CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance gibberellins (GA_4, GA_7)[1] (approved as giberelline)

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SUMMARY

Gibberellins are one of the 295 substances of the fourth stage of the review programme covered by Commission Regulation (EC) No 2229/2004[3], as amended by Commission Regulation (EC) No 1095/2007[4].

Gibberellins were included in Annex I to Directive 91/414/EEC on 1 September 2009 pursuant to Article 24b of the Regulation (EC) No 2229/2004 (hereinafter referred to as 'the Regulation') and have subsequently been deemed to be approved under Regulation (EC) No 1107/2009[5], in accordance with Commission Implementing Regulation (EU) No 540/2011[6], as amended by Commission Implementing Regulation (EU) No 541/2011[7]. In accordance with Article 25a of the Regulation, as amended by Commission Regulation (EU) No 114/2010[8], the European Food Safety Authority (EFSA) is required to deliver by 31 December 2012 its view on the draft review report submitted by the European Commission in accordance with Article 25(1) of the Regulation. This review report was established as a result of the initial evaluation provided by the designated rapporteur Member State in the Draft Assessment Report (DAR). The EFSA therefore organised a peer review of the DAR. The conclusions of the peer review are set out in this report.

Hungary being the designated rapporteur Member State submitted the DAR on gibberellins in accordance with the provisions of Article 22(1) of the Regulation, which was received by the EFSA on 16 August 2006. The peer review was initiated on 12 June 2008 by dispatching the DAR to the notifiers Valent Biosciences, Globachem NV and Fine Agrochemicals Ltd, and on 24 February 2011 to the Member States. Following consideration of the comments received on the DAR, it was concluded that EFSA should conduct a focused peer review in the area of mammalian toxicology and deliver its conclusions on gibberellins.

[1] On request from the European Commission, Question No EFSA-Q-2009-00258, issued on 16 December 2011.
[2] Correspondence: pesticides.peerreview@efsa.europa.eu
[3] OJ L 379, 24.12.2004, p.13
[4] OJ L 246, 21.9.2007, p.19
[5] OJ L 309, 24.11.2009, p.1
[6] OJ L 153, 11.6.2011, p.1
[7] OJ L 153, 11.6.2011, p.187
[8] OJ L 37, 10.2.2010, p.12

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The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of mixtures of GA_4 and GA_7 as a plant growth regulator on apple, pear and cherries, as proposed by the notifiers. Full details of the representative uses can be found in Appendix A to this report.

In the area of identity, physical/chemical/technical properties and methods of analysis data requirements were identified for some of the supporting data for all specifications. A data gap was identified for the hydrolysis study. For the formulations various data gaps were identified. For residue monitoring methods data gaps were identified for soil, water and air.

Only the datapackage submitted by Valent has been considered complete enough to perform a risk assessment and data gaps have been identified for Globachem and Fine agrochemicals (risk assessment inconclusive). It was not possible to conclude whether the batches used in the toxicology studies are representative of the technical specification (both missing) leading to an issue that could not be finalised. Data gaps were identified for acute toxicity datapackage for 'Regulex 10 SG' and medical data of gibberellins.

Data gaps were identified in the residue section for the submission of information on the natural background levels of gibberellins in the edible parts of crops and for storage stability studies. No MRLs were proposed for pome fruits as the residue levels in both treated and control samples were below the LOQ and since it would not be possible to distinguish between exogenous and natural occurring gibberellins.

With the available information (pertinent to the assessment of environmental fate and behaviour in soil and water), a high potential for groundwater exposure of the active compounds GA_4 and GA_7 above the parametric legal limit of 0.1µg/L over a wide range of geoclimatic conditions was identified from all the representative uses assessed. This is identified as a critical area of concern. Data gaps are identified for additional experimental results that may allow a more refined environmental exposure assessment to be completed.

A data gap was identified to address the risk to aquatic macrophytes and the chronic risk to aquatic organisms. The acute risk to aquatic organisms was assessed as low. A low risk was also concluded for birds, mammals, bees, non-target arthropods, earthworms and soil micro-organisms, non-target plants and biological methods of sewage treatment. A data gap was also identified to address the representativeness of the material tested in the ecotoxicological studies to the technical specification.

KEY WORDS

Gibberellins, gibberellin 4, GA_4, gibberellin 7, GA_7, peer review, risk assessment, pesticide, plant growth regulator.

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BACKGROUND

Gibberellins is one of the 295 substances of the fourth stage of the review programme covered by Commission Regulation (EC) No 2229/2004[9], as amended by Commission Regulation (EC) No 1095/2007[10].

Gibberellins were included in Annex I to Directive 91/414/EEC on 1 September 2009 pursuant to Article 24b of the Regulation (EC) No 2229/2004 (hereinafter referred to as 'the Regulation') and has subsequently been deemed to be approved under Regulation (EC) No 1107/2009[11], in accordance with Commission Implementing Regulation (EU) No 540/2011[12], as amended by Commission Implementing Regulation (EU) No 541/2011[13]. In accordance with Article 25a of the Regulation, as amended by Commission Regulation (EU) No 114/2010[14] the European Food Safety Authority (EFSA) is required to deliver by 31 December 2012 its view on the draft review report submitted by the European Commission in accordance with Article 25(1) of the Regulation (European Commission, 2008). This review report was established as a result of the initial evaluation provided by the designated rapporteur Member State in the Draft Assessment Report (DAR). The EFSA therefore organised a peer review of the DAR. The conclusions of the peer review are set out in this report.

Hungary being the designated rapporteur Member State submitted the DAR on gibberellins in accordance with the provisions of Article 22(1) of the Regulation, which was received by the EFSA on 16 August 2006 (Hungary, 2006). The peer review was initiated on 12 June 2008 by dispatching the DAR to the notifiers Valent Biosciences, Globachem NV and Fine Agrochemicals Ltd, and on 24 February 2011 to the Member States, for consultation and comments. In addition, the EFSA conducted a public consultation on the DAR. 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 notifiers were invited to respond to the comments in column 3 of the Reporting Table. The comments were evaluated by the RMS in column 3 of the Reporting Table.

The scope of the peer review was considered in a telephone conference between the EFSA, the RMS, and the European Commission on 20 June 2011. On the basis of the comments received and the RMS' evaluation thereof it was concluded that the EFSA should organise a consultation with Member State experts in the area of mammalian toxicology.

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 consultation with Member State experts, and additional information to be submitted by the notifiers, 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 discussions where these took place, were reported in the final column of the Evaluation Table.

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 November – December 2011.

[9] OJ L 379, 24.12.2004, p.13
[10] OJ L 246, 21.9.2007, p.19
[11] OJ L 309, 24.11.2009, p.1
[12] OJ L 153, 11.6.2011, p.1
[13] OJ L 153, 11.6.2011, p.187
[14] OJ L 37, 10.2.2010, p.12

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 growth regulator on apple, pear and cherries, as proposed by the notifiers. 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, 2011) 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 DAR,
- the Reporting Table (20 June 2011),
- the Evaluation Table (7 December 2011),
- the report(s) of the scientific consultation with Member State experts,
- the comments received on the assessment of the points of clarification,
- the comments received on the draft EFSA conclusion.

Given the importance of the DAR including its addendum (compiled version of October 2011 containing all individually submitted addenda (Hungary, 2011)) and the Peer Review Report, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Gibberellins is the generic name given to these compounds. The compounds considered in this conclusion are Gibberellin 4 (GA_4) and Gibberellin 7 (GA_7). The IUPAC names are:

GA_4 (3*S*,3a*R*,4S,4a*R*,7*R*,9a*R*,9b*R*,12*S*)-12-hydroxy-3-methyl-6-methylene-2-oxoperhydro-4a,7-methano-3,9b-propanoazuleno[1,2-b]furan-4-carboxylic acid.

GA_7 (3*S*,3a*R*,4*S*,4a*R*,7*R*,9a*R*,9b*R*,12*S*)-12-hydroxy-3-methyl-6-methylene-2-oxoperhydro-4a,7-methano-9b,3-propenoazuleno[1,2-b]furan-4-carboxylic acid.

There are no ISO common names for these compounds.

The IUPAC names are specific to just one of the possible (64) isomers for each of GA_4 and GA_7. In this conclusion the use of the names GA_4 and GA_7 are expected to pertain to just each single isomer, though the analytical methodologies used in different studies may not always have been isomer specific, so there is some uncertainty regarding this.

The representative formulated products for the evaluation were 'Regulex 10 SG' a soluble granule formulation containing 10 % w/w GA_4/GA_7, 'Novagib' and 'Gibb Plus' soluble concentrate formulations containing 10 g/l GA_4/GA_7.

The representative uses evaluated comprise outdoor foliar spraying as a plant growth regulator on apple, pear and cherries. Full details of the GAP 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/10597/2003 rev. 8.1 (European Commission, 2009), and SANCO/825/00 rev. 7 (European Commission, 2004a).

It was considered that the presented sources were not equivalent on the basis of a Tier I assessment and therefore see the Tier II assessment in sections 2 and 5. It should be noted that only one of the Fine Agrochemicals sources was considered as there was only one batch analysis.

The minimum purity of GA_4/GA_7 is 852 g/kg. The purity of the individual sources and the accepted ranges of GA_4 and GA_7 can be found in the list of end points in Appendix A. Data gaps were identified for some of the supporting data for all specifications.

In the hydrolysis study the breakdown products were not identified and this has been identified as a data gap. For the formulations the following data gaps were identified:

- 'Novagib': acidity or alkalinity, identification of the break down products in the shelf-life study, method of analysis for the formulation.
- 'Regulex 10 SG': bulk or tap density, accelerated storage study, shelf-life study.
- 'Gibb plus': shelf-life study.

Methods of analysis for products of plant and animal origin are not required as no MRLs are proposed. A method of analysis is available for surface water but data gaps are identified for methods of analysis for drinking/ground water, soil and air. A method of analysis for body fluids and tissues is not required as the active substance 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, 2004b), SANCO/10597/2003 rev. 8.1 (European Commission, 2009).

Gibberellins GA_4/GA_7 was discussed at the Pesticide Peer Review Expert Meeting 88.

Based on the available information it is not possible to conclude on whether the presented sources are equivalent on the basis of a Tier II assessment. Only the Valent datapackage is complete enough to perform a risk assessment and data gaps have been established for Globachem and Fine agrochemicals leading to an issue that could not be finalised. Thus, the following conclusion only refers to the Valent source.

Based on available data it is not possible to conclude on whether the technical specification is supported by the batches used in the toxicological studies leading to an issue that could not be finalised (both missing, see section 1); the relevance of the impurities has not been adequately addressed and a data gap is identified.

Absorption and excretion of gibberellins GA_4/GA_7 were rapid. Oral absorption was estimated at 40% in females and 18% in males. They are widely distributed. There was no evidence for accumulation. The main metabolic pathway identified was hydroxylation and glucuronide conjugation of parent compound and hydroxyls.

Low acute toxicity is observed when gibberellins GA_4/GA_7 are administered by the oral, dermal and inhalation routes. No skin or eye irritation was observed and there was no potential for skin sensitisation.

In short-term oral studies with rats and dogs, the critical effects were observed in the liver (hepatocelular vacuolation in rats and increased weight in dogs) and kidney (tubule-interstitial nephritis and nephron loss in rats and increased weight in dogs). Non-specific critical effects as reduced food consumption and body weight gain were also observed in rats and dogs. The relevant short-term oral NOAELs are 500 mg/kg bw/d (90-d rat study) and 650 mg/kg bw/d (90-d dog study).

The weight-of-evidence suggests that gibberellins GA_4/GA_7 are unlikely to be genotoxic.

Fertility and overall reproductive performance was not impaired. The parental NOAEL is 300 mg/kg bw/d, the offspring NOAEL is 600 mg/kg bw/d and the reproductive NOAEL is 1000 mg/kg bw/d. In the rabbit developmental toxicity study there was no evidence of teratogenicity, and the relevant maternal and developmental NOAELs are 300 mg/kg bw/d.

No potential for neurotoxicity was observed in the standard genotoxicity studies.

No acceptable long-term and carcinogenicity studies (i.e. performed with gibberellic acid) were available and no developmental rat study was submitted. It was also considered that similar molecular structure and biological effects are not a sufficient reason to bridge information from other gibberellins (e.g. gibberellic acid). However, no further data are required to conclude on the risk assessment since these uncertainties (i.e. missing information) have been taken into account for setting references values (see below).

Based on the effects described above, no classification and labelling are proposed. However, the database is not suitable to assess adequately the hazard for reproductive toxicity and carcinogenic potential.

Based on available data and the toxicological profile of gibberellins GA4/GA7 the agreed acceptable daily intake (**ADI**) is 0.3 mg/kg bw/d, based on the parental NOAEL of 300 mg/kg bw/d in the multigeneration study and applying a standard uncertainty factor of 100 plus an additional uncertainty factor of 10 because of the use of short-term toxicity and also due to a general database weakness. The agreed acceptable operator exposure level (**AOEL**) is 0.18 mg/kg bw/d based on the NOAEL of 300 mg/kg bw/d in the multigeneration study (parental NOAEL) and rabbit developmental study (maternal and developmental NOAEL) and applying a standard uncertainty factor of 100 plus an additional uncertainty factor of 3 because of the lack of developmental study in rats and a correction for 18% oral absorption. The setting of an acute reference dose (**ARfD**) is considered not justified.

The relevant dermal absorption values for 'Regulex 10 SG' are 18% for the concentrate and dilution based on the oral absorption value. An acute toxicity datapackage with 'Regulex 10 SG' and medical data are missing (data gaps).

Considering the representative use of 'Regulex 10 SG' on apples (highest dose representative use[15]) the estimated operator exposure is below the AOEL (3.12 and 1.8% respectively for tractor-mounted and handheld sprayer respectively according to German model) without personal protective equipment (PPE). Worker and bystander exposure is below the AOEL (12 and 0.66% respectively).

3. Residues

The assessment in the residue section below is based on the guidance documents listed in the document SANCO/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 and 2007).

Plant or animal metabolism studies were not submitted as gibberellins are plant hormones, naturally occurring in plants, especially in growing tissues (shoots, developing seeds…) and information on gibberellins is available from published literature. Information was reported in the DAR on the mode of actions of gibberellins, their nature in different plant species, their metabolism in plants and rat and their natural concentrations in some specific parts of plants (e.g. fruit exudates…). However, no reliable information was provided on the natural background levels of gibberellins in the edible part of the crops, to confirm that the use of GA_4 and GA_7 as a plant protection product will result in residue levels similar to the natural levels in plants. A data gap was set to provide such data.

Residue trials on pome fruits were submitted where samples were analysed for gibberellins GA_4 and GA_7, achieving an LOQ of 0.05 mg/kg. Applications were done in compliance with the recommended timing and growth stages but using dose rates representing 75% of the supported rate for apples and 150% for pears. Residues in control and treated samples were all below the LOQ. Storage stability studies on apples and pears to support the residue trial results were not provided and therefore identified as a data gap. Animal metabolism studies, processing studies and rotational crop studies were not submitted but considered not necessary.

No MRLs are proposed for apple and pear as residue levels were shown to be below the LOQ of 0.05 mg/kg in both treated and control samples and since it would not be possible to distinguish between exogenous and natural gibberellins. It should be noted that considering the LOQ value for pome fruits in the EFSA PRIMo model, the highest TMDI is calculated to be less than 0.3 % of the proposed ADI (0.3 mg/kg bw/d).

No conclusions are drawn for cherries as residue trials or information on the natural background levels were not provided (data gap).

[15] Operator and bystander exposure was calculated by the RMS using an application rate of 0.018 kg a.s./ha instead of the correct value of 0.020 kg a.s./ha.. The results in the EFSA conclusion have been re-calculated using 0.020 kg a.s./ha and do not vary significantly compared to the calculations made by the RMS.

4. Environmental fate and behaviour

The only experimental measurement results for GA_4 and GA_7 available in the notifiers' dossier useful for assessing their environmental fate and behaviour are:

- a water solubility (20◦C, pH 7) of 40 g/L;
- a sterile aqueous hydrolysis study indicating these two compounds are stable to hydrolysis at environmentally relevant temperatures and pH;
- a sterile aqueous photolysis study indicating these two compounds are stable to aqueous photolysis;
- a ready biodegradability study (OECD 301B) indicating these compounds are readily biodegradable under the conditions of this test that uses a sewage sludge inoculum (76% mineralisation occurred in 28 days);
- a log Pow (log octanol water partition coefficient, 20◦C, pH 7) of 0.146.

Measurements of behaviour in soil or natural sediment water systems were not available.

Using these data (primarily the classification as readily biodegradable from the results of the OECD 301B test) and following REACH guidance (ECHA, 2010), half-lives (single first order DT_{50}) in water, soil and sediment of 15, 30 and 300 days were estimated respectively. GA_4 and GA_7 will exhibit very high mobility in soil based on a QSAR[16] soil adsorption estimate (K_{doc}) of 0.5747 mL/g. Soil adsorption is expected to be pH dependent (water solubility increases and Log Pow decreases as pH increases).

It was also appropriately indicated that the plant organs shoot tips and the endosperm and cotyledons of seeds, contain gibberellin compounds (maybe including GA_4 and GA_7), so the natural soil and surface water systems and biota will be naturally exposed to related compounds. However no quantitative assessment of the levels that will occur in soil or natural surface water systems was provided in the dossier or RMS assessment.

The DT_{50} and K_{doc} values indicated above were used to calculate the necessary predicted environmental concentrations (PEC) that are included in appendix A consequent to the representative uses applied for. PEC calculations in surface water and sediment were carried out for GA_4 and GA_7 using the FOCUS (FOCUS, 2001) step 1 and step 2 approach (version 1.1 of the Steps 1-2 in FOCUS calculator). The necessary groundwater exposure assessments were appropriately carried out using FOCUS (FOCUS, 2000) scenarios and the models PEARL 3.3.3 and PELMO 3.3.2[17] for GA_4 and GA_7. The potential for groundwater exposure from the representative use of the product 'Regulex 10 SG' on apples (highest dose representative use) above the parametric drinking water limit of 0.1 µg/L was concluded to be high in geoclimatic situations that are represented by all 9 FOCUS groundwater scenarios (9 of 9 for GA_4 and 8 of 9 for GA_7). The potential for groundwater exposure from the representative use of the product 'Regulex 10 SG' on pears (lowest total dose representative use) above the parametric drinking water limit of 0.1 µg/L was concluded to be high in geoclimatic situations that are represented by 5 of the 9 FOCUS groundwater scenarios (5 of 9 for GA_4 and none for GA_7, the sum of GA_4 and GA_7 was > 0.1 µg/L in 6 of 9 but <0.5µg/L[18] for all 9 scenarios). The potential for groundwater exposure from the representative use of the product 'Novagib' on pears (lowest individual dose representative use) above the parametric drinking water limit of 0.1 µg/L was concluded to be high in geoclimatic situations that are represented by 7 of the 9 FOCUS groundwater

[16] calculation using KOCWIN V2.0; EPISUITE 4.0 software (Syracuse Research Corporation) based on the pH 7 Log Pow value.

[17] Simulations complied with EFSA (EFSA, 2004) and utilised a Q10 of 2.2 and Walker equation coefficient of 0.7.

[18] 0.5µg/L is the legal parametric limit that applies to the sum of all pesticides (the definition of which includes plant growth regulators). 0.1µg/L is the legal parametric limit that applies to individual pesticides.

scenarios (7 of 9 for GA_4 and none for GA_7, the sum of GA_4 and GA_7 was also > 0.1 µg/L in 7 of 9 but <0.5µg/L for all 9 scenarios). As for all the representative uses groundwater contamination is indicated above the parametric limit at more than half the pertinent FOCUS scenarios, this is indicated as a critical area of concern (see section 9 of this conclusion).

It is currently accepted that it is likely (based on the high proportion of mineralisation in a relatively short time in the available ready biodegradability study) that transformation products of GA_4 and GA_7 (excepting CO_2) will not be formed at levels that would trigger further consideration for environmental exposure and risk assessment. However this conclusion might have to be revisited in the context of mass balance results from any soil or sediment water incubations that might become available in the future should the data gaps discussed below (and indicated in section 7) be filled.

Consequent to the high potential for groundwater contamination indicated above and non demonstration of low chronic risk to aquatic organisms in section 5, data gaps for laboratory incubations of GA_4 and GA_7 in soils and natural sediment water systems and batch soil adsorption measurements are identified to reduce the uncertainty in the available environmental exposure assessment (see section 7). In the context of addressing the risk to aquatic organisms information (that would need to be traceable back to reliable observations or measurements) on the levels of GA_4 and GA_7 naturally present in pertinent natural waters would be an alternative way of addressing this missing risk characterisation.

5. Ecotoxicology

The risk assessment was based on the following documents: European Commission (2002a, 2002b, 2002c) and SETAC (2001).

A Tier II technical equivalence assessment for ecotoxicology was not presented and therefore it is not possible to conclude that the presented sources are ecotoxicologically equivalent. The representativeness of the material tested in the ecotoxicological studies to the technical specification should be addressed once the technical specification has been defined.

Acute and short-term avian studies were provided for gibberellic acid (GA_3) and used for first-tier risk assessment. No reliable acute and short-term avian toxicity data were available for GA_4 and GA_7. The acute and short-term risk assessment presented for gibberellic acid (GA_3) resulted in TER values which were far above the Annex VI triggers and therefore indicated a low risk. On the basis of the high margin of safety obtained for the risk assessment with gibberellic acid (GA_3), the similarities between gibberellic acid and GA_4 and GA_7 and available additional information, the acute and short-term risk from the representative use of GA_4 and GA_7 could be considered as low. No avian long-term reproductive toxicity data for GA_4 and GA_7 was available. However, a low reproductive risk to birds was concluded on the basis of weight-of-evidence taking into account the results of the mammal multi-generation study and also the low exposure to birds from the representative use. The acute and reproductive risk to mammals was assessed to be low based on first tier risk assessment.

Acute toxicity data with the formulated product 'GA_4/GA_7 10g/l SL' were available for fish, aquatic invertebrates and algae and were used to assess the risk from the active substance. The risk to algae, fish and aquatic invertebrates was assessed as low. Data on the chronic toxicity of GA_4 and GA_7 to fish, aquatic invertebrates and aquatic macrophytes were not available and therefore a quantified risk assessment could not be performed. Since GA_4 and GA_7 are plant growth regulators the risk to non-target aquatic plants should be considered. As for terrestrial plants, it is expected that GA_4 and GA_7 are natural components of aquatic plants and may not exhibit phytotoxic effects. However, no reliable quantitative assessment of the levels of GA_4 and GA_7 that occur naturally in surface water was available, allowing concluding negligible exposure following the representative use. Therefore, a data gap was identified to address the risk to aquatic macrophytes. The representative use of GA_4 and

GA_7 includes four applications and the estimated aquatic DT_{50} is 15 days. Therefore, long-term exposure of aquatic organisms cannot be excluded. Data and/or risk assessment are required to address the chronic risk to fish and to aquatic invertebrates.

A first tier risk assessment indicated a low risk to bees. A first tier risk assessment according to SETAC (2001) indicated a low in-field and off-field risk to non-target arthropods for the representative use.

A first tier risk assessment demonstrated a low acute risk to earthworms. No data indicating the chronic toxicity of earthworms was available. GA_4 and GA_7 are expected to exhibit low to moderate persistence in soil (see section 4), therefore a low chronic risk to earthworms was concluded. Toxicity data indicated a low risk to soil micro-organisms.

No standard non-target plant studies were available. A low risk to non-target terrestrial plants was concluded on the basis a qualitative argument concerning the non-toxic mode-of-action and the fact that GA_4 and GA_7 occur naturally in many terrestrial plants. A low risk was concluded for biological methods of sewage treatments.

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
GA_4	Data gap	The risk to soil-dwelling organisms was assessed as low.
GA_7	Data gap	The risk to soil-dwelling 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
GA_4	Data gap Very high mobility, A QSAR estimate at pH7 gives a Kdoc of 0.5747 mL/g pH dependent mobility is expected	Yes between 5 of 9 (1x10g/ha) and 9 of 9 (4x20g/ha) FOCUS scenarios	Yes	Yes	The acute risk to aquatic organisms was assessed as low. A data gap was identified to address the risk to aquatic macrophytes and the chronic risk to fish and aquatic invertebrates.

GA_7	Data gap Very high mobility, A QSAR estimate at pH7 gives a Kdoc of 0.5747 mL/g pH dependent mobility is expected	Yes up to 7 of 9 FOCUS scenarios (4x20g/ha)	Yes	Yes	The acute risk to aquatic organisms was assessed as low. A data gap was identified to address the risk to aquatic macrophytes and the chronic risk to fish and aquatic invertebrates.

6.3. Surface water and sediment

Compound (name and/or code)	**Ecotoxicology**
GA_4	The acute risk to aquatic organisms was assessed as low. A data gap was identified to address the risk to aquatic macrophytes and the chronic risk to fish and aquatic invertebrates.
GA_7	The acute risk to aquatic organisms was assessed as low. A data gap was identified to address the risk to aquatic macrophytes and the chronic risk to fish and aquatic invertebrates.

6.4. Air

Compound (name and/or code)	**Toxicology**
GA_4	GA_4/GA_7: Low acute toxicity to rats LC_{50}> 2.98 mg/L air /4h (nose only)
GA_7	GA_4/GA_7: Low acute toxicity to rats LC_{50}> 2.98 mg/L air /4h (nose only)

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

This is a complete list of the 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 7 of Directive 91/414/EEC concerning information on potentially harmful effects).

- Batch analysis for fumonisins (relevant for the Globachem source; submission date proposed by the notifier: unknown; see section 1)
- Validation of the method of analysis for fumonisin (relevant for the Fine Agrochemicals source ; submission date proposed by the notifier: unknown; see section 1)
- Structure of impurity BP3 (relevant for the Globachem source; submission date proposed by the notifier: unknown; see section 1)
- Batch analysis for fumonisins and water by the Karl Fisher method (relevant for the Valent source; submission date proposed by the notifier: unknown; see section 1)
- Validation for the method of analysis for impurities (relevant for the Fine Agrochemicals and Valent sources; submission date proposed by the notifier: unknown; see section 1)
- Method of analysis for the technical material capable of separating GA_4 and GA_7 and other gibberellins (relevant for the 'Regulex 10 SG' formulation; submission date proposed by the notifier: unknown; see section 1)
- Identification of the formed hydrolysis compounds (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 1)
- For the formulation 'Novagib': acidity or alkalinity, identification of the break down products in the shelf-life study, method of analysis for the formulation. (relevant for the 'Novagib formulation; submission date proposed by the notifier: unknown; see section 1)
- For the formulation 'Regulex 10 SG': bulk or tap density, accelerated storage study, shelf-life study (relevant for the 'Regulex 10 SG' formulation; submission date proposed by the notifier: unknown; see section 1)
- For the formulation 'Gibb plus': shelf-life study (relevant for the 'Gibb plus' formulation; submission date proposed by the notifier: unknown; see section 1)
- Methods of analysis for water (ground/drinking), soil and air (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 1).
- The representativeness of the material tested in the toxicological studies to the technical specification and the toxicological relevance of impurities should be addressed once the technical specification has been defined (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 2).
- The toxicological profile of the gibberellins Globachem and Fine agrochemicals sources should be adequately addressed (relevant for the representative uses evaluated in pears and cherries ('Novagib' formulation) and apples ('Novagib' and 'Gibb plus' formulations), submission date proposed by the notifier: unknown; see section 2.).

- Acute toxicity datapackage with 'Regulex 10 SG' (relevant for the representative uses evaluated in pears and apples ('Regulex 10 SG' formulation), already submitted by the notifier but not accepted according to Regulation 1095/2007 ; see section 2).

- Medical data of gibberellins (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 2).

- Information on the natural background levels of gibberellins in the edible parts of crops are required (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 3).

- Supervised residue trials on cherries and information on the natural background levels of gibberellins are required (relevant for the representative use evaluated on cherries; submission date proposed by the notifier: unknown; see section 3).

- Storage stability studies for gibberellins GA_4 and GA_7 supporting the supervised residue trial results are required (relevant for the representative uses evaluated on apple and pear; submission date proposed by the notifier: data already submitted but not considered according to the article 11 of Regulation 1095/2007 concerning the submission of new studies; see section 3).

- Because a high potential for groundwater contamination is identified, measured data: on at least degradation in soil (laboratory incubations, minimum 4 soils) and adsorption to soil (laboratory batch adsorption investigations in soils (minimum 4) with a range of pH) for GA_4 and GA_7, would be needed to provide a less uncertain / more refined groundwater exposure assessment (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 4)

- Information to address the chronic risk to fish and aquatic invertebrates from exposure to GA4 and GA7 is outstanding. Any information provided could include chronic toxicity data or a scientific argumentation based on either the provision of information demonstrating rapid dissipation in natural sediment water systems (laboratory incubations) or information (that would need to be traceable back to reliable observations or measurements) on the levels of GA4 and GA7 naturally present in pertinent natural waters, compared to levels estimated to occur from the representative uses, (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see sections 4 and 5)

- Information to address the risk to aquatic macrophytes from exposure to GA4 and GA7 is outstanding. Any information provided could include toxicity data or a scientific argumentation based on of the provision of information (that would need to be traceable back to reliable observations or measurements) on the levels of GA4 and GA7 naturally present in pertinent natural waters, compared to levels estimated to occur from the representative uses, (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see sections 4 and 5)

- The representativeness of the material tested in the ecotoxicological studies to the technical specification should be addressed once the technical specification has been defined (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 5).

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

- none.

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 of Annex VI to Directive 91/414/EEC and where the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

1. The representativeness of the batches used in the toxicology and ecotoxicology studies to the technical specification (both missing).

2. The toxicological profile of Globachem and Fine agrochemicals sources and therefore the risk assessment to operators, workers and bystanders (‘Gibb plus’ and ‘Novagib’).

3. The risk to aquatic macrophytes and the chronic risk to fish and aquatic invertebrates.

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 of Annex VI to Directive 91/414/EEC, 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.

4. With the available data, a high potential for groundwater exposure by the components of the active substance above the parametric drinking water limit of 0.1 µg/L are predicted over a wide range of geoclimatic conditions. (Between 9 out of 9 FOCUS scenarios for one of the representative uses on apples and 5 out of 9 FOCUS scenarios for the least challenging representative use (one of those on pears)).

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9.3. Overview of the concerns 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.)

All columns are grey as the representativeness of the material tested in the toxicological and ecotoxicological studies to the technical specification could not be defined (both missing).

Representative use		Apples Regulex 10 SG 4x20g/ha	Apples Novagib SL 5x5g/ha	Apples Gibb Plus 4x5g/ha	Pears Regulex 10 SG 1x10g/ha	Pears Novagib SL 3x5g/ha	Cherries Novagib SL 2x10g/ha
Operator risk	Risk identified						
	Assessment not finalised		X[2]	X[2]		X[2]	X[2]
Worker risk	Risk identified						
	Assessment not finalised		X[2]	X[2]		X[2]	X[2]
Bystander risk	Risk identified						
	Assessment not finalised		X[2]	X[2]		X[2]	X[2]
Consumer risk	Risk identified						
	Assessment not finalised						
Risk to wild non target terrestrial vertebrates	Risk identified						
	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	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]
Groundwater exposure active substance	Legal parametric value breached	X[4]	situation similar to Pears Novagib SL anticipated	situation similar to Pears Novagib SL anticipated	5 of 9 FOCUS scenarios[4]	7 of 9 FOCUS scenarios[4]	situation similar to Pears Novagib SL anticipated
	Assessment not finalised						
Groundwater exposure metabolites	Legal parametric value breached						
	Parametric value of 10µg/L[(a)] breached						
	Assessment not finalised						

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

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

REFERENCES

ECHA (European Chemicals Agency), 2010. Guidance on information requirements and chemical safety assessment. Chapter R.16: Environmental exposure estimation, version 2 May 2010. EC Document Reference ECHA-10-G-06-EN 05/2010. http://guidance.echa.europa.eu (updated from: Technical Guidance Document on Risk Assessment in support of Commission Directive 93/67/EEC on Risk Assessment for new notified substances, Commission Regulation (EC) No 1488/94 on Risk Assessment for existing substances and Directive 98/8/EC concerning placement of biocides products on the market, Part II, European Commission Joint Research Centre, EUR 20418 EN/2 (2003))

EFSA (European Food Safety Authority), 2004. Opinion of the Scientific Panel on Plant Health, Plant Protection Products and their Residues on a request of EFSA related to FOCUS groundwater models comparability and the consistency of this risk assessment of groundwater contamination. The EFSA Journal (2004) 93, 1-20.

EFSA (European Food Safety Authority), 2011. Peer Review Report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance gibberellins.

European Commission, 1999. Guidelines for the generation of data concerning residues as provided in Annex II part A, section 6 and Annex III, part A, section 8 of Directive 91/414/EEC concerning the placing of plant protection products on the market, 1607/VI/97 rev.2, 10 June 1999.

European Commission, 2000. Technical Material and Preparations: Guidance for generating and reporting methods of analysis in support of pre- and post-registration data requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414. SANCO/3030/99 rev.4, 11 July 2000.

European Commission, 2002a. Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC. SANCO/10329/2002 rev.2 final, 17 October 2002.

European Commission, 2002b. Guidance Document on Aquatic Ecotoxicology Under Council Directive 91/414/EEC. SANCO/3268/2001 rev 4 (final), 17 October 2002.

European Commission, 2002c. Guidance Document on Risk Assessment for Birds and Mammals Under Council Directive 91/414/EEC. SANCO/4145/2000.

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

European Commission, 2004a. Guidance document on residue analytical methods. SANCO/825/00 rev. 7, 17 March 2004.

European Commission, 2004b. Guidance Document on Dermal Absorption. SANCO/222/2000 rev. 7, 19 March 2004.

European Commission, 2008. Review Report for the active substance giberellin finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 28 October 2008 in view of the inclusion of giberellin in Annex I of Directive 91/414/EEC. SANCO 2614/08 – rev. 1, 8 July 2008.

European Commission, 2009. Guidance Document on the Assessment of the Equivalence of Technical Materials of Substances Regulated under Council Directive 91/414/EEC. SANCO/10597/2003 – rev. 8.1, May 2009.

FOCUS, 2000. "FOCUS Groundwater Scenarios in the EU review of active substances". Report of the FOCUS Groundwater Scenarios Workgroup, EC Document Reference SANCO/321/2000-

rev.2. 202 pp, as updated by the Generic Guidance for FOCUS groundwater scenarios, version 1.1 dated April 2002.

FOCUS, 2001. "FOCUS Surface Water Scenarios in the EU Evaluation Process under 91/414/EEC". Report of the FOCUS Working Group on Surface Water Scenarios, EC Document Reference SANCO/4802/2001-rev.2. 245 pp.

Hungary, 2006. Draft Assessment Report (DAR) on the active substance gibberellins, prepared by the rapporteur Member State Hungary in the framework of Directive 91/414/EEC, August 2006.

Hungary, 2011. Final Addendum to Draft Assessment Report on gibberellins, compiled by EFSA, October 2011.

JMPR, 2004. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues Rome, Italy, 20–29 September 2004, Report 2004, 383 pp.

JMPR, 2007. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues Geneva, Switzerland, 18–27 September 2007, Report 2007, 164 pp.

SETAC (Society of Environmental Toxicology and Chemistry), 2001. Guidance Document on Regulatory Testing and Risk Assessment procedures for Plant Protection Products with Non-Target Arthropods. ESCORT 2.

APPENDICES

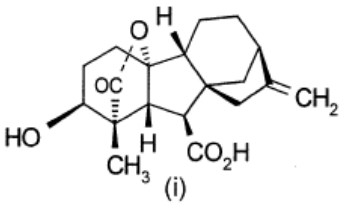
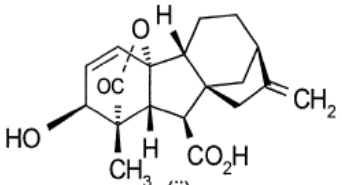
APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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

Active substance (ISO Common Name) ‡	Gibberellins - GA_4/GA_7 there is no ISO common name for these compounds
Function (*e.g.* fungicide)	Plant growth regulator
Rapporteur Member State	Hungary
Co-rapporteur Member State	-

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	GA_4: (3*S*,3a*R*,4*S*,4a*R*,7*R*,9a*R*,9b*R*,12*S*)-12-hydroxy-3-methyl-6-methylene-2-oxoperhydro-4a,7-methano-3,9b-propanoazuleno[1,2-*b*]furan-4-carboxylic acid GA_7: (3*S*,3a*R*,4*S*,4a*R*,7*R*,9a*R*,9b*R*,12*S*)-12-hydroxy-3-methyl-6-methylene-2-oxoperhydro-4a,7-methano-9b,3-propenoazuleno[1,2-*b*]furan-4-carboxylic acid
Chemical name (CA) ‡	GA4: (1α,2β,4aα,4bβ,10β)-2,4a-dihydroxy-1-methyl-8-methylenegibbane-1,10-dicarboxylic acid 1,4a-lactone GA7: (1α,2β,4aα,4bβ,10β)-2,4a-dihydroxy-1-methyl-8-methylenegibb-3-ene-1,10-dicarboxylic acid 1,4a-lactone
CIPAC No ‡	904
CAS No ‡	GA_4: 468-44-0 GA_7: 510-75-8 GA_4A_7 mixture: 8030-53-3
EC No (EINECS or ELINCS) ‡	EEC: GA_4: 207-406-9 GA_7: 208-117-0
FAO Specification (including year of publication) ‡	-
Minimum purity of the active substance as manufactured ‡	1. Fine Agrochemicals Ltd. GA_4 905 g/kg-919 g/kg GA_7 19.5 g/kg-27 g/kg GA_4/GA_7 min. 924 g/kg 2. Globachem NV GA_4 648 g/kg-653 g/kg GA_7 248 g/kg-253 g/kg GA4/GA7 min. 885 g/kg 3.Valent Biosciences Ltd. GA_4 631 g/kg-778 g/kg

	GA_7 130 g/kg-288 g/kg GA_4/GA_7 min. 852 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	Open
Molecular formula ‡	GA_4 $C_{19}H_{24}O_5$ GA_7 $C_{19}H_{22}O_5$
Molecular mass ‡	GA_4 332.40 g/mol GA_7 330.40 g/mol
Structural formula ‡	GA_4  (i) GA_7  (ii)

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	205.5-231°C (92.5-99%)
Boiling point (state purity) ‡	Not applicable
Temperature of decomposition (state purity)	≥ 210°C (92.5-99%)
Appearance (state purity) ‡	Pure material: white powder (99%) Technical material: white powder (92.5%)
Vapour pressure (state temperature, state purity) ‡	between 7.68 x 10^{-6} Pa and 1.6 x 10^{-1} Pa (92.5-99%)
Henry's law constant ‡	between 2 x 10^{-5} Pa m^3 mol^{-1} and 6.5 x 10^{-2} Pa m^3 mol^{-1} (92.5-99%)
Solubility in water (state temperature, state purity and pH) ‡	at 20°C (99 %) Pure water 127 ± 1.6 mg/l pH 4 buffer 141 ± 4.2 mg/l pH 7 buffer 40.0 ± 1.7 g/l pH 9 buffer >250 g/l
Solubility in organic solvents ‡ (state temperature, state purity)	Solubility at 20 °C in g/L (92.5 %) n-Heptane < 0.5 mg/l Xylene 78.9 ± 1.4 mg/l 1,2-dichloroethane 3380 ± 220 mg/l Methanol >250 g/l Acetone >250 g/l Ethyl acetate 56 ± 2.4 g/l
Surface tension ‡ (state concentration and temperature, state purity)	64 mN/m at 114 mg/l; at 20°C (99%) not surface active
Partition co-efficient ‡ (state temperature, pH and purity)	at 20°C (99%): pH 4: log P_{ow} = 2.47 pH 7: log P_{ow} = 0.146 pH 10: log P_{ow} = -1.23; at 20°C (92.5%), without pH control: GA_4: log P_{ow} = 2.34 GA_7: log P_{ow} = 2.25
Dissociation constant (state purity) ‡	at 23°C, 99% pKa: 4.30
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	In methanol solution GA_4/GA_7 absorbed UV at wavelengths below ca. 250 nm. No maxima were observed above 210 nm. ε values at, or above 298 nm: < 10 l cm^{-1} mol^{-1}
Flammability ‡ (state purity)	not highly flammable (99% and 90.8%) not autoflammable (99%)
Explosive properties ‡ (state purity)	not explosive (99% and 90.8%)
Oxidising properties ‡ (state purity)	not oxidising (99% and 90.8%))

Summary of representative uses evaluated (Gibberellins GA_4/GA_7)

Crop and/or situation (a)	Member State or Country	Product Name	F G or I (b)	Pests or Group of pests controlled function (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks (m)
					Type (d-f)	Conc. of a.s. (i)	Method Kind (f-h)	Growth stage & season (j)	Number min max (k)	Interval between apps. (min)	kg a.s. /hL min-max	Water (L/ha) min-max	kg a.s ./ha min-max		
Apple		**Regulex 10 SG**	F	PGR	SG	10 % w/w	spraying	First application at petal fall BBCH 65, latest application at BBCH 72	1-4	7-12 days	0.5-2.0	1000	0.005-0.020	Not relevant	
Apple		**Novagib**	F	PGR	SL	10 g/l	spraying	First application at petal fall BBCH 65, latest application at BBCH 72	1-5	7-10 days	0.2-0.5	1000-3000	0.002-0.005	Not relevant	specific rates vary with cultivar and growing conditions
Apple		**Gibb Plus**	F	PGR	SL	10 g/l	spraying	First application at petal fall BBCH 65, latest application at BBCH 72	**4**	10 days	0.2 -2.0	1000	0.002-0.005	Not relevant	
Pear	North and South EU	**Regulex 10 SG**	F	PGR	SG	10 % w/w	spraying	First application at petal fall BBCH 65, latest application at BBCH 72	1	-	1.0	500	0.010	Not relevant	
Pear	North and South EU	**Novagib**	F	PGR	SL	10 % w/w	spraying	First application at petal fall BBCH 65, latest	1-3	7	0.5	500	0.005	Not relevant	

Crop and/or situation (a)	Member State or Country	Product Name	F G or I (b)	Pests or Group of pests controlled function (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks (m)
					Type (d-f)	Conc. of a.s. (i)	Method Kind (f-h)	Growth stage & season (j)	Number min max (k)	Interval between apps. (min)	kg a.s. /hL min-max	Water (L/ha) min-max	kg a.s ./ha min-max		
								application at BBCH 72							
Cherries	North and South EU	**Novagib**	F	PGR	SL	10 % w/w	spraying	First application at petal fall BBCH 65, latest application at BBCH 72	2	14	0.5-1.0	500	0.005-0.010	Not relevant	

(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)
(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)
(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) All abbreviations used must be explained
(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated
(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants. **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant.**
(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)	HPLC-UV
Impurities in technical as (analytical technique)	HPLC-UV; HPLC-MS
Plant protection product (analytical technique)	HPLC-UV

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin	Not required
Food of animal origin	Not required
Soil	GA_4 and GA_7
Water surface	GA_4 and GA_7.
drinking/ground	GA_4 and GA_7
Air	GA_4 and GA_7

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	Not required as no MRLs are proposed
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Not required as no MRLs are proposed
Soil (analytical technique and LOQ)	Open
Water (analytical technique and LOQ)	Open for ground/drinking water. Surface water: No. 1880-1 method Concentrated by C18extraction cartridge, eluted with methanol. LC/MS/MS 10 µg/L
Air (analytical technique and LOQ)	Open
Body fluids and tissues (analytical technique and LOQ)	Not required. Gibberellins are not classified as toxic (T) or very toxic (T^+)

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

	RMS/peer review proposal
Active substance	No classification proposed

Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	40% in females and 18% in males (based on urinary excretion within 48 h).
Distribution ‡	Widely distributed.
Potential for accumulation ‡	No evidence of accumulation.
Rate and extent of excretion ‡	Rapid and extensive (app. 98%) within 48 h; mainly via urine, faeces and bile.
Metabolism in animals ‡	Hydroxylation and glucuronide conjugation of parent compounds and hydroxyls.
Toxicologically relevant compounds ‡ (animals and plants)	Parent compound (Gibberellins GA_4/GA_7)
Toxicologically relevant compounds ‡ (environment)	Parent compound (Gibberellins GA_4/GA_7)

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	> 5000 mg/kg bw	
Rat LD_{50} dermal ‡	> 2000 mg/kg bw	
Rat LC_{50} inhalation ‡	> 2.98 mg/L air /4h (nose only)	
Skin irritation ‡	Non-irritant	
Eye irritation ‡	Moderate irritant	
Skin sensitisation ‡	Non-sensitising (M & K)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Liver (hepatocelular vacuolation in rats; increased weight in dogs) Kidney (tubule-interstitial nephritis and nephron loss in rats and increased weight in dogs). Reduced food consumption and body weight gain (rats and dogs).	
Relevant oral NOAEL ‡	90-day dog 650 mg/kg bw/day 90-day rat: 500 mg/kg bw/day	
Relevant dermal NOAEL ‡	No data – not required	
Relevant inhalation NOAEL ‡	No data - not required	

Genotoxicity ‡ (Annex IIA, point 5.4)

Gibberellins GA_4/GA_7 are unlikely to be genotoxic	

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

Target/critical effect ‡	Limited data available; no further data needed.	
Relevant NOAEL ‡	-	
Carcinogenicity ‡	-	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Parental: kidney (nephropathy, medulary tubular dilation, fibroplasias and interstitial basophilia) and reduced body weight gain and food consumption Reproductive: none. Offspring: reduced body weight and spleen weight.	
Relevant parental NOAEL ‡	300 mg/kg bw/day (females)	
Relevant reproductive NOAEL ‡	1000 mg/kg bw/day	
Relevant offspring NOAEL ‡	600 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	Rabbit Maternal: mortality, reduced body weight gain and food consumption. Developmental: increased resorptions and decreased live foetuses. Rat: no data; no further data needed.	
Relevant maternal NOAEL ‡	Rabbit: 300 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rabbit: 300 mg/kg bw/day	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data; no further data needed.	
Repeated neurotoxicity ‡	No data; no further data needed.	
Delayed neurotoxicity ‡	No data; no further data needed.	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No data; no further data needed.
Studies performed on metabolites or impurities ‡	No data; no further data needed.

Medical data ‡ (Annex IIA, point 5.9)

Limited information available. Further data are required.

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.3 mg/kg bw/day	Rat, Multigeneration	1000
AOEL ‡	0.18 mg/kg bw/day	Rat, Multigeneration; rabbit, developmental	300x0.18*
ARfD ‡	Not needed		

*Correction for low oral absorption (18%)

Dermal absorption ‡ (Annex IIIA, point 7.3)

Regulex 10SG: 18 % based on oral absorption.

Exposure scenarios (Annex IIIA, point 7.2)

Operator	The estimated exposure for 'Regulex 10 SG' according to the German model (highest rate representative use of 0.020 kg a.s./ha) was below the AOEL. Tractor-mounted equipment: Without PPE: 3.12% of AOEL Handheld equipment: Without PPE: 1.8% of AOEL 'Gibb plus' and 'Novagib': risk assessment inconclusive.
Workers	'Regulex 10 SG': 12% of AOEL 'Gibb plus' and 'Novagib': risk assessment inconclusive.
Bystanders	'Regulex 10 SG': 0.66% of AOEL 'Gibb plus' and 'Novagib': risk assessment inconclusive.

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

	Peer review proposal
Substance classified (gibberellins GA_4/GA_7)	None. However, the database is not suitable to assess adequately the reproductive toxicity and carcinogenic potential.

Residues

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

Plant groups covered	Gibberellins are a group of naturally-occurring diterpenoid acids that function as plant growth regulators by influencing a range of developmental processes in higher plants including stem elongation, germination, dormancy, flowering, sex expression, enzyme induction and leaf and fruit senescence. Specific plant metabolism studies were not conducted since the metabolism of gibberellins in plants is widely documented in literature accessible in the public domain.
Rotational crops	Not provided and not required
Metabolism in rotational crops similar to metabolism in primary crops?	Not relevant
Processed commodities	Not relevant
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Not relevant
Plant residue definition for monitoring	Not necessary as no MRLs proposed and since not possible to distinguish exogenous and natural gibberellins
Plant residue definition for risk assessment	Not necessary as no MRLs proposed and since not possible to distinguish exogenous and natural gibberellins
Conversion factor (monitoring to risk assessment)	Not relevant

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

Animals covered	Not provided and not required
Time needed to reach a plateau concentration in milk and eggs	Not relevant
Animal residue definition for monitoring	Not relevant
Animal residue definition for risk assessment	Not relevant
Conversion factor (monitoring to risk assessment)	Not relevant
Metabolism in rat and ruminant similar (yes/no)	Not relevant
Fat soluble residue: (yes/no)	Not relevant

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

	Not provided and not required since Gibberellins GA_4/GA_7 are applied to a perennial orchard crop.

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

A study investigating the stability of gibberellins GA_4/GA_7 in frozen crop matrices is on-going Gibberellins GA_4 and GA_7 are stable in crop extracts stored refrigerated for at least 4 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)	No	No	No
Potential for accumulation (yes/no):	Not relevant	Not relevant	Not relevant
Metabolism studies indicate potential level of residues ≥ 0.01 g/kg in edible tissues (yes/no)	Not relevant	Not relevant	Not relevant
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle			
Liver			
Kidney			
Fat			
Milk			
Eggs			

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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 Souther Region field or glasshou se	Trials results relevant to the representativ e uses (a)	Recommendation/comments	**MRL** estimated from trials according to representativ e use	**HR** (c)	**STMR** (b)
Apples	Northern	2x <0.05	PHI 104 to 131 days	(no MRL proposed)		
	Southern	6x <0.05	PHI 103 to 126 days.			
Pears	Northern	2x <0.05	PHI 148 to 152 days	(no MRL proposed)		

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3x <0.01, 0.01, 6x 0.02, 0.04, 2x 0.15, 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

Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8)[7]

ADI	0.3 mg/kg bw/day
TMDI (% ADI) according to EFSA PRIMo Model	Informative only since no MRLs proposed Highest TMDI 0.2% ADI when LOQ value of 0.05 mg/kg considered for pome fruits.
TMDI (% ADI) according to national (to be specified) diets	Not necessary
IEDI (WHO European Diet) (% ADI)	Not necessary
NEDI (specify diet) (% ADI)	Not necessary
Factors included in IEDI and NEDI	-
ARfD	No ARfD value proposed and not necessary
IESTI (% ARfD)	Not relevant
NESTI (% ARfD) according to national (to be specified) large portion consumption data	Not relevant
Factors included in IESTI and NESTI	Not relevant

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

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%)
		Transfer factor	Yield factor	
Not provided and not required	-			

Proposed MRLs

No MRLs proposed

Fate and behaviour in the environment

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

Mineralization after 100 days ‡	No data were submitted
Non-extractable residues after 100 days ‡	No data were submitted
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	No data were submitted

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

Anaerobic degradation ‡

Mineralization after 100 days	No data were submitted
Non-extractable residues after 100 days	No data were submitted
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No data were submitted

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No data were submitted

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

Laboratory studies ‡	No data were submitted, Data gap for measured data to refine assessments
	Estimated DT_{50} both GA_4 and GA_7: 30 days*
	* Technical Guidance Document on Risk Assessment in support of Commission Directive 93/67/EEC on Risk Assessment for new notified substances, Commission Regulation (EC) No 1488/94 on Risk Assessment for existing substances and Directive 98/8/EC concerning placement of biocides products on the market, Part II, European Commission Joint Research Centre, EUR 20418 EN/2 (2003)
Field studies ‡	No data were submitted

pH dependence ‡ (yes / no) (if yes type of dependence)	No data were submitted
Soil accumulation and plateau concentration ‡	No data were submitted

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡	Estimated Koc both GA4 and GA7: 0.5747 ml/g (Kom 0.33335ml/g) (KOCWIN v2.00; EPISUITE 4.0), for a pH of 7 from the Log Pow value measured at pH 7 (0.146, see endpoints, Annex IIA, point 2). Adsorption is expected to be pH dependent. Data gap for measured data to refine assessments
Metabolite ‡	No data were submitted

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

Column leaching ‡	No data were submitted
Aged residues leaching ‡	No data were submitted
Lysimeter/ field leaching studies ‡	No data were submitted

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	"DT_{50} (d): 30 days" Extrapolation of the results from ready biodegradation tests is possible according to the EU Technical Guidance Document on Risk Assessment.
Application data	Crop: apple Depth of soil layer: 5 cm Soil bulk density: 1.5 g/cm^3 % plant interception: 50% Number of applications: 4 Interval (d): 7 Application rate(s): 20 g as/ha

$PEC_{(s)}$ (µg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	13.3		42.4	
Short term				
24h	13.0	13.2	41.4	41.9
2d	12.7	13.0	40.5	41.4
4d	12.2	12.7	38.7	40.5
Long term				
7d	11.3	12.3	36.1	39.1
28d	7.0	9.8	22.2	31.2
50d	4.2	7.9	13.4	25.1
100d	1.3	5.2	4.2	16.5

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	**pH 4**: GA_4/GA_7: stable at 50°C; extrapolation: DT_{50} > 1 year at 20°C; GA_4 stable at 50°C; extrapolation: DT_{50} > 1 year at 20°C; GA_7: after 5 days declined ca. 50%
	pH 7: GA_4/GA_7: stable at 50°C; extrapolation: DT^{50} > 1 year at 20°C ;GA_4: stable at 50°C; extrapolation: DT_{50} > 1 year at 20°C; GA_7: stable at 50°C; extrapolation: DT_{50} > 1 year at 20°C
	pH 9: GA_4/GA_7: stable at 50°C; extrapolation: DT_{50} > 1 year at 20°C ; GA_4: stable at 50°C; extrapolation: DT_{50} > 1 year at 20°C; GA_7: after 5 days completely decline
Photolytic degradation of active substance and metabolites above 10 % ‡	DT_{50} : GA_4/GA_7 ranged 104 – 206 days at pH5 – pH9 respectively DT_{50}: GA_4 ranged 101 – 163 days at pH5 – pH9 respectively DT_{50} : GA_7 114 days at pH5 ; 145 days at pH7; 57 days at pH9
Quantum yield of direct phototransformation in water at Σ > 290 nm	No data were submitted
Readily biodegradable ‡ (yes/no)	yes
Degradation in water / sediment ‡	No data were submitted, Data gap for measured data to refine assessments Estimated DT_{50} both GA_4 and GA_7: water 15 days, sediment 200 days* * Technical Guidance Document on Risk Assessment in support of Commission Directive 93/67/EEC on Risk Assessment for new notified substances, Commission Regulation (EC) No 1488/94 on Risk Assessment for existing substances and Directive 98/8/EC concerning placement of biocides products on the market, Part II, European Commission Joint Research Centre, EUR 20418 EN/2 (2003)

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

Parent Parameters used in FOCUSsw step 1 and 2	Molecular weight (g/mol): 332.4 GA_4; 330.7 GA_7 Water solubility (mg/L): 340 for both compounds Koc (L/kg): 0.5747 for both compounds 1/n: 0.9 DT_{50} soil (d): 30 days for both compounds (extrapolated) DT50 water (d): 15 DT50 sediment (d): 300
Application rate	Crop: apple Crop interception: minimal crop cover Number of applications: 4 Interval (d): 7 Application rate(s): 20 g as/ha Depth of water body: 30 cm
Main routes of entry	29.197 % drift from 3 meter (FOCUSsw Step 1) 10% runoff/drainage (FOCUSsw Step 1) 23.6% drift from 3 meter (FOCUSsw Step 2) 2% runoff/drainage (at FOCUSsw Step 1 and 2)at N 4% runoff/drainage (at FOCUSsw Step 1 and 2)at S

Results:

Parent (name) Gibberellins GA_4/GA_7

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	0	34.4321		0.1531	
	24	34.3467	34.3894	0.1974	0.1753
	2d	34.2674	34.3482	0.1969	0.1862
	4d	34.1095	34.2683	0.1960	0.1913
	7d	33.8738	34.1497	0.1947	0.1931
	14d	33.3304	33.8755	0.1915	0.1931
	21d	32.7957	33.6045	0.1885	0.1921
	28d	32.2695	33.3363	0.1855	0.1908
	42d	31.2424	32.8086	0.1796	0.1880
	50d	30.6702	32.5121	0.1763	0.1864
	100d	27.3241	30.7385	0.1570	0.1764

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0	6.53		0.04	
	24	6.24	6.39	0.04	0.04
	2d	5.96	6.24	0.03	0.04
	4d	5.43	5.97	0.03	0.03
	7d	4.73	5.58	0.03	0.03
	14d	3.42	4.81	0.02	0.03
	21d	2.48	4.18	0.01	0.02
	28d	1.79	3.67	0.01	0.02
	42d	0.94	2.88	0.01	0.02
	50d	0.65	2.55	0.00	0.01
	100d	0.06	1.40	0.00	0.01
Southern EU	0	9.63		0.05	
	24	9.20	9.42	0.05	0.05
	2d	8.78	9.20	0.05	0.05
	4d	8.01	8.80	0.05	0.05
	7d	6.97	8.23	0.04	0.05
	14d	5.05	7.10	0.03	0.04
	21d	3.65	6.17	0.02	0.04
	28d	2.64	5.41	0.02	0.03
	42d	1.39	4.25	0.01	0.02
	50d	0.96	3.76	0.01	0.02
	100d	0.10	2.070.05	0.00	0.01

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

Method of calculation and type of stud/y: modelling,	* <u>For FOCUS gw modelling, values used –</u> Modelling using FOCUS model(s), with appropriate FOCUS gw scenarios, according to FOCUS guidance. Model(s) used: FOCUS PELMO 3.3.2 and FOCUS PEARL 3.3.3 Scenarios : all 9 FOCUS scenarios
Parent parameters	Parent DT_{50}: 30 days* Q10=2.2, Walker coefficient 0.7. * Estimated from ready biodegradation study (both GA_4 and GA_7) K_{oc}: 0.5747 ml/g* (K_{om}:0.33335ml/g)* * Estimated Koc value for both GA_4 and GA_7 1/n: 0.9 (FOCUS default value) Molecular weight (g/mol): 332.4 GA_4; 330.7 GA_7 Water solubility (mg/L): 340 for both compounds Vapour pressure:0.160 Pa for GA4; 0.067 PA for GA7. Plant uptake factor: 0.5
Application data	Crop: apple Application rate: 4 x 20 g/ha GA4 : GA7 = 70 : 30 Crop interception. 65 % Effective application rate: 4 x 4.9 g/ha GA4; 4 x 2.1 g/ha GA7 Interval: 7 days Crop: pears Application rate: 3 x 5 g/ha GA4 : GA7 = 97 : 3 Crop interception. 65 % Effective application rate: 3 x 1.6975 g/ha GA4; 3 x 0.0525 g/ha GA7 Interval: 7 days Crop: pears Application rate: 1 x 10 g/ha GA4 : GA7 = 70 : 30 Crop interception. 65 % Effective application rate: 1 x 2.45 g/ha GA4; 1 x 1.05 g/ha GA7
1st application date	Châteaudun 1 April Hamburg 15 April Jokioinen 10 May Kremsmünster 15 April Okehampton 25 March Piacenza 1 April Porto 15 March Sevilla 15 March Thiva 15 March

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

Model PELMO 3.3.2 /Crop Apple 4x20g/ha	Scenario	GA_4 (µg/L)	GA_7 (µg/L)	Total GA_4A_7 (µg/L)
	Châteaudun	**0.113**	0.053	0.166
	Hamburg	0.027	0.023	0.050
	Jokioinen	0.019	0.019	0.038
	Kremsmünster	0.059	0.055	0.114
	Okehampton	0.040	0.035	0.075
	Piacenza	0.046	0.036	0.082
	Porto	0.025	0.026	0.051
	Sevilla	0.005	0.006	0.011
	Thiva	0.005	0.004	0.009

Model PEARL 3.3.3 /Crop Apple 4x20g/ha	Scenario	GA_4 (µg/L)	GA_7 (µg/L)	Total GA_4A_7 (µg/L)
	Châteaudun	**0.777**	**0.343**	**1.121**
	Hamburg	**0.932**	**0.435**	**1.367**
	Jokioinen	**1.495**	**0.698**	**2.193**
	Kremsmünster	**0.917**	**0.402**	**1.319**
	Okehampton	**0.763**	**0.336**	**1.099**
	Piacenza	**0.628**	**0.278**	**0.906**
	Porto	**0.184**	0.080	0.264
	Sevilla	**0.495**	**0.223**	**0.718**
	Thiva	**0.346**	**0.154**	**0.500**

Model PEARL 3.3.3 /Crop Pear 3 x5g/ha	Scenario	GA_4 (µg/L)	GA_7 (µg/L)	Total GA_4A_7 (µg/L)
	Châteaudun	**0.209**	0.006	0.216
	Hamburg	**0.243**	0.008	0.251
	Jokioinen	**0.377**	0.013	0.390
	Kremsmünster	**0.235**	0.007	0.242
	Okehampton	**0.196**	0.006	0.202
	Piacenza	**0.170**	0.005	0.175
	Porto	0.055	0.002	0.056
	Sevilla	**0.124**	0.004	0.128
	Thiva	0.088	0.003	0.091

Model PEARL 3.3.3 /Crop Pear 1x10g/ha	Scenario	GA_4 (µg/L)	GA_7 (µg/L)	Total GA_4A_7 (µg/L)
	Châteaudun	**0.104**	0.045	0.149
	Hamburg	**0.121**	0.053	0.174
	Jokioinen	**0.166**	0.083	0.250
	Kremsmünster	**0.109**	0.047	0.155
	Okehampton	**0.108**	0.046	0.155
	Piacenza	0.095	0.041	0.136
	Porto	0.033	0.015	0.048
	Sevilla	0.053	0.025	0.078
	Thiva	0.039	0.017	0.056

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

Direct photolysis in air ‡	Not studied - no data requested
Photochemical oxidative degradation in air ‡	DT_{50} of GA_4 1.67 hours derived by the Atkinson model DT50 of GA_7 0.99 hours derived by the Atkinson model
Volatilisation ‡	Not studied - no data requested
	Not studied - no data requested

PEC (air)

Method of calculation	Expert judgement, based on vapour pressure, dimensionless Henry's Law Constant and information on volatilisation from plants and soil.

$PEC_{(a)}$

Maximum concentration	negligible

Residues requiring further assessment

Environmental occurring residues requiring further assessment by other disciplines (toxicology and ecotoxicology) and or requiring consideration for groundwater exposure.	Soil: GA_4/GA_7 Surface Water: GA_4/GA_7 Sediment: GA_4/GA_7 Groundwater:GA_4/GA_7 Air: GA_4/GA_7

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

Soil (indicate location and type of study)	No data provided – not requested
Surface water (indicate location and type of study)	No data provided – not requested
Ground water (indicate location and type of study)	No data provided – not requested
Air (indicate location and type of study)	No data provided – not requested

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

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Ecotoxicology

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)
Birds ‡				
Bobwhite quail	Gibberellic acid (GA_3)	Acute	LD_{50} >2250 mg/kg bw	-
	Preparation	Acute	Not required	-
	Metabolite 1	Acute	Not required	-
Bobwhite quail	Gibberellic acid (GA_3)	Short-term	LD_{50} >1376	LC_{50} >5620
	a.s.	Long-term	No data available	No data available
Mammals ‡				
Rat	Gibberellins (GA_4/GA_7)	Acute	LD_{50}>5000 mg/kg bw	-
	Preparation	Acute	Not required	-
	Metabolite 1	Acute	Not required	-
Rat	Gibberellins (GA_4/GA_7)	Long-term	NOAEL = 300	
Additional higher tier studies ‡				
not required				

[1] NOAEL based on parental toxicity (F0) in female rats in a multi-generation study.

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)
Orchards (4 applications of 20 g a.s./ha with a 7 day interval between applications)

Indicator species/Category	Time scale	ETE (mg a.s./kg bw/day)	TER	Annex VI Trigger
Tier 1 (Birds)				
Insectivorous bird	Acute	1.08	>2080[1]	10
Insectivorous bird	Short-term	0.60	>2281[1]	10
Insectivorous bird	Long-term	-	-[2]	5
Higher tier refinement (Birds)				
	Acute		Not required	10
	Short-term		Not required	10
	Long-term		Not required	5
Tier 1 (Mammals)				
	Acute	7.1	>704	10
	Long-term	2.5	122	5
Higher tier refinement (Mammals)				
	Acute		Not required	10
	Long-term		Not required	5

[1] For the representative use of GA4/GA7 a risk assessment using data for gibberellic acid (GA3) was considered to be reasonable given the high margin of safety in the TERs and evidence from additional information.
[2] TER was not calculated but a low reproductive risk to birds was concluded on the basis of weight-of-evidence.

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 (mg a.s./L)
Laboratory tests				
Fish				
Oncorhynchus mykiss	Gibberellins (GA_4/GA_7)	96 h (semi-static)	Mortality, LC_{50}	100 (~~mm~~ nom)
Oncorhynchus mykiss	Gibberellic acid (GA_3)	96 h (static)	Mortality, LC_{50}	120 (~~mm~~ nom)
Oncorhynchus mykiss	Gibberellic acid (GA_3)	96 h	Mortality, LC_{50}	>150
Oncorhynchus mykiss	Formulation GA_4/GA_7 10g/l SL	96 h (semi-static)	Mortality, LC_{50}	>1.2998 (mm)
Aquatic invertebrate				
Daphnia magna	Gibberellins (GA_4/GA_7)	48 h (static)	Immobility, EC_{50}	>100 (~~mm~~ nom)
Daphnia magna	Gibberellic acid (GA_3)	48 h (static)	Immobility, EC_{50}	> 120 (~~mm~~ nom)
Daphnia magna	Gibberellic acid (GA_3)	48 h	Immobility, EC_{50}	>143
Daphnia magna	Formulation GA_4/GA_7 10g/l SL	48 h (semi-static)	Immobility, EC_{50}	>1.4162 (mm)
Algae				
Pseudokirchneriella subcapitata	Gibberellins (GA_4/GA_7)	96 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	>100 (nom) >100 (nom)
Pseudokirchneriella subcapitata	Gibberellic acid (GA_3)	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	>100 (nom) >100 (nom)
Pseudokirchneriella subcapitata	Formulation GA_4/GA_7 10g/l SL	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	>1.4647 (mm) >1.4647 (mm)
Microcosm or mesocosm tests				
Not required				

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

FOCUS Step1
Apple, 4 applications of 20 g a.s./ha each.

Test substance	Organism	Toxicity end point (mg a.s./l)	Time scale	PEC_{swi} (mg a.s./l)	TER	Annex VI Trigger
Formulation GA_4/GA_7 10g/l SL	Fish	> 1.2998	Acute	0.03443	>38	100

Test substance	Organism	Toxicity end point (mg a.s./l)	Time scale	PEC_{swi} (mg a.s./l)	TER	Annex VI Trigger
Formulation GA_4/GA_7 10g/l SL	Aquatic invertebrates	> 1.4162	Acute	0.03443	>41	100
Formulation GA_4/GA_7 10g/l SL	Algae	> 1.4647		0.03443	>43	10

FOCUS Step 2
Apple, 4 applications of 20 g a.s./ha each.

Test substance	N/S[1]	Organism	Toxicity end point (mg a.s./L)	Time scale	PEC_{swi} (mg a.s./L)	TER	Annex VI Trigger
Formulation GA_4/GA_7 10g/l SL	N	Fish	> 1.2998	Acute	0.00653	>199	100
Formulation GA_4/GA_7 10g/l SL	S	Fish	> 1.2998	Acute	0.00963	>135	100
Formulation GA_4/GA_7 10g/l SL	N	Aquatic invertebrates	> 1.4162	Acute	0.00653	>217	100
Formulation GA_4/GA_7 10g/l SL	S	Aquatic invertebrates	> 1.4162	Acute	0.00963	>147	100

[1] Northern or Southern Europe

Bioconcentration

	Active substance
$logP_{O/W}$ Gibberellins (GA_4/GA_7)	2.34, 2.25
Bioconcentration factor (BCF)	Not required
Annex VI Trigger for the bioconcentration factor	Not relevant
Clearance time (days) (CT_{50})	Not relevant
(CT_{90})	Not relevant
Level and nature of residues (%) in organisms after the 14 day depuration phase	Not relevant

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)
Gibberellins (GA_4/GA_7)	>87	>100
Gibberellic Acid (GA_3)[1]	-	>25
Preparation	Not required	Not required
Metabolite 1	Not required	Not required
Field or semi-field tests		
not required		

[1]Data for gibberellic acid used for supportive information

Hazard quotients for honey bees (Annex IIIA, point 10.4)
Crop and application rate
Orchards (4 applications of 20 g a.s./ha with a 7 day interval between applications)

Test substance	Route	Hazard quotient	Annex VI Trigger
Gibberellins (GA_4/GA_7)	Contact	<0.20	50
Gibberellins (GA_4/GA_7)	oral	<0.8	50
Preparation	Contact	Not required	50
Preparation	oral	Not required	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 a.s.//ha)
Typhlodromus pyri ‡	Gibberellins (GA_4/GA_7)	Mortality	>40
Aphidius rhopalosiphi ‡	Gibberellins (GA_4/GA_7)	Mortality	>40

Crop and application rate

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field	Trigger
Gibberellins (GA_4/GA_7)	*Typhlodromus pyri*	>40	<1.35	Not calculated[1]	2
Gibberellins (GA_4/GA_7)	*Aphidius rhopalosiphi*	>40	<1.35	Not calculated[1]	2

[1] The off-field risk to non-target arthropods is covered by the in-field hazard quotients being less than the trigger value.

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, substrate and duration	Dose (g/ha)	End point	% effect	Trigger value
Not required						50 %

Field or semi-field tests
Not required

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
Earthworms			
Eisenia fetida	Gibberellins (GA_4/GA_7)	Acute 14 days	LC_{50} >1,250 mg a.s./kg d.w.soil LC_{50CORR} >625 mg a.s./kg d.w.soil[1]
	a.s. ‡	Chronic 8 weeks	Not required
	Preparation	Acute	Not required
	Preparation	Chronic	Not required
	Metabolite 1	Acute	Not required
	Metabolite 1	Chronic	Not required

Test organism	Test substance	Time scale	End point
Other soil macro-organisms			
Soil mite	a.s. ‡		Not required
	Preparation		Not required
	Metabolite 1		Not required
Collembola			
	a.s. ‡	Chronic	Not required
	Preparation		Not required
	Metabolite 1		Not required
Soil micro-organisms			
Nitrogen mineralisation	Gibberellins (GA_4/GA_7)	28 days	Application of gibberellins (GA_4/GA_7) at a concentration of 0.013 mg/kg dry soil had no biologically significant effect on the transformation of organic nitrogen in either of two soils tested. Application at the higher concentration of 0.13 mg/kg dry soil suppressed the mineralisation and subsequent nitrification of organic nitrogen by the indigenous soil microflora in both soils. This effect was transient and the differences between these processes in the presence and absence of the test substance had diminished to less than 15% within 28 days. Gibberellins (GA_4/GA_7) caused no permanent effect on nitrogen transformation processes in soils at the concentrations applied.
	Metabolite 1		Not required

Test organism	Test substance	Time scale	End point
Carbon mineralisation	Gibberellins (GA_4/GA_7)	28 days	Application of gibberellins (GA_4/GA_7) at concentrations of 0.013 and 0.13 mg/kg dry soil suppressed respiration by the indigenous soil microflora in one of the two soils tested. This effect was transient and the differences between respiration measured in the presence and absence of the test substance had diminished to less than 15% within 28 days. Gibberellins (GA_4/GA_7) caused no permanent effect on carbon oxidation processes in soils at the concentrations applied.
	Metabolite 1		Not required
Field studies			
Not required			

[1] In accordance with SANCO/10329/2002 rev 2 final, as the log P_{ow} > 2, the toxicity endpoint was divided by 2 to take account the different amount of organic carbon between laboratory and natural soils (corrected toxicity endpoint labelled as LC_{50CORR})

Toxicity/exposure ratios for soil organisms

Crop and application rate

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Earthworms					
	Gibberellins (GA_4/GA_7)	Acute	0.0424	>14741	10
	a.s. ‡	Chronic		Not required	5
	Preparation	Acute		Not required	10
	Preparation	Chronic		Not required	5
	Metabolite 1	Acute		Not required	10
	Metabolite 1	Chronic		Not required	5
Other soil macro-organisms					
Soil mite	a.s. ‡			Not required	
	Preparation			Not required	
	Metabolite 1			Not required	
Collembola	a.s. ‡			Not required	
	Preparation			Not required	
	Metabolite 1			Not required	

[1] Chronic risk to earthworms for the representative use of gibberellins was assessed as low on the basis that the estimated soil DT_{50} for gibberllins was 30 days.

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

Not required

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

Test type/organism	Activated sludge
Activated sludge	3h EC_{50}: > 100 mg GA_4/GA_7/l

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

Compartment	
soil	GA_4/GA_7
water	GA_4/GA_7
sediment	GA_4/GA_7
groundwater	GA_4/GA_7

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

	RMS/peer review proposal
Active substance	Hazard symbol: None. Indication of danger: None. Risk phrases: None. Safety phrases: None.

	RMS/peer review proposal
Preparation	Hazard symbol: None. Indication of danger: None. Risk phrases: None. Safety phrases: None.

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
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase (SGOT)
AV	avoidance factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstracts Service
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticides Analytical Council Limited
CL	confidence limits
cm	centimetre
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
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_{50}	emergence rate/effective rate, median
ErC_{50}	effective concentration (growth rate)
EU	European Union
EUROPOEM	European Predictive Operator Exposure Model
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
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)
GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathion
h	hour(s)
ha	hectare
Hb	haemoglobin
Hct	haematocrit
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography – mass spectrometry
HQ	hazard quotient
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	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
m	metre
M/L	mixing and loading
MAF	multiple application factor
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
mg	milligram
mL	millilitre
mm	millimetre
mN	milli-newton
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
MWHC	maximum water holding capacity
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
OECD	organisation for economic co-operation and development
OM	organic matter content
Pa	pascal
PD	proportion of different food types
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
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIE	potential inhalation exposure
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between *n*-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
REACH	registration, evaluation, authorisation and restriction of chemicals regulation
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
$t_{1/2}$	half-life (define method of estimation)
TER	toxicity exposure ratio
TER_A	toxicity exposure ratio for acute exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TK	technical concentrate
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDS	unscheduled DNA synthesis
UV	ultraviolet
W/S	water/sediment
w/v	weight per volume
w/w	weight per weight
WBC	white blood cell

WG	water dispersible granule
WHO	World Health Organisation
wk	week
yr	year