residues in sed. max x % after n d	Non-extractable residues in sed. max x % after n d (end of the study)
Rhine River	8.6	n.d.	9.5 after 363 days	26.4 after 363 days	26.4 after 363 days
Pond	7.1	n.d.	9.6 after 363 days	36.2 after 363 days	36.2 after 363 days

n.d.: not determined

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

Parent Parameters used in FOCUSsw step 1 and 2	FOCUS calculator : FOCUS Step 1-2 version 1.1 Molar weight (g/mol): 210.3 Water solubility at 25°C (mg/L): 7.7 Kf_{OC} (L/kg): 1650 DT_{50} soil (d): 0.131(step2) DT_{50} water/sediment system (d): 0.709 DT_{50} water (d): 1000 (level P-I) DT_{50} sediment (d): 0.709
Parameters used in FOCUSsw step 3 (if performed)	As above FOCUS SWASH 3.1 package EVA 2.1 for deposition single and multiple applications (single worst case except in some ponds)
Application rate	4 x 25 g a.s./ha (tobacco) 6 x 100 g a.s./ha (apples) 6 x 25 g a.s./ha (tomatoes) single applications since worst case (step 2)
Main routes of entry	Drift

FOCUS STEP 1						
Scenario	Application Timing	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	Max. TWA 21 d	Actual	Max. TWA 21 d
Tobacco		0	2.83	0.141	43.0	2.23
Pome fruits North Europe	early application	0	20.15	0.85	172	10.16
Tomato South Europe	June-Sept.	0	2.83	0.141	43.0	2.23
FOCUS STEP 2						
Scenario	-	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	Max. TWA 21 d	Actual	Max. TWA 21 d
Tobacco North Europe	March-May	0	0.230	0.015	0.217	0.031
Tobacco South Europe		0	0.230	0.015	0.217	0.031
Tobacco North Europe	June-Sept.	0	0.230	0.015	0.217	0.031
Tobacco South Europe		0	0.230	0.015	0.217	0.031
Pome fruits North Europe	June-Sept.	0	3.44	0.324	4.74	0.660
Pome fruits South Europe		0	3.44	0.324	4.74	0.660
Tomato North Europe	March-May	0	0.143	0.013	0.190	0.027
Tomato South Europe		0	0.143	0.013	0.190	0.027
Tomato North Europe	June-Sept.	0	0.143	0.013	0.190	0.027
Tomato South Europe		0	0.143	0.013	0.190	0.027

STEP 3	**Scenario**	**Water body**	**Max. PEC_{SW} (µg/L)**	**Max. PEC_{Sed} (µg/kg)**	**Max. TWA in Water (µg/L)**			**Date of Global Maximum PEC_{SW}**
					7 days	**21 days**	**28 days**	
tobacco (single)	R3	Stream	0.117	0.023	0.006	0.002	0.001	03-Jun-75
tobacco (multiple)	R3	Stream	0.079	0.015	0.004	0.003	0.003	15-Jul-75
pome fruits late scenario (single application)	D3	Ditch	3.66	1.67	0.655	0.218	0.164	17-May-92
	D4	Pond	0.164	0.171	0.146	0.118	0.107	30-May-85
	D4	Stream	3.54	0.294	0.060	0.020	0.015	30-May-85
	D5	Ditch	0.164	0.176	0.146	0.118	0.107	11-May-78
	D5	Stream	3.60	0.156	0.032	0.011	0.008	11-May-78

	R1	Pond	0.164	0.206	0.145	0.116	0.104	15-May-84
	R1	Stream	2.76	0.257	0.053	0.018	0.013	15-May-84
	R2	Stream	3.70	0.221	0.046	0.015	0.011	22-Apr-77
	R3	Stream	3.94	0.697	0.163	0.054	0.041	18-May-80
	R4	Stream	2.81	0.382	0.081	0.027	0.020	15-Apr-84
pome fruits late scenario (multiple applications)	D3	Ditch	2.21	1.09	0.917	0.64	0.48	06-Jul-92
	D4	Pond	0.341	0.305	0.305	0.272	0.261	11-Jul-85
	D4	Stream	2.24	0.377	0.091	0.080	0.060	11-Jul-85
	D5	Ditch	0.383	0.378	0.344	0.302	0.292	23-Jun-78
	D5	Stream	2.42	0.551	0.265	0.132	0.134	23-Jun-78
	R1	Pond	0.331	0.322	0.293	0.273	0.267	04-Jul-84
	R1	Stream	1.71	0.235	0.100	0.051	0.050	04-Jul-84
	R2	Stream	2.29	0.178	0.071	0.035	0.035	03-Jun-77
	R3	Stream	2.42	0.498	0.258	0.129	0.122	21-Jun-80
	R4	Stream	1.71	0.252	0.099	0.059	0.052	20-Apr-84
pome fruits early application (single application)	D3	Ditch	7.753	3.507	1.392	0.464	0.348	17 May
	D4	Pond	0.470	0.438	0.419	0.341	0.309	30 May
	D4	Stream	7.933	0.658	0.135	0.045	0.034	30 May
	D5	Pond	0.470	0.495	0.419	0.341	0.310	12 May
	D5	Stream	8.068	0.350	0.0723	0.0241	0.0181	11 May
	R1	Pond	0.470	0.439	0.415	0.332	0.299	13-June
	R1	Stream	6.300	0.835	0.183	0.061	0.046	13-June
	R2	Stream	8.309	0.495	0.103	0.034	0.025	22 Apr
	R3	Stream	8.833	1.557	0.366	0.122	0.09	18 May
	R4	Stream	6.298	0.855	0.182	0.061	0.045	15 Apr
tomatoes (single application)	D6	Ditch	0.155	0.033	0.008	0.003	0.002	24-Apr-86
	R2	Stream	0.138	0.009	0.002	0.001	<0.001	22-Apr-77
	R3	Stream	0.147	0.030	0.008	0.003	0.002	01-Jun-80
	R4	Stream	0.101	0.008	0.002	0.001	<0.001	04-May-84
tomatoes (multiple application)	D6	Ditch	0.093	0.028	0.012	0.009	0.008	24-Jun-86
	R2	Stream	0.082	0.006	0.001	0.001	0.001	06-May-77
	R3	Stream	0.086	0.018	0.005	0.005	0.005	18-Jun-80
	R4	Stream	0.061	0.008	0.002	0.002	0.001	06-Jun-84

STEP 4	**Scenario**	**Water body**	**Max. PEC_{SW} (µg/L)**	**Max. PEC_{Sed} (µg/kg)**	**Max. TWA in Water (µg/L)**			**Date of Global Maximum PEC_{SW}**
					7 days	**21 days**	**28 days**	
pome fruits late application (single) 50 % spray drift reduction single application (without deposition)	D3	Ditch	1.98	1.13	0.167	0.137	0.124	17-May-92
	D4	Pond	0.185	0.198	0.043	0.015	0.011	31-May-85
	D4	Stream	1.94	0.177	0.167	0.137	0.124	30-May-85
	D5	Ditch	0.185	0.204	0.023	0.008	0.006	12-May-78
	D5	Stream	1.92	0.092	0.166	0.134	0.121	11-May-78

	R1	Pond	0.185	0.239	0.038	0.013	0.010	16-May-84
	R1	Stream	1.54	0.156	0.033	0.011	0.008	15-May-84
	R2	Stream	2.00	0.133	0.117	0.039	0.029	22-Apr-77
	R3	Stream	2.22	0.437	0.059	0.020	0.015	18-May-80
	R4	Stream	1.61	0.236	0.167	0.137	0.124	15-Apr-84
pome fruits late application 10 m spray buffer distance single Application (including deposition)	D3	Ditch	1.103	0.608	0.262	0.0875	0.0656	26-Sep
	D4	Pond	0.110	0.228	0.101	0.0841	0.0771	30-Oct
	D4	Stream	1.268	0.155	0.033	0.011	0.0084	30-Oct
	D5	Ditch	0.110	0.191	0.102	0.0846	0.0775	28-Nov
	D5	Stream	1.384	0.350	0.0803	0.0268	0.0201	27-Nov
	R1	Pond	0.110	0.230	0.101	0.0823	0.0748	23-Nov
	R1	Stream	0.993	0.152	0.0317	0.0106	0.00792	14-Nov
	R2	Stream	1.332	0.099	0.0221	0.00736	0.00552	09-Oct
	R3	Stream	1.385	0.317	0.078	0.026	0.019	27-Oct
	R4	Stream	0.884	0.0278	0.0059	0.0019	0.0015	19-Oct
pome fruits late application 10 m spray buffer distance multiple applications (including deposition)	D3	Ditch	0.769	0.759	0.408	0.292	0.228	29-Oct
	D4	Pond	0.270	0.424	0.249	0.222	0.211	9-Oct
	D4	Stream	0.865	0.171	0.0705	0.0354	0.0351	27-Aug
	D5	Ditch	0.302	0.297	0.277	0.249	0.236	22-Sep
	D5	Stream	0.929	0.219	0.110	0.0733	0.0825	17-Sep
	R1	Pond	0.249	0.410	0.228	0.205	0.194	18-Oct
	R1	Stream	0.672	0.115	0.0435	0.0217	0.0217	11-Oct
	R2	Stream	0.900	0.0676	0.0303	0.0152	0.0114	24-Sep
	R3	Stream	0.934	0.187	0.107	0.0535	0.0402	28-Sep
	R4	Stream	0.672	0.0892	0.0433	0.0252	0.0189	15-Sep
pome fruit early application 10 m spray buffer Distance (including deposition)	D3	Ditch	3.739	1.731	0.682	0.227	0.170	17 May
	D4	Pond	0.292	0.310	0.267	0.217	0.196	30 May
	D4	Stream	4.197	0.350	0.0726	0.0242	0.0181	30 May
	D5	Pond	0.292	0.318	0.266	0.217	0.197	11 May
	D5	Stream	4.266	0.186	0.0387	0.0129	0.0097	11 May
	R1	Pond	0.292	0.282	0.264	0.211	0.190	13-Jun
	R1	Stream	3.332	0.445	0.0983	0.0328	0.0246	13-Jun
	R2	Stream	4.396	0.263	0.055	0.0183	0.0138	22 Apr
	R3	Stream	4.665	0.831	0.196	0.0653	0.049	18 May
	R4	Stream	3.331	0.456	0.0976	0.0326	0.0244	15 Apr
pome fruit early with 20 m spray buffer distance (including deposition)	D3	Ditch	0.854	0.395	0.159	0.0531	0.0398	17 May
	D4	Pond	0.096	0.104	0.0881	0.0714	0.0646	30 May
	D4	Stream	0.964	0.0811	0.017	0.0056	0.0043	30 May
	D5	Pond	0.0962	0.107	0.088	0.0714	0.0648	11 May
	D5	Stream	0.979	0.043	0.0091	0.003	0.0023	11 May
	R1	Pond	0.0962	0.095	0.0873	0.0696	0.0625	13-Jun
	R1	Stream	0.766	0.103	0.0230	0.0077	0.0058	13-Jun
	R2	Stream	1.009	0.0611	0.0129	0.0043	0.003	22 Apr
	R3	Stream	1.068	0.194	0.0458	0.0153	0.0115	18 May

	R4	Stream	0.766	0.106	0.0229	0.0076	0.0057	14 Apr

CGA 210007 Parameters used in FOCUSsw step 1 and 2	FOCUS calculator : FOCUS Step 1-2 version 1.1 Molar weight (g/mol): 180.2 Water solubility at 25°C (mg/L): 39000 Kf_{OC} (L/kg): 113 DT_{50} soil (d): 19 DT_{50} water/sediment system (d): 418 DT_{50} water (d): 418 DT_{50} sediment (d): 418
Parameters used in FOCUSsw step 3 (if performed)	Not used
Application rate	4 x 25 g a.s./ha (tobacco) 6 x 100 g a.s./ha (apples) 6 x 25 g a.s./ha (tomatoes) multiple applications since worst case

FOCUS STEP 1						
Scenario	Application Timing	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	Max. TWA 21 d	Actual	Max. TWA 21 d
Tobacco		0	25.1	24.6	28.3	27.8
Pome fruits late North Europe		0	168	162	186	183
Tomato South Europe	June-Sep	0	37.7	37.0	42.4	41.7
FOCUS STEP 2						
Scenario	-	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	Max. TWA 21 d	Actual	Max. TWA 21 d
Tobacco North Europe	March-May	0	2.76	2.70	3.10	3.05
Tobacco South Europe		0	5.17	5.07	5.82	5.72
Tobacco North Europe	June-Sep	0	2.76	2.70	3.10	3.05
Tobacco South Europe		0	3.97	3.89	4.46	4.38
Pome fruits late North Europe	June-Sep	0	20.6	19.8	22.8	22.4
Pome fruits late South Europe		0	25.7	24.8	28.5	28.0
Tomato North Europe	March-May	0	3.23	3.15	3.62	3.56
Tomato South Europe		0	6.00	5.87	6.74	6.62

Tomato North Europe	June-Sep	0	3.23	3.15	3.62	3.56
Tomato South Europe		0	4.61	4.51	5.18	5.09

SYN 546642 Parameters used in FOCUSsw step 1 and 2	FOCUS calculator : FOCUS Step 1-2 version 1.1 Molar weight (g/mol): 196.2 Water solubility at 25°C (mg/L): 7.7 Kf_{OC} (L/kg): 4201 DT_{50} soil (d): 604 DT_{50} water/sediment system (d): 1000 DT_{50} water (d): 1000 DT_{50} sediment (d): 1000
Parameters used in FOCUSsw step 3 (if performed)	Not used
Application rate	4 x 25 g a.s./ha (tobacco) 6 x 100 g a.s./ha (apples) 6 x 25 g a.s./ha (tomatoes) multiple applications since worst case

FOCUS STEP 1						
Scenario	Application Timing	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	Max. TWA 21 d	Actual	Max. TWA 21 d
Tobacco		0	1.92	1.90	80.5	80.0
Pome fruits North Europe		0	11.5	11.4	483	480
Tomato South Europe	June-Sep	0	2.88	2.86	121	120
FOCUS STEP 2						
Scenario	-	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	Max. TWA 21 d	Actual	Max. TWA 21 d
Tobacco North Europe	March-May	0	0.302	0.300	12.7	12.6
Tobacco South Europe		0	0.604	0.599	25.4	25.2
Tobacco North Europe	June-Sep	0	0.302	0.300	12.7	12.6
Tobacco South Europe		0	0.453	0.449	19.0	18.9
Pome fruits late North Europe	June-Sep	0	1.35	1.34	56.9	56.5
Pome fruits late South Europe		0	2.03	2.02	85.4	84.7

Tomato North Europe	March-May	0	0.421	0.418	17.7	17.6
Tomato South Europe		0	0.842	0.836	35.4	35.1
Tomato North Europe	June-Sep	0	0.421	0.418	17.7	17.6
Tomato South Europe		0	0.631	0.627	26.5	26.3

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

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	FOCUS Groundwater Modelling ; FOCUS PELMO 4.4.3 and FOCUS PEARL 4.4.4

Tobacco, 4 x 25 g a.s./ha at BBCH 13 - 89 Pome fruit, 6 x 100 g a.s./ha at BBCH 59 – 87 Tomatoes, 6 x 25 g a.s./ha in at BBCH 16 – 79 acibenzolar-S-methyl: Molar weight (g/mol): 210.3 Water solubility at 25°C (mg/L): 7.7 Saturated vapour pressure at 20°C (Pa): 4.6×10^{-4} Kf_{OC} (L/kg): 1650 Freundlich exponent (1/n): 0.829 DT_{50} soil (d): 0.131 Q10: 2.58 Plant uptake factor : 0.5 Crop interception (%): Tobacco 50/50/70/70 Apple 65/65/70/70/70/70 Tomatoes 50/50/70/70/70/70 CGA 210007 Molar weight (g/mol): 180.2 Water solubility at 20°C (mg/L): 39000 Kf_{OC} (L/kg): 113 Freundlich exponent (1/n): 0.856 DT_{50} soil (d): 19 Plant uptake factor : 0 Q10: 2.58 ffm:1 (from parent) SYN 546642 Molar weight (g/mol): 196.2 Water solubility at 20°C (mg/L): 39000 Saturated vapour pressure at 20°C (Pa): 0 (default) Kf_{OC} (L/kg): 3765 Freundlich exponent (1/n): 1 DT_{50} soil (d): 218 Plant uptake factor : 0 Q10: 2.58 ffm: 1 from CGA 210007

PEC (gw) – FOCUS modelling result (80th percentile annual average concentration at 1m)

	Scenario	Parent (µg/L)	Metabolite (µg/L)	
			CGA 210007	SYN 546642
Tobacco Apple Tomatoes	Chateaudun	< 0.001	< 0.001	< 0.001
	Hamburg	< 0.001	< 0.001	0.001
	Jokioinen	< 0.001	< 0.001	< 0.001
	Kremsmunster	< 0.001	< 0.001	< 0.001

	Okehampton	< 0.001	< 0.001	0.002
	Piacenza	< 0.001	< 0.001	0.007
	Porto	< 0.001	< 0.001	0.001
	Sevilla	< 0.001	< 0.001	< 0.001
	Thiva	< 0.001	< 0.001	< 0.001

PEC (gw) From lysimeter / field studies

Parent	1st year	2nd year	3rd year
Annual average (µg/L)	No data	No data	No data

Metabolites CGA 210007 SYN 546642	1st year	2nd year	3rd year
Annual average (µg/L)	No data	No data	No data

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

Direct photolysis in air ‡	No data
Quantum yield of direct phototransformation	0.036 mol. einstein^{-1} at 289 nm 0.021 mol. einstein^{-1} at 327 nm
Photochemical oxidative degradation in air ‡	DT_{50}: 19-40 h (Atkinson)
Volatilisation ‡	from plant surfaces: estimated < 10 % (experiment) from soil: estimated to be negligible (experiment)
Metabolites	No data

PEC (air)

Method of calculation	Not calculated

PEC (a)

Maximum concentration	Not calculated

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: Acibenzolar-S-methyl (rapidly degraded) CGA 210007, SYN 546642 Groundwater water : Acibenzolar-S-methyl (rapidly degraded), CGA 210007, SYN 546642 Surface water : Acibenzolar-S-methyl (rapidly degraded) CGA 210007

Air: Acibenzolar-S-methyl Candidate for R53 (not ready biodegradable)

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

Soil (indicate location and type of study)	No data
Surface water (indicate location and type of study)	No data
Ground water (indicate location and type of study)	No data
Air (indicate location and type of study)	No data

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

Acibenzolar-S-methyl id rapidly degraded into CGA 210007 in soil and water under aerobic condition.

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

Species	Test substance	Time scale	End point (mg/kg bw/day	End point (mg/kg feed)
Bird				
Bobwhite quail	a.s.	Acute (oral), LD50	> 2000 mg/kg bw	-
Mallard duck	a.s.	Acute (oral), LD50	> 2000 mg/kg bw	-
			-	-
Bobwhite quail	a.s.	Short-term (dietary), LC50	> 1835 mg/kg b.w./d	> 5200 mg/kg diet
Mallard duck	a.s.	Short-term (dietary), LC50	> 1539 mg/kg b.w./d	> 5200 mg/kg diet
Bobwhite quail	a.s.	Long-term (reproduction), NOEC	61 mg/kg b.w./d	600 mg/kg diet
Mallard duck	a.s.	Long-term (reproduction), NOEC	160 mg/kg b.w./d	1000 mg/kg diet
Mammals				
Rat	a.s.	Acute (oral), LD50	> 2000 mg/kg bw	-
Rat	Preparation A9180A (CGA-245704 50 WG)	Acute (oral), LD50	> 5000 mg/kg bw	-
Rat	Metabolite CGA 210007	Acute (oral), LD50	> 2000 mg/kg bw	-
Rat	a.s.	Long-term (2-generation feeding study), NOAEL	15 mg/kg bw/d	200 mg/kg diet
Additional higher tier studies ǂ				
- None submitted				

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

Tobacco (4 x 0.025 kg a.s./ha, 7 days interval)

Indicator species	Time scale	DDD	TER	Annex VI Trigger
BIRDS				
Screening step				
Small omnivorous bird	Acute	7.15	> 280	10
	Long-term	1.89	32	5
Tier 1 (Birds)				

Not necessary				
MAMMALS				
Screening step				
Small herbivorous mammal	Acute	6.14	> 325	10
	Long-term	2.11	7.1	5
Tier 1 (Mammals)				
Not necessary				

Tomato (6 x 0.025 kg a.s./ha, 7 days interval)

Indicator species	Time scale	DDD	TER	Annex VI Trigger
BIRDS				
Screening step				
Small omnivorous bird	Acute	7.54	> 270	10
	Long-term	2.15	28	5
Tier 1 (Birds)				
Not necessary				
MAMMALS				
Screening step				
Small herbivorous mammal	Acute	6.48	> 308	10
	Long-term	2.39	6.3	5
Tier 1 (Mammals)				
Not necessary				

Pome fruit (6 x 0.100 kg a.s./ha, 5 days interval)

Indicator species	Time scale	DDD	TER	Annex VI Trigger
BIRDS				
Screening step				
Small insectivorous bird	Acute	10.3	> 190	10
	Long-term	2.89	21	5
Tier 1 (Birds)				
Not necessary				
MAMMALS				
Screening step				
Small herbivorous mammal	Acute	30.0	> 67	10
	Long-term	11.5	**1.3**	5

Tier 1 (Mammals)				
Small herbivorous mammal (vole)	Long-term	3.45	**4.3**	5
Frugivorous mammal (dormouse)	Long-term	3.61	**4.2**	
Large herbivorous mammal (lagomorph)	Long-term	0.68	22	
Small omnivorous mammal (mouse)	Long-term	0.37	41	

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)	End point	Toxicity (µg/L)
Laboratory tests				
Fish				
Oncorhynchus mykiss	a.s.	Acute 96H (static)	LC_{50}	400 (initial measured)
Oncorhynchus mykiss	a.s.	Acute 96H (flow-through)	LC_{50}	1100 (initial measured)
Oncorhynchus mykiss	a.s.	Acute 96H (flow-through)	LC_{50}	680 - 950 Extrapolated: 880 (mm)
Lepomis macrochirus	a.s.	Acute 96H (static)	LC_{50}	>2700 Extrapolated: 2800 (mm)
Lepomis macrochirus	a.s.	Acute 96H (flow-through)	LC_{50}	1600 (mm)
Cyprinodon variegatus	a.s.	Acute 96H (flow-through)	LC_{50}	1700 (mm)
Oncorhynchus mykiss	a.s.	ELS 87d (flow through)	NOEC	26 (mm)
Oncorhynchus mykiss	CGA 210007	Acute 96H (static)	LC_{50}	> 100000 (nom)
Oncorhynchus mykiss	CGA 210007	Acute 96H (static)	LC_{50}	> 180000 (nom)
Oncorhynchus mykiss	A9180A	Acute 96H (static)	LC_{50}	1300 (equivalent to 650 µg a.s./L) (mm)
Aquatic invertebrate				
Daphnia magna	a.s.	Acute 48H (static)	EC_{50}	2400 (mm)
Daphnia magna	a.s.	Acute 48H (flow-through)	EC_{50}	2900 (mm)
Mysidopsis bahia	a.s.	Acute 96H (flow-through)	EC_{50}	880 (mm)

Crassostrea virginica (aquatic molluscs)	a.s.	Acute 96H (flow-through)	EC_{50}	610 (mm)
Daphnia magna	a.s.	Chronic 22d (semi-static)	NOEC	44 (mm)*
Daphnia magna	CGA 210007	Acute 48H (static)	EC_{50}	58000 (nom)
Daphnia magna	CGA 210007	Chronic 21d (static)	NOEC	30000 (nom)
Daphnia magna	A9180A	Acute 48H (static)	EC_{50}	2800 (equivalent to 1400 µg a.s./L) (mm)
Algae				
Scenedesmus subspicatus	a.s.	72H (static)	EbC_{50} ErC_{50}	500 (final measured) 1700 (final measured)
Pseudokirchneriella subcapitata	a.s.	96H (static)	EC_{50}	1340 (mean measured)**
Selenastrum capricornutum	CGA 210007	72H (static)	EbC_{50} ErC_{50}	90000 (nom) 108000 (nom)
Anabaena flos-aquae	CGA 210007	96H (static)	EbC_{50} ErC_{50}	46000 (nom) 63000 (nom)
Selenastrum capricornutum	A9180A	72H (static)	EbC_{50} ErC_{50}	1600 (equivalent to 800 µg a.s./L) (final measured) 4800 (equivalent to 2400µg a.s./L) (final measured)
Microcosm or mesocosm tests				
not required				

($_{nom}$): nominal

($_{mm}$): mean measured

*: the recoveries of the test solutions were low in general. The mean measured values were calculated by using the arithmetic mean, which was a best case approach compared with other, more preferred methods.

**: the recoveries of the test solutions at the end of the study, were low.

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

FOCUS Step 1

Risk assessment has been conducted directly from FOCUS Step 2 for metabolite CGA 210007 and Step 3 for the active substance.

FOCUS Step 2

TER were calculated using FOCUS Step 2 PEC value for metabolite CGA 210007 only and a worst-case PEC value was used based on pome fruit scenario that covers all following uses:
Tobacco, 4 x 0.025 kg a.s./ha (BBCH 13-89)
Tomato, 6 x 0.025 kg a.s./ha (BBCH 16-79)
Pome fruit, 6 x 0.100 kg a.s./ha (BBCH 59-87)

Test substance	Organism	Toxicity end point (µg/L)	Time scale	PEC	TER	Annex VI Trigger
CGA210007	Fish	> 100000	LC_{50}	57.62*	> 1730	100
CGA210007	Aquatic invertebrates	58000	EC_{50}	57.62*	1000	100
CGA210007	Aquatic invertebrates	30000	NOEC	57.62*	520	100
CGA210007	Algae	63000	EC_{50}	57.62*	1090	10

* Plateau concentration

Refined aquatic risk assessment using higher tier FOCUS modelling

FOCUS Step 3

Tobacco, 4 x 0.025 kg a.s./ha (BBCH 13-89)

Test substance	Scenario[1]	Water body type[2]	Test organism	Time scale	Toxicity end point (µg/L)	PEC	TER	Annex VI Trigger
a.s.	R3	stream	Fish	LC_{50}	400	0.117	3400	100
a.s.	R3	stream	Fish	NOEC	26	0.117	220	10
a.s.	R3	stream	Aquatic invertebrates	EC_{50}	610	0.117	5210	100
a.s.	R3	stream	Aquatic invertebrates	NOEC	44	0.117	380	10
a.s.	R3	stream	Algae	EC_{50}	500	0.117	4300	10

[1] R3 is a run-off scenario

Tomato, 6 x 0.025 kg a.s./ha (BBCH 16-79)

Test substance	Scenario[1]	Water body type	Test organism	Time scale	Toxicity end point (µg/L)	PEC	TER	Annex VI Trigger
a.s.	D6	ditch	Fish	LC_{50}	400	0.155	2 600	100
	R2	stream				0.138	2 900	
	R3	stream				0.147	2 700	
	R4	stream				0.101	4 000	
a.s.	D6	ditch	Fish	NOEC	26	0.155	170	10
	R2	stream				0.138	190	
	R3	stream				0.147	180	
	R4	stream				0.101	260	

a.s.	D6	ditch	Aquatic invertebrates	EC_{50}	610	0.155	3930	100
	R2	stream				0.138	4420	
	R3	stream				0.147	4150	
	R4	stream				0.101	6040	
a.s.	D6	ditch	Aquatic invertebrates	NOEC	44	0.155	280	10
	R2	stream				0.138	320	
	R3	stream				0.147	300	
	R4	stream				0.101	440	
a.s.	D6	ditch	Algae	EC_{50}	500	0.155	3 200	10
	R2	stream				0.138	3 600	
	R3	stream				0.147	3 400	
	R4	stream				0.101	5 000	

[1] drainage (D1-D6) and run-off (R1-R4)

Pome fruit, 6 x 0.100 kg a.s./ha (BBCH 59-87), early stage scenario (worst-case)

Test substance	Scenario[1]	Water body type	Test organism	Time scale	Toxicity end point (µg/L)	PEC	TER	Annex VI Trigger
a.s.	D3	ditch	Fish	LC_{50}	400	7.753	**51**	100
	D4	pond				0.470	850	
	D4	stream				7.933	**50**	
	D5	pond				0.470	850	
	D5	stream				8.068	**49**	
	R1	pond				0.470	850	
	R1	stream				6.300	**63**	
	R2	stream				8.309	**48**	
	R3	stream				8.833	**45**	
	R4	stream				6.298	**63**	
a.s.	D3	ditch	Fish	NOEC	26	7.753	**3.3**	10
	D4	pond				0.470	55.3	
	D4	stream				7.933	**3.2**	
	D5	pond				0.470	55.3	
	D5	stream				8.068	**3.2**	
	R1	pond				0.470	55	
	R1	stream				6.300	**4.1**	
	R2	stream				8.309	**3.1**	

	R3	stream				8.833	**2.9**	
	R4	stream				6.298	**4.1**	
a.s.	D3	ditch	Aquatic invertebrates	EC_{50}	610	7.753	**78**	100
	D4	pond				0.470	1297	
	D4	stream				7.933	**76**	
	D5	pond				0.470	1297	
	D5	stream				8.068	**75**	
	R1	pond				0.470	1297	
	R1	stream				6.300	**96**	
	R2	stream				8.309	**73**	
	R3	stream				8.833	**69**	
	R4	stream				6.298	**96**	
a.s.	D3	ditch	Aquatic invertebrates	NOEC	44	7.753	**5.6**	10
	D4	pond				0.470	93	
	D4	stream				7.933	**5.5**	
	D5	pond				0.470	93	
	D5	stream				8.068	**5.4**	
	R1	pond				0.470	93	
	R1	stream				6.300	**7.0**	
	R2	stream				8.309	**5.3**	
	R3	stream				8.833	**5.0**	
	R4	stream				6.298	**7.0**	
a.s.	D3	ditch	Algae	EC_{50}	500	7.753	64.5	10
	D4	pond				0.470	1060	
	D4	stream				7.933	63.0	
	D5	pond				0.470	1060	
	D5	stream				8.068	62.0	
	R1	pond				0.470	1060	
	R1	stream				6.300	79.3	
	R2	stream				8.309	60.0	
	R3	stream				8.833	56.6	
	R4	stream				6.298	79.4	

[1] drainage (D1-D6) and run-off (R1-R4)

FOCUS Step 4

Pome fruit, 6 x 0.100 kg a.s./ha (BBCH 59-87), early stage scenario (worst-case)

Scenario[1]	Water body type	Test organism	Time scale	Toxicity end point (µg/L)	Buffer zone distance	PEC	TER	Annex VI Trigger
D3	ditch	Fish	LC_{50}	400	10 m	3.739	106	100
D4	stream					4.197	**95**	
D5	stream					4.266	**95**	
R1	stream					3.332	120	
R2	stream					4.396	**91**	
R3	stream					4.665	**85**	
R4	stream					3.331	120	
D4	stream				20 m	0.964	415	
D5	stream					0.979	408	
R2	stream					1.009	396	
R3	stream					1.068	374	
D3	ditch	Fish	NOEC	26	10 m	3.739	**6.9**	10
D4	stream					4.197	**6.2**	
D5	stream					4.266	**6.1**	
R1	stream					3.332	**7.8**	
R2	stream					4.396	**5.9**	
R3	stream					4.665	**5.6**	
R4	stream					3.331	**7.8**	
D3	ditch				20 m	0.854	30.4	
D4	stream					0.964	27	
D5	stream					0.979	26.5	
R1	stream					0.766	33.9	
R2	stream					1.009	25.7	
R3	stream					1.068	24.3	
R4	stream					0.766	33.9	
D3	ditch	Aquatic invertebrates	EC_{50}	610	10 m	3.739	163	100
D4	stream					4.197	145	
D5	stream					4.266	143	
R1	stream					3.332	183	
R2	stream					4.396	138	
R3	stream					4.665	130	
R4	stream					3.331	183	
D3	ditch	Aquatic invertebrates	NOEC	44	10 m	3.739	11.8	10
D4	stream					4.197	10.5	
D5	stream					4.266	10.3	
R1	stream					3.332	13.2	

R2	stream					4.396	10.0	
R3	stream					4.665	**9.4**	
R4	stream					3.331	13.2	
R3	stream				20 m	1.068	41	

	Acibenzolar-S-methyl	CGA 210007
$logP_{O/W}$	3.1	-0.64 (pH 5.8)
Bioconcentration factor (BCF)	whole fish = 118 edible parts = 48 non-edible parts = 199	-
Annex VI Trigger for the bioconcentration factor	-	-
Clearance time (days) (CT_{50})	0.35	-
(CT_{90})	Not determined	-
Level and nature of residues (%) in organisms after the 14 day depuration phase	-	-

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)
a.s.	> 128 µg a.s./bee	> 100 µg a.s./bee
Preparation	> 199 µg A9180A/bee (> 99.3 µg a.s./bee)	> 200 µg A9180A/bee (> 99.8 µg a.s./bee)
Field or semi-field tests		
None submitted		

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

Worst-case use (among the EU representative uses): Pome fruit (6 x 0.100 kg a.s./ha)

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	Contact	< 1	50
a.s.	oral	< 0.78	50

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

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR_{50} g/ha)

Species	Test Substance	End point	Effect (LR_{50} g/ha)
Typhlodromus pyri	A9180A	Mortality	>200 g a.s./ha
Typhlodromus pyri	A9180A	Mortality/reproduction	>200 g a.s./ha No significant difference in number eggs/female at 200 g a.s./ha (only dose tested)
Aphidius rhopalosiphi	A9180A	Mortality	>200 g a.s./ha

Tobacco (4 x 0.025 kg a.s./ha)

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field (1 m)	Trigger
A9180A	*Typhlodromus pyri*	>200 g a.s./ha	< 0.34	< 0.009	2
A9180A	*Aphidius rhopalosiphi*	>200 g a.s./ha	< 0.34	< 0.009	2

Tomato (6 x 0.025 kg a.s./ha)

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field (1 m)	Trigger
A9180A	*Typhlodromus pyri*	>200 g a.s./ha	< 0.40	< 0.011	2
A9180A	*Aphidius rhopalosiphi*	>200 g a.s./ha	< 0.40	< 0.011	2

Pome fruit (6 x 0.100 kg a.s./ha)

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field (3 m)	Trigger
A9180A	*Typhlodromus pyri*	>200 g a.s./ha	< 1.60	< 0.252	2
A9180A	*Aphidius rhopalosiphi*	>200 g a.s./ha	< 1.60	< 0.252	2

Further laboratory and extended laboratory studies (A9180A)

Species	Life stage	study design	Dose (g a.s./ha)	End point	% effect[3]	Trigger value

Species	Life stage	study design	Dose (g a.s./ha)	End point	% effect[3]	Trigger value
Typhlodromus pyri	nymphal stage/adult	Tier II, 2-D	30	reproduction	<50% effects	50 %
Orius laevigatus	nymphal stage	Tier II, 3-D	10-200	fecundity	22% effects at 200 g a.s./ha	50 %
Orius insidiosus	nymphal stage	Tier II, 2-D	30	reproduction	<50% effects	50 %

Field or semi-field tests
None submitted.

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	End point[1]
Earthworms			
	a.s.	Acute 14 days	LC_{50} >1000 mg a.s./kg dry soil [2] LC_{50} corr. > 500 mg a.s./kg dry soil
	CGA 210007	Chronic 8 weeks	NOEC: 2.675 mg/kg dry soil[4]
	CGA 210007	Chronic 8 weeks	NOEC: 13.09 mg/kg dry soil
Other soil macro-organisms			
	-	-	-
Collembolan			
	SYN 546642	Chronic	NOEC= 500 mg/kg d.w.soil
Soil micro-organisms			
Nitrogen mineralisation	a.s.	28 days	< 25 % effect at 0.4 mg a.s./kg d.w.soil
	SYN 546642	28 days	< 25 % effect at 1.3 mg/kg d.w.soil
Carbon mineralisation	a.s.	28 days	< 25 % effect at 0.4 mg a.s./kg d.w.soil
	SYN 546642	28 days	< 25 % effect at 1.3 mg/kg d.w.soil
Field studies[3]			
not required			

[1] indicate where end point has been corrected due to log Pow >2.0 (e.g. LC_{50corr})
[2] There is some uncertainty about the acute endpoint of LC50 > 1000 mg/kg soil for earthworms due to the significantly lower response (mortality) in the highest concentration than at the lower levels. A clear concentration related response was observed at the lower levels approaching 50% already at the 333 mg/kg concentration level.
[3] litter bag, field arthropod studies not included at 8.3.2/10.5 above, and earthworm field studies
[4] this endpoint was included in the Review Report for acibenzolar-S-methyl, however the study was not reassessed

Toxicity/exposure ratios for soil organisms

Tobacco at 6 x 0.025 kg a.s./ha

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Earthworms					
	a.s.	Acute	0.041	> 12000	10
	CGA 210007	Chronic	0.187*	70	5

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Other soil macro-organisms					
Collembola	SYN 546642	Chronic	0.425 **	1176	5

* PEC worst-case for pome fruit scenario
** Plateau concentration for use on pome fruit (worst case)

Tomato at 4 x 0.025 kg a.s./ha

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Earthworms					
	a.s.	Acute	0.041	> 12000	10
	CGA 210007	Chronic	0.187*	70	5
Other soil macro-organisms					
Collembola	SYN 546642	Chronic	0.425 **	1176	5

* PEC worst-case for pome fruit scenario
** Plateau concentration for use on pome fruit (worst case)

Pome fruit at 6 x 0.100 kg a.s./ha

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Earthworms					
	a.s.	Acute	0.191	> 2600	10
	CGA 210007	Chronic	0.187	70	5
Other soil macro-organisms					
Collembola	SYN 546642	Chronic	0.425	1176	5

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

Preliminary screening data

No data

Laboratory dose response tests

Most sensitive species	Test substance	ER_{50} (g/ha)[2] vegetative vigour	ER_{50} (g/ha) emergence	Exposure (g/ha)[2]	TER	Trigger
-	A9180A	>250	>250	15.73	>16	5

Additional studies (e.g. semi-field or field studies)

Not required

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

Test type/organism	end point
Activated sludge	The 3-hour EC_{50} was higher than the highest test concentration of 106 mg/L

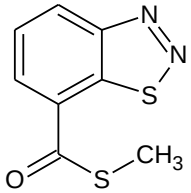
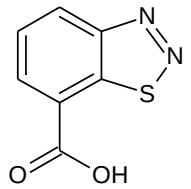
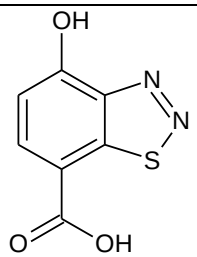
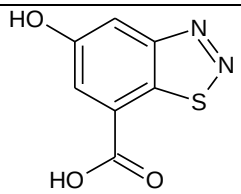
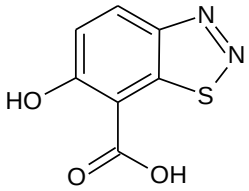
Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)

Compartment	
soil	Acibenzolar-S-methyl (rapidly degraded), CGA 210007, SYN 546642
water	Acibenzolar-S-methyl (rapidly degraded), CGA 210007, SYN 546642
sediment	Acibenzolar-S-methyl, CGA 210007, SYN 546642
groundwater	Acibenzolar-S-methyl (rapidly degraded), CGA 210007

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

	Harmonized classification
Active substance	**Classification acc. to Dir. 67/549/EEC:** Symbol: N Risk phrases: R50/53
	Classification acc. to Reg. 1272/2008: Indication of danger: Aquatic Acute Category 1, Chronic Category 1 Risk phrases: H400, H410
	RMS proposal
	M-factor: 1

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name*	Chemical name/SMILES**	Structural formula**
acibenzolar-S-methyl **CGA 245704**	*S*-methyl benzo[1,2,3]thiadiazole-7-carbothioate O=C(SC)c1cccc2nnsc12	
acibenzolar acid **CGA 210007**	1,2,3-benzothiadiazole-7-carboxylic acid O=C(O)c1cccc2nnsc12	
4-OH acibenzolar acid **CGA 323060**	4-hydroxy-1,2,3-benzothiadiazole-7-carboxylic acid O=C(O)c1ccc(O)c2nnsc12	
CGA 324041	5-hydroxy-1,2,3-benzothiadiazole-7-carboxylic acid O=C(O)c1cc(O)cc2nnsc12	
6-OH acibenzolar acid **SYN 546642**	6-hydroxy-1,2,3-benzothiadiazole-7-carboxylic acid O=C(O)c1c(O)ccc2nnsc12	

* The metabolite name in bold is the name used in the conclusion.
** ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008)

ABBREVIATIONS

1/n	slope of Freundlich isotherm
λ	wavelength
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AR	applied radioactivity
AR	androgen receptor
ARfD	acute reference dose
BCF	bioconcentration factor
BE	
bw	body weight
CAS	Chemical Abstracts Service
CI	confidence interval
CIPAC	Collaborative International Pesticides Analytical Council Limited
CL	confidence limits
cm	centimetre
d	day
DAR	draft assessment report
DAT	days after treatment
DFOP	double first order in parallel
DT_{50}	period required for 50 percent disappearance (define method of estimation)
DT_{90}	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
ECHA	European Chemical Agency
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER	oestrogen receptor
ER_{50}	emergence rate/effective rate, median
ErC_{50}	effective concentration (growth rate)
EU	European Union
EUROPOEM	European Predictive Operator Exposure Model
EVA	exposure via air
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
FID	flame ionisation detector
FIR	Food intake rate
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram
GAP	good agricultural practice
GC	gas chromatography
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GC-FID	gas chromatography with flame ionisation detector
GM	geometric mean

GRL	guidline residue level
GS	growth stage
h	hour(s)
H361d	hazard statement for reproductive developmental toxicity according to Reg. (EC) No. 1272/2008
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS/MS	high performance liquid chromatography with tandem mass spectrometry
HPLC-UV	high performance liquid chromatography with ultra violet detector
HQ	hazard quotient
HR	highest residue
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting on the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K_{doc}	organic carbon linear adsorption coefficient
kg	kilogram
K_{Foc}	Freundlich organic carbon adsorption coefficient
L	litre
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)
m	metre
min	minute
M&K	maximisation test of Magnusson & Kligman
M/L	mixing and loading
µg	microgram
mg	milligram
mL	millilitre
mm	mean measured
mm	millimetre
mN	milli-newton
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MWHC	maximum water holding capacity
N/A	not applicable
NEDI	national estimated daily intake
NESTI	national estimated short-term intake
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
nc	not calculated
nom	not measured
nr	not reported
OC	organic carbon

OECD	Organisation for Economic Co-operation and Development
Pa	pascal
PEARL	Pesticide Emission Assessment at Regional and Local scales
PELMO	Pesticide Leaching Model
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in ground water
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
pH	pH-value
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
POEM	Predictive Operator Exposure Model
P_{ow}	partition coefficient between *n*-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
RAC	raw agricultural commodity
RBC	red blood cells
REACH	Registration, Evaluation, Authorisation of CHemicals
RMS	rapporteur Member State
SANCO	Directorate-General for Health and Consumers
SD	standard deviation
SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
STOT SE	specific target organ toxicity – single exposure
$t_{1/2}$	half-life (define method of estimation)
TER	toxicity exposure ratio
TMDI	theoretical maximum daily intake
TWA	time weighted average
UF	uncertainty factor
UV	ultraviolet
w/v	weight per volume
w/w	weight per weight
WG	water dispersible granule
WHO	World Health Organization
wk	week
yr	year