DETERMINATION ON WHETHER A SUBSTANCE IS A HAZARDOUS SUBSTANCE PURSUANT TO SECTION 26 OF THE HSNO ACT

25 August 2009

Application Code	HAZ09001
Application Type	To determine whether a substance is hazardous under Section 26 of the Hazardous Substances and New Organisms Act 1996 ("the Act").
Applicant	Orion Crop Protection Ltd
Date Application Received	22 May 2009
Consideration Date	6 August 2009
Considered by	A Committee of the Authority ("the Committee")
Purpose of the Application	To determine whether GIB 32SL is hazardous.

1 Application process

1.1 The Agency received an application requesting a formal determination on whether GIB 32SL, a formulation of gibberellic acid, is a hazardous substance under section 26 of the HSNO Act.

1.2 The application was formally received on 22 May 2009.

1.3 The evaluation of the application was undertaken by the ERMA New Zealand project team ("the Agency") which comprised the following staff members:

Jo Prankerd	Advisor (Hazardous Substances)
Cora Drijver	Advisor (Hazardous Substances)
Jim Waters	Senior Advisor (Hazardous Substances)

1.4 The report was reviewed and signed out by:

Lynne Waterson	Applications Manager (Hazardous Substances).

1.5 No external experts were used in the consideration of this application.

1.6 The following members of the Authority considered the application: Richard Woods (Chair) and Shaun Ogilvie.

1.7 The information available to the Committee comprised:

- the application; and
- this report including a confidential appendix.

2 Background to the application

Purpose of the application

2.1 To determine whether GIB 32SL is hazardous.

Identification of GIB 32SL and gibberellic acid (GA3)

2.2 The Hazardous Substances (Chemicals) Transfer Notice 2006 (Issue 72 of 28 June 2006) assigned two substances classifications as follows:

2.2.1 Gibberellic acid (>90% A3) {CAS 77-06-5}: 6.4A (eye irritant)

2.2.2 Gibberellic acid A4/A7 (45-70% A4 and 25- 55% A7) {No CAS}: 6.4A (eye irritant).

2.3 The first isomer is referred to as GA3 in this report. Where gibberellic acid is mentioned in this report, unless otherwise stated, GA3 is being referred too.

2.4 GIB 32SL is a formulation containing gibberellic acid in a non-hazardous solvent.

2.5 The structural formula of and general information on gibberellic acid can be found below in Table 2.1 and Figure 1.

Table 2.1: Identification of gibberellic acid (GA3).

	CAS number: 77-06-5
IUPAC name	3S,3aS,4S,4aS,7S,9aR,9bR,12S)-7,12-dihydroxy-3-methyl-6-methylene-2-oxoperhydro-4a,7-methano,9b,3-propenol(1,2-b)furan-4-carboxylic acid
Common name	Gibberellic acid (GA3)
Molecular formula	$C_{19}H_{22}0_6$
Molecular weight	346.37
Structural formula	A tetracyclic dihydroxylactonic acid. See figure 1
Purity	The application indicates 90% content of gibberellic acid (GA3)
Significant impurities/additives (% concentration)	ISO gibberellic acid GA3: 4% ISO gibberellic acid A3: 5% gibberellic acid GA8: 0.5% (Water: 0.5%)
Known uses	Plant growth regulator
HSNO classification	**6.4A, 9.1D**
Other classification & labelling	No information

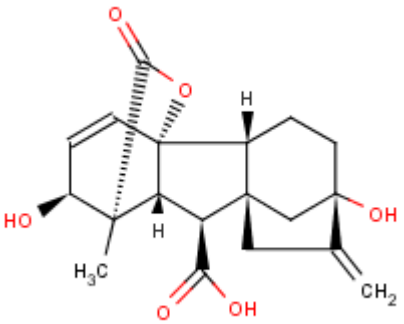

Figure 1: Structural formula of gibberellic acid.

3 Hazardous property assessment

Hazard classification

3.1 The Agency has classified component B (refer to Confidential Appendix 3), gibberellic acid and GIB 32SL as follows:

Table 3.1: Summary of the Agency's classifications of Component B

Hazardous Property	Component B
Explosiveness	No
Flammability	No
Oxidiser	ND#
Metal corrosive	ND#
Acute Oral Toxicity	No
Acute Dermal Toxicity	No
Acute Inhalation Toxicity	ND#
Skin Irritancy	No
Eye Irritancy	ND#
Respiratory Sensitisation	ND#
Contact Sensitisation	ND#
Mutagenicity	No
Carcinogenicity	No
Reproductive/developmental toxicity	No
Reproductive/developmental toxicity via lactation	ND#
Target Organ Toxicity	No
Aquatic ecotoxicity	No
Soil ecotoxicity	No
Terrestrial vertebrate ecotoxicity	No
Terrestrial invertebrate ecotoxicity	ND#

ND represents insufficient data or lack of data for this endpoint.

Table 3.2: Summary of the Agency's physical classifications of gibberellic acid and GIB 32SL

Hazardous Property	Gibberellic acid (GA3)	GIB 32SL
Explosiveness	No	No
Flammability	No	No
Oxidiser	No	No
Metal corrosive	ND	ND

Table 3.3: Summary of the Agency's toxicity classifications of gibberellic acid and GIB 32SL

Hazardous Property	Gibberellic acid (GA3)	GIB 32SL
Acute Oral Toxicity	No	No
Acute Dermal Toxicity	ND#	ND#
Acute Inhalation Toxicity	ND#	ND#
Skin Irritancy	No	No
Eye Irritancy	6.4A	No$
Respiratory Sensitisation	ND	ND
Contact Sensitisation	ND#	ND#
Mutagenicity	ND#	ND#
Carcinogenicity	ND#	ND#
Reproductive/developmental toxicity	ND#	ND#
Reproductive/developmental toxicity via lactation	ND#	ND#
Target Organ Toxicity	No	No

ND represents insufficient data or lack of data for this endpoint.

$ See comment in mixture rules for this endpoint (Confidential Appendix 3).

Table 3.4: Summary of the Agency's ecotoxicity classifications of gibberellic acid and GIB 32SL

Hazardous Property	Gibberellic acid (GA3)	GIB 32SL
Aquatic ecotoxicity	9.1D	No*
Soil ecotoxicity	ND#	ND#
Terrestrial vertebrate ecotoxicity	No	No
Terrestrial invertebrate ecotoxicity	No	No

ND represents insufficient data or lack of data for this endpoint.

* based on mixture rules

3.2 The information available to the Agency with respect to component B indicates that this component is non-hazardous. The Agency has located no information to indicate that this component is hazardous.

3.3 The classification of GIB 32SL was estimated using information on the effects of the components of GIB 32SL and mixture rules as formulation data were not provided for any endpoint. Further information on the classification of GIB 32SL can be found in Appendix 2.

3.4 A summary of the hazardous property assessment is provided below. Refer to Appendix 2 and Confidential Appendix 3 for further information.

Class 1: Substances with Explosive Properties

3.5 Both gibberellic acid and component B are not considered to be explosive. Therefore the Agency considers GIB 32SL will not trigger this endpoint.

Classes 2-4: Flammability

3.6 The Agency considers that GIB 32SL is not a flammable substance. Gibberellic acid does not meet the threshold for flammability and based on the low content of gibberellic acid in component B (a non-hazardous solvent) it is unlikely that GIB 32SL will be flammable. It is therefore considered that GIB 32SL does not trigger this endpoint.

Class 5: Oxidisers/Organic Peroxides

3.7 The Agency considers that GIB 32SL does not meet the HSNO criteria for an oxidiser or an organic peroxide. Gibberellic acid has no oxidising properties and based on its content in component B (a non-hazardous solvent) it is therefore considered that GIB 32SL does not trigger this endpoint.

Sub-class 8.1: Metal Corrosiveness

3.8 No information was located to indicate that gibberellic acid or component B would be corrosive to metals. In addition, due to the low concentration of gibberellic acid in GIB 32SL, the Agency considers it is unlikely this substance would meet the HSNO criteria for a metallic corrosive. It is therefore considered that GIB 32SL is unlikely to trigger this endpoint.

Class 6: Toxicity

Sub-class 6.1 – Acute toxicity

3.9 The Agency considers gibberellic acid not to exceed the threshold for acute oral toxicity based on the available information. Thus considering the low concentration of gibberellic acid in a non-hazardous solvent it is the opinion of the Agency that GIB 32SL will also not exceed the thresholds for acute oral toxicity.

3.10 The Agency considers there is insufficient information to classify gibberellic acid as an acute dermal toxicant. A single study on gibberellic acid was located; this study concluded gibberellic acid is relatively harmless in rats and mice when administered orally, parenterally, by inhalation or by topical application.

3.11 The Agency considers there is insufficient information to classify gibberellic acid as an acute inhalation toxicant. A single study on gibberellic acid was located; this study concluded that gibberellic acid is relatively harmless in rats

and mice when administered orally, parenterally, by inhalation or by topical application.

3.12 In summary, the Agency notes there is clear information (albeit of Klimisch Score 2 at best, refer to Appendix 2 for further information on this data reliability scoring system) to indicate gibberellic acid and thus the substance do not trigger for 6.1 (oral). While data on gibberellic acid are not sufficient to assign "no classification" for the dermal and inhalation routes, the Agency considers the substance is very unlikely to trigger by these routes. This assessment permits a reliable conclusion in respect to the mixture (GIB 32SL) due to the low concentration of this active ingredient in the formulation.

Sub-class 6.3 – Skin Irritation

3.13 The Agency considers gibberellic acid not to exceed the 6.3 threshold.

3.14 The Agency notes that that the formulation in the study identified in Appendix 2 contained less than 10% of the active ingredient and therefore it is not possible to use these data as a basis for classification of the pure substance. Nevertheless, the Agency considers the supporting data for a mixture of gibberellic isomers GA4 and GA7 (90%), for which the primary irritation index is reported as zero, can be read across to support "no classification" for 6.3 skin irritation for the GA3 gibberellic acid isomer.

3.15 As gibberellic acid is considered not to exceed the threshold for skin irritation it is reasonable to conclude that a low percentage of gibberellic acid in a non-hazardous solvent also will not exceed the 6.3 threshold. Thus it is the opinion of the Agency that GIB 32SL will not be a skin irritant.

Sub-class 6.4 – Eye Irritation

3.16 The Agency considers that gibberellic acid is correctly classified as a 6.4A substance.

3.17 The Agency notes that data are lacking for the pure material. However, the Agency has identified one study in which a formulation containing 7.5% active ingredient was used, caused eye irritation, and therefore considers it is reasonable to assume a higher percentage of active ingredient would be an eye irritant (at least). If it was only the active ingredient which is an eye irritant, this may suggest it is corrosive in pure form. In another study assumed to be with the pure material, the substance is reported to cause "moderate to severe conjunctival irritation"; this supports the classification as an eye irritant, rather than an eye corrosive.

3.18 Based on the relevant mixture rules and the composition of GIB 32SL, the Agency considers GIB 32SL does not trigger the classification as an eye irritant or corrosive (refer to Confidential Appendix 3 for further information on the classification of GIB 32SL).

Sub-class 6.5 – Respiratory (6.5A) and Contact (6.5B) Sensitisation

3.19 No information was located to indicate that gibberellic acid or component B would be respiratory sensitisers (6.5A). It is therefore considered there is no information to classify GIB 32SL for respiratory sensitisation.

3.20 With respect to contact sensitisation (6.5B), the Agency notes that a negative finding was found for gibberellic acid as a 10% formulation. However, this is not suitable information to form a basis for classification of the pure active ingredient.

3.21 The Agency therefore considers there is insufficient data to classify GIB 32SL for contact sensitisation.

Sub-class 6.6 – Mutagenicity

3.22 The Agency notes that the results for gibberellic acid (GA3 and GA4/GA7 mixtures) are negative with the possible exception of tests for clastogenicity in human lymphocytes and Chinese hamster cells. The Agency notes that, although one study indicates a possible positive response, the detail provided in the study, including dose levels, is inappropriate.

3.23 The Agency also notes there appear to be no *in vivo* data available for any gibberellins.

3.24 Overall, the information available does not provide sufficient evidence to support a mutagenicity classification for gibberellic acid. Therefore considering the low concentration of gibberellic acid in a non-hazardous solvent the Agency concludes there are insufficient data to assign a classification to GIB 32SL as well.

Sub-class 6.7 – Carcinogenicity

3.25 The Agency notes two carcinogenicity studies on gibberellic acid were located. However due to an insufficient level of detail, including a lack of information on study design, justification for species, route and dosing regime and a lack of information on appropriate background data, neither study was considered of adequate reliability to assign a carcinogenicity classification. The Agency therefore considers that insufficient information is available to assign gibberellic acid a 6.7 classification.

3.26 Thus based on component data and mixture rules there is insufficient information to assign a carcinogenicity classification to GIB 32SL.

Sub-class 6.8 – Reproductive/Developmental Toxicity

3.27 The developmental studies identified support the view that gibberellic acid is unlikely to be a developmental toxicant.

3.28 With respect to reproductive toxicity via lactation, the Agency considers the data are insufficient.

3.29 Overall, the Agency considers there is insufficient information to support a developmental/reproductive classification conclusion for gibberellic acid.

3.30 Thus there is insufficient information to assign developmental or reproductive classifications to GIB 32SL.

Sub-class 6.9 – Target Organ Toxicity

3.31 The Agency notes that the repeat dose studies carried out on gibberellic acid, most notably the 13 week study in rats for which sufficient information is available, indicate that the LOAEL (Lowest Observable Adverse Effect Level) value is above the threshold for classification for target organ systemic toxicity.

3.32 The Agency therefore considers that gibberellic acid does not trigger the threshold for target organ toxicity and therefore it is concluded that the information available supports a "no classification" conclusion.

3.33 Considering the low concentration of gibberellic acid in a non-hazardous solvent the Agency considers that target organ toxicity classification will not be triggered for GIB 32SL either.

Summary of the Class 6 Toxicity classifications of GIB 32SL

3.34 As reported in Table 3.3, the Agency considers gibberellic acid to be an eye irritant and is assigned a 6.4A classification. Based on component data, GIB 32SL does not trigger the classification as an eye irritant.

3.35 The Agency considers the available information indicates gibberellic acid is not classified as an acute oral toxicant, a skin irritant, or a target organ toxicant. Based on component data and mixture rules, GIB 32SL does not trigger these classifications either.

3.36 With respect to the remainder of the class 6 hazard classifications, the Agency notes there is insufficient data or a lack of data to classify gibberellic acid for these endpoints.

3.37 In summary, based on component information and mixture rules GIB 32SL is not expected to exceed any of the Class 6 toxicity hazard thresholds.

Class 9: Ecotoxicity and environmental fate

Sub-class 9.1 – Aquatic ecotoxicity, fate and degradation

3.38 The Agency considered the acute and chronic aquatic toxicity of gibberellic acid and it's bioaccumulative and persistence properties when classifying it under this sub-class (refer to Appendix 2 for further information).

3.39 With respect to the aquatic fate and degradation of gibberellic acid, the Agency considers gibberellic acid is not bioaccumulative based on the log Kow and is considered to be rapidly degradable. Based on component data and mixture rules, the Agency expects GIB 32SL not to be bioaccumlative and rapidly degradable.

3.40 With respect to the aquatic toxicity of gibberellic acid, gibberellic acid is classified as 9.1D due to its toxicity to algae, lack of bioaccumulation and rapid degradability. However based on component data and mixture rules, the Agency considers that GIB 32SL will not trigger any 9.1 classification.

Sub-class 9.2 – Soil ecotoxicity and terrestrial fate

3.41 With respect to terrestrial fate and degradation, based on the data (summarised in Table A2.8), gibberellic acid is considered to meet the HSNO criteria for degradability in the soil in less than 30 days.

3.42 A summary of the information available on the toxicity of gibberellic acid to soil dwelling macro-organisms, soil microbial function and terrestrial plants is provided in Table A2.9.

3.43 Based on the lack of data, the Agency is not able to classify gibberellic acid or GIB 32SL as being ecotoxic in the soil environment.

Sub-class 9.3 – Terrestrial vertebrate ecotoxicity

3.44 The Agency notes the mammalian toxicity of gibberellic acid has been addressed under sub-class 6. Table A2.10 in Appendix 2 summarises the key endpoints for both mammalian and avian toxicity.

3.45 Based on the information shown in this table, the Agency considers gibberellic acid and thus GIB 32SL does not exceed the threshold for toxicity to terrestrial vertebrates.

Sub-class 9.4 – Terrestrial invertebrate ecotoxicity

3.46 The Agency considers that based on the information that is provided in Table A2.11, gibberellic acid and thus GIB 32SL does not exceed the threshold for toxicity to terrestrial invertebrates.

Summary of the Class 9 Ecotoxicity classifications of GIB 32SL

3.47 The Agency considers gibberellic acid triggers the classification as an aquatic ecotoxicant. However, there is insufficient information in order to classify gibberellic acid as a soil ecotoxicant.

3.48 With respect to both the terrestrial vertebrate and terrestrial invertebrate ecotoxicity of gibberellic acid, the Agency considers the information supports a "no classification" conclusion for gibberellic acid.

3.49 The Agency has used component data and the mixture rules to determine that GIB 32SL does not exceed the threshold for aquatic ecotoxicity.

Recommended Determination

If the Authority is of the view that GIB 32SL is not hazardous under the HSNO Act, then the Authority may:

a) determine that GIB 32SL as defined is not hazardous pursuant to section 26 of the HSNO Act 1996; and

b) direct the Chief Executive to arrange for notice of this determination to be placed in the Gazette.

Lynne Waterson, Applications Manager, Hazardous Substances Group

Date:

Determination by the Authority

The recommended determination is approved.

Richard Woods

Chair

Date: 25 August 2009

APPENDIX 1: REFERENCES

ERMA New Zealand (2008a). User Guide to HSNO Thresholds and Classifications. ERMA New Zealand, Wellington.

European Union (2006). Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC. http://reach.jrc.it/

EU (2008). DAR Gibberellic acid

Klimisch, HJ, Andreae, E, Tillman, U (1997). A systematic approach for evaluating the quality of experimental and ecotoxicological data. *Regulatory Toxicology and Pharmacology* 25: 1–5.

OECD (1990). Manual for Investigation of HPV Chemicals. http://www.oecd.org/document/21/0,3343,en_2649_34379_1939669_1_1_1_1,00.html Retrieved 23 January 2008.

HSDB Hazardous Substances Data Bank (USA): http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~a7FMjT:1 (Record for gibberellic acid, CAS 77-06-5)

APPENDIX 2: HAZARD CLASSIFICATION

Classification of GIB 32SL

Formulation data were not provided for any endpoint for GIB 32SL so classification was estimated using information on the effects of the components and mixture rules. Details of the components and the methods used to derive the classifications are presented in Table A2.1. The relevant sections of the User Guide to Thresholds and Classifications under the HSNO Act (ERMA 2008a) that describe the mixture rules are listed in Table A2.2.

The Agency has provided a summary of the toxicity, ecotoxicity and environmental fate data in Tables A2.5 to A2.12.

Data quality – overall evaluation

The Agency has adopted the Klimisch et al (1997) data reliability scoring system for evaluating data used in the hazard classification and risk assessment of chemicals (section 1.2.4 in ERMA 2008a). The data used by The Agency to classify GIB 32SL are predominantly the classifications which have been officially gazetted during the transfer process and are publicly available through the HSNO Chemical Classification Information Database (CCID) (ERMA 2008b). The Agency also searched and found information to fill the existing data gaps as much as possible and to update the existing information.

Table A2.0: Physical and chemical properties of GIB 32SL.

Test	GIB 32SL	Method	Reference
Appearance	Amber translucent liquid	No information	Application
Odour	No information	-	-
Density at 20°C	1.046 g/ml at 20°C	No information	Application
Surface tension	No information	-	-
pH	7.0 (1% v/v)	No information	Application
Dynamic viscosity	No information	-	-
Flash point	No information	-	-
Auto flammability	No information	-	-
Explosive properties	No information	-	-

Table A2.1: Summary of the toxicity and ecotoxicity hazard classifications of GIB 32SL

Hazardous Property	Agency's Classification	Classification Method	Component(s) driving classification
6.1 oral	None	Mixture rules	None
6.1 dermal	None	Mixture rules	None
6.1 inhalation	None	Mixture rules	None
6.3/8.2 Skin irritation/corrosion	None	Mixture rules	None
6.4/8.2 Eye irritation/corrosion	None	Mixture rules, and "expert judgment" (see comment in appendix)	None
6.5 Respiratory sensitization	None	Mixture rules	None
6.5 Contact	None	Mixture rules	None

Hazardous Property	Agency's Classification	Classification Method	Component(s) driving classification
sensitisation			
6.6 Mutagenicity	None	Mixture rules	None
6.7 Carcinogenicity	None	Mixture rules	None
6.8 Reproductive developmental toxicity	None	Mixture rules	None
6.9 Target organ systemic toxicity	None	Mixture rules	None
9.1 Aquatic ecotoxicity	None	Mixture rules	None
Aquatic Persistence	None	Mixture rules	None
Bioaccumulative	None	Mixture rules	None
9.2 Soil ecotoxicity	ND	NA	NA
Soil Persistence	None	Mixture rules	None
9.3 Terrestrial vertebrate ecotoxicity	None	NA	No components trigger this classification
9.4 Terrestrial invertebrate ecotoxicity	None	NA	No components trigger this classification

ND= no data,
NA= not applicable

Table A2.2: Location of mixture rules within the HSNO Thresholds and Classifications User Guide (V2.0. March 2008).

Hazard	User Guide to HSNO Thresholds and Classifications Reference
Subclass 6.1 Acute Toxicity	Part V, Chapter 10, Page 12
Subclass 6.3/8.2 Skin Irritancy/Corrosivity	Part V, Chapter 11, Page 7
Subclass 6.4/8.3 Eye Irritancy/Corrosivity	Part V, Chapter 12, Page 9
Subclass 6.5 Contact and Respiratory Sensitisation	Part V, Chapter 13, Page 8
Subclass 6.6 Mutagenicity	Part V, Chapter 14, Page 5
Subclass 6.7 Carcinogenicity	Part V, Chapter 15, Page 8
Subclass 6.8 Reproductive Developmental Toxicity	Part V, Chapter 16, Page 11
Subclass 6.9 Target Organ Systemic Toxicity	Part V, Chapter 17, Page 10
Subclass 9.1 Aquatic Ecotoxicity	Part VI, Chapter 19, Page 18
Subclass 9.2 Soil Ecotoxicity	Part VI, Chapter 20, Page 8
Subclass 9.3 Terrestrial Vertebrate Ecotoxicity	Part VI, Chapter 21, Page 7
Subclass 9.4 Terrestrial Invertebrate Ecotoxicity	Part VI, Chapter 22, Page 5

Identity of the Active Ingredient

General data about gibberellic acid are provided in the Tables A2.3 and A2.4.

Table A2.3: Identification of gibberellic acid (GA3).

	CAS number: 77-06-5
IUPAC name	3S,3aS,4S,4aS,7S,9aR,9bR,12S)-7,12-dihydroxy-3-methyl-6-methylene-2-oxoperhydro-4a,7-methano,9b,3-propenol(1,2-b)furan-4-carboxylic acid
Common name	Gibberellic acid (GA3)
Molecular formula	$C_{19}H_{22}0_6$
Molecular weight	346.37
Structural formula	A tetracyclic dihydroxylactonic acid. See figure 1

Purity	The application indicates 90% content of gibberellic acid (GA3)
Significant impurities/additives (% concentration)	ISO gibberellic acid GA3: 4% ISO gibberellic acid A3: 5% gibberellic acid GA8: 0.5% (Water: 0.5%)
Known uses	Plant growth regulator
HSNO classification	**6.4A, 9.1D**
Other classification & labelling	No information

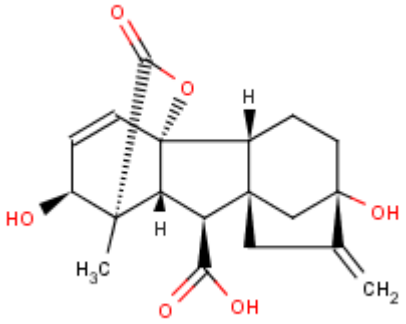

Figure 1: Structural formula of gibberellic acid.

Physical and chemical properties of gibberellic acid relevant to the interpretation of ecotoxicity test, environmental fate and exposure assessment are summarised in Table A2.4.

Table A2.4: Physical and chemical properties of gibberellic acid (GA3)

Property	Result	Test method	Reference
Colour	ND		
Physical state	ND		
Odour	ND		
Vapour pressure	2.1×10^{-13} mm Hg at 25°C. (Equivalent to 2.8×10^{-11} Pa.)	No information	HSDB
Henry's Law constant	7.5×10^{-7} Pa m^3 /mol at 25°C	calculated	EU assessment 2008
Melting range	233 – 235°C	No information	ERMA internal database
Relative Density	0.6 g/ml at 20°C.	No information	HSDB
Water Solubility	5000 mg/L	No information	ERMA internal database
Solvent Solubility (20°C)	At 20 °C (98%) n-hexane < 0.01 g/L toluene < 0.01 g/L dichloromethane 0.032 g/L methanol 273 g/L acetone 30.8 g/L ethyl acetate 3.1 g/L	No information	EU assessment 2008
pH	4	No information	ERMA internal database
Log Kow	log Kow = 0.24	No information	Hansch, C., Leo, A., D. Hoekman.

			Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society., 1995
Flammability	GA_3 is not highly flammable		EU assessment 2008
Autoflammability	The compound is not auto-flammable		EU assessment 2008
Explosive properties	GA_3 is not considered as explosive		EU assessment 2008
Surface Tension	ND		
Oxidizing properties	GA_3 has no oxidizing properties		EU assessment 2008

ND= no data

Biological Hazards: Class 6 Toxicity

Table A2.5: Summary of toxicity data on gibberellic acid (GA3).

ACUTE TOXICITY
Acute oral toxicity
SPECIES: Mice STRAIN: No information TEST SUBSTANCE: acid DOSE LEVELS: 25 g/kg bw NO/SEX/GROUP: No information ENDPOINT: Lethality REMARKS: No deaths observed in mice given single oral doses of 25 g/kg. VALUE: >25,000 mg/kg bw GLP: No informaton TEST GUIDELINES: No information REFERENCE SOURCE: Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984., p. II-351 cited in HSDB, USA. RELIABILITY (KLIMISCH SCORE): 2
SPECIES: Rats/Mice STRAIN: No information TEST SUBSTANCE: acid DOSE LEVELS: No information NO/SEX/GROUP: No information ENDPOINT: Lethality and signs of toxicity. REMARKS: In rats & mice it is relatively harmless when admin orally, parenterally, by inhalation, or by topical application. VALUE: No information GLP: No information TEST GUIDELINES: No information REFERENCE SOURCE: Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984., p. II-351 cited in HSDB, USA. RELIABILITY (KLIMISCH SCORE): 2
Oral: Human Exposure

If gibberellic acid has been swallowed there is no reason to expect adverse effects.

REFERENCE SOURCE: U.S. Environmental Protection Agency/Office of Prevention, Pesticides, and Toxic Substances. Reigart, J.R., Roberts, J.R. Recognition and Management of Pesticide Poisonings. 5th ed. 1999. EPA Document No. EPA 735-R-98-003, and available in electronic format at: http://www.epa.gov/pesticides/safety/healthcare p. 65] cited in HSDB, USA.
RELIABILITY (KLIMISCH SCORE): 2

Conclusion on classification: No classification for 6.1 (oral)

Acute dermal toxicity

SPECIES: Rats/Mice
STRAIN: No information
TEST SUBSTANCE: acid
DOSE LEVELS: No information
NO/SEX/GROUP: No information
ENDPOINT: Lethality and signs of toxicity.
REMARKS: In rats & mice it is relatively harmless when admin orally, parenterally, by inhalation, or by topical application.
VALUE: No information
GLP: No information
TEST GUIDELINES: No information
REFERENCE SOURCE: Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984., p. II-351 cited in HSDB, USA.
RELIABILITY (KLIMISCH SCORE): 2

Conclusion on classification: Insufficient information

Acute inhalation toxicity

SPECIES: Rats/Mice
STRAIN: No information
TEST SUBSTANCE: acid
DOSE LEVELS: No information
NO/SEX/GROUP: No information
ENDPOINT: Lethality
REMARKS: In rats & mice it is relatively harmless when admin orally, parenterally, by inhalation, or by topical application.
VALUE: No information
GLP: No information
TEST GUIDELINES: No information
REFERENCE SOURCE: Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984., p. II-351 cited in HSDB, USA.
RELIABILITY (KLIMISCH SCORE): 2

Conclusion on classification: Insufficient information

The Agency notes that there is clear information (albeit of Klimisch Score 2 at best) to indicate the substance does not trigger for 6.1 (oral). While data are not sufficient to assign "no classification" for the dermal and inhalation routes, the substance is very unlikely to trigger by these routes. This conclusion permits a reliable conclusion in respect to the mixture (GIB 32SL) due to the low concentration of this active ingredient in the formulation.

IRRITATION

Eye irritation

SPECIES: Unknown
STRAIN: Unknown
TEST SUBSTANCE: Formulation containing 7.5% gibberellic acid (GA3)
REMARKS:

Report 1: Eye irritation clearing in 7 days or less. AI 7.5% Tox category III (MRID 41591106) [USEPA RED 1995]

Report 2: Moderate to severe conjunctival irritation, reversible in 7 days, was found in eye irritation test in rabbits with gibberellic acid. http://www.horizononline.com/MSDS_Sheets/353.txt [MSDS]

GLP: No information
TEST GUIDELINES: No information
REFERENCE SOURCE:
1. USEPA RED 1995
2. http://www.horizononline.com/MSDS_Sheets/353.txt [MSDS]
RELIABILITY (KLIMISCH SCORE):

The Agency notes that data are lacking for the pure material. Since one study a formulation containing 7.5% active ingredient caused eye irritation, it is reasonable to assume higher % of active ingredient would be an eye irritant (at least). If it was only the active ingredient which is an eye irritant, this may suggest it is corrosive in pure form. In the other study assumed to be with the pure material the substance is reported to cause "moderate to severe conjunctival irritation" this supports classification as an eye irritant, not an eye corrosive.

Conclusion on classification: 6.4A.

Skin irritation

SPECIES: Rabbit
STRAIN: No information
TEST SUBSTANCE: Formulation containing 7.5% gibberellic acid (GA3)
REMARKS: Mild or slight irritant. AI 7.5% Tox category IV (MRID 41591107)
GLP: No information
TEST GUIDELINES: No information
REFERENCE SOURCE: US EPA RED 1995
RELIABILITY (KLIMISCH SCORE): 4

SPECIES: Rabbit
STRAIN: No information
TEST SUBSTANCE: Formulation containing GA4 and GA7 (90%) [Note this is a different GA isomer].
REMARKS: Primary Irritation Score (PIS) is 0.
GLP: No information
TEST GUIDELINES: No information
REFERENCE SOURCE: US EPA RED 1995
RELIABILITY (KLIMISCH SCORE): 2

Agency conclusion
The Agency notes that since the formulation contained less than 10% of the active ingredient it is not possible to use these data as a basis for classification of the pure substance. Nevertheless, the Agency considers the supporting data for a mixture of GA4 and GA7 (90%) for which the primary irritation index is reported as zero can be read across to support *no classification* for 6.3 skin irritation for GA3.

Conclusion on classification: No classification.

SENSITISATION

Respiratory sensitisation	**Contact sensitization**
No information available.	SPECIES: No information STRAIN: No information NO./SEX/GROUP: No information TEST SUBSTANCE: Formulation containing 10% gibberellic acid REMARKS: Not a contact dermal sensitizer. Tox category IV (MRID 41560406)

	GLP: No information TEST GUIDELINES: No information REFERENCE SOURCE: USEPA RED 1995 RELIABILITY (KLIMISCH SCORE): 4 The Agency notes that since negative finding was for the substance as a 10% formulation this is not suitable information to from a basis for classification of the pure active ingredient.
Conclusion on classification: No information	***Conclusion on classification: Insufficient data.***
MUTAGENICITY	
***In vitro* studies**	
STUDY TYPE: Bacteria CELL TYPE: *Salmonella typhimurium* strains (TA 98, TA 100, TA 1535, and TA 1537) in the presence and absence of Aroclor-induced rat or hamster liver S-9. TEST SUBSTANCE: acid DOSE RATE: 0, 100, 333, 1000, 3333, and 10,000 µg/plate in the presence and absence of Aroclor-induced rat or hamster liver S-9. RESPONSE: Negative. GLP: No information TEST GUIDELINE: No guideline (but NTP protocol) REFERENCE SOURCE: Zeiger E et al; Environ Mutagen 9:1-110 (1987) RELIABILITY (KLIMISCH SCORE): 2	
STUDY TYPE: Bacteria CELL TYPE: *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537, and TA 1538 TEST SUBSTANCE: acid (GA3) DOSE RATE: 0 to 10,000 µg/plate with negative test results up to limit dose of 5,000 and 10,000 ug/plate. RESPONSE: Negative GLP: No information TEST GUIDELINE: No information REFERENCE SOURCE: USEPA/Office of Pesticide Programs; Reregistration Eligibility Decision Document - Acid. EPA 738-R-96-005 December 1995. RELIABILITY (KLIMISCH SCORE): 2	
STUDY TYPE: Mammalian CELL TYPE: Human lymphocytes TEST SUBSTANCE: acid DOSE RATE: No information RESPONSE: A 2-3 fold increase of the chromosome aberrations was induced irrespective of the time of 3-aminobenzamide addition to the cultures (the 28th, 46th, 72th hr of the cultivation) GLP: No information TEST GUIDELINE: No information REFERENCE SOURCE: Zalinyan GG et al; Tsitol Genet 24 (3): 31-4 (1990) RELIABILITY (KLIMISCH SCORE): 4 [The Agency notes that although this study indicates a possible positive response, the detail provided in the study, including dose levels, is inadequate. (See Cal EPA reports for clastogenicity below.]	
STUDY TYPE: Mammalian CELL TYPE: Mouse lymphoma L5178Y cells TEST SUBSTANCE: acid (technical, 91%) DOSE RATE: 0 (DMSO; dimethyl sulfoxide), 300, 600, 1250, 2500, 3750 or 5000 ug/mL for 3 hr in the absence and presence Aroclor 1254 male rat liver S-9 preparation. RESPONSE: There was little cytotoxicity up to and including 5000 ug/mL. There was no increase in mutation frequency with treatment under the conditions of the test. No adverse effect.	

GLP: No information
TEST GUIDELINE: No information
REFERENCE SOURCE: California Environmental Protection Agency/Department of Pesticide Regulation; Toxicology Data Review Summaries. Available from: http://www.cdpr.ca.gov/docs/toxsums/toxsumlist.htm on Gibberellins as of January 26, 2006.
RELIABILITY (KLIMISCH SCORE): 2

STUDY TYPE: Clastogenicity in human lymphocytes (*in vitro*)
CELL TYPE: Human lymphocytes
TEST SUBSTANCE: acid technical.
DOSE RATE: 9.8 – 5000 µg/mL
RESPONSE: Positive (Possible adverse effect) at 2500 µg/mL without activation and at 4500 µg/mL with S9 activation
GLP: No information
TEST GUIDELINE: No information
REFERENCE SOURCE: Cal EPA summary.
http://www.cdpr.ca.gov/docs/risk/toxsums/pdfs/310.pdf
RELIABILITY (KLIMISCH SCORE): 4

[The Agency notes that due to the incompleteness of the report the Cal EPA did not consider this study was able to be validated. "Unacceptable, possibly upgradeable with submission of the data from the other trial or an explanation why the data were not included. (Gee, 12/16/97)]

The Agency notes that the Cal EPA accepted a chromosomal aberration study in Chinese hamster ovary cells for GA4/GA7,which also gave a "Possible adverse effect":

STUDY TYPE: Clastogenicity in Chinese hamster ovary (CHO) cells (*in vitro*)
CELL TYPE: CHO cells
TEST SUBSTANCE: GA4/GA7
DOSE RATE: 0 (ethanol), 262, 655, 1310, 1970 or 2620 µg/mL
REMARKS: In one assay, treatment with the test material was for only 6 hours with continued incubation and harvest at 24 hours. With activation, harvest times were 12, 24 or 48 hours in two separate trials. Positive controls were mitomycin C without activation and cyclophosphamide with activation. Concentrations were 0 (ethanol), 262, 655, 1310, 1970 or 2620 µg/ml. Cytotoxicity was seen at 1970 and 2620 µg/ml in terms of cell debris, percent of confluency and mitotic index.

Chromosomal aberrations were increased in percentage at 1970 and 2620 µg/ml at 24 hours (2 assays), at 1970 µg/ml at 48 hours but not at 2620 µg/ml when CHO were treated for 6 hours followed by incubation until the 24-hour harvest.

Results with activated cultures were negative at all concentrations tested in one assay but positive in a second assay at 2620 µg/ml with a suggestion of a concentration-related increase at lower concentrations. Because of the lack of reproducibility with S9 activation, the results for a positive effect are less clear.

RESPONSE: Possible adverse effect: A reproducible increase in chromosomal aberrations was found without activation at concentrations with cytotoxicity.
GLP: No information
TEST GUIDELINE: No information
REFERENCE SOURCE: Cal EPA summary. [H. Murli, Hazleton Washington, 15393-0-437Z, August 17, 1994] http://www.cdpr.ca.gov/docs/risk/toxsums/pdfs/310.pdf
RELIABILITY (KLIMISCH SCORE): 2

STUDY TYPE: Unscheduled DNA synthesis in the rat.
CELL TYPE: Primary hepatocytes
TEST SUBSTANCE: acid (GA3), 90%
DOSE RATE: 0 (ethanol), 50, 100, 250, 500, 602, 1000 or 1260 µg/ml for 18 hours.

RESPONSE: Negative. The study was evaluated as unacceptable but upgradeable with submission of more detailed results of the net nuclear grain counts. (Gee, 12/17/97).
Record 166958 contained the response consisting of 2 pages of the results for each of the three slides per concentration with the relevant data. With this submission, the study was upgraded to acceptable status with no evidence for the induction of unscheduled DNA synthesis under the conditions of the study. (Gee, 7/21/99)

GLP: No information
TEST GUIDELINE: No information
REFERENCE SOURCE: Cal EPA summary. [M. A. Cifone, Hazleton Biotechnologies, No. 20991, May, 1986, amended July, 1986; response dated 1/22/99] http://www.cdpr.ca.gov/docs/risk/toxsums/pdfs/310.pdf
RELIABILITY (KLIMISCH SCORE): 2

STUDY TYPE: Unscheduled DNA synthesis in the rat.
CELL TYPE: Primary hepatocytes
TEST SUBSTANCE: acid (GA4/GA7)
DOSE RATE: 0.5 to 1500 µg/ml for 18-20 hours.

RESPONSE: No evidence for the induction of UDS was found. Acceptable.

GLP: No information
TEST GUIDELINE: No information
REFERENCE SOURCE: Cal EPA summary. [R. D. Curren, Microbiological Associates, T8201.380009, October 21] http://www.cdpr.ca.gov/docs/risk/toxsums/pdfs/310.pdf
RELIABILITY (KLIMISCH SCORE): 2

***In vivo* studies**

No data for *in vivo* studies for any gibberellins were identified.

Agency conclusion

The Agency notes that the results for gibberellic acid (GA3 and GA4/GA7 mixtures) are negative with the possible exception of tests for clastogenicity in human lymphocytes and Chinese hamster cells. The study in human lymphocytes was not upgraded by the Cal EPA.

Overall, the database does not provide sufficient evidence to support classification. The Agency notes there appear to be no *in vivo* data available for any GA isomers.

Conclusion on classification: Insufficient data to assign a classification.

CARCINOGENICITY

TYPE OF STUDY: Carcinogenicity in mice
SPECIES: Mice
STRAIN: Swiss
NO.ANIMALS/SEX/GROUP: No information.
TEST SUBSTANCE: acid (GA3)
DOSE LEVELS: 0, 3ppm in 0.3 ml saline, twice per week for 22 months. [There appears to have been only one treatment group. The dose would be very low, if the substance was administered only twice weekly at 3ppm in 0.3ml per dose. This represents approximately 0.9 µg/dose (0.0009 mg). For an adult mouse weighing 20g this represents a dose that day of 0.045 mg/kg bw. The daily dose is actually lower than this.]
ROUTE: Oral gavage
GLP: No information
TEST GUIDELINES: No information
REMARKS: No details

a. Non-neoplastic effects
LOAEL: No information

NOAEL: No information

b. Neoplastic effects

Males
LOAEL: Approximately 0.02 mg/kg bw/day
NOAEL: No information

TUMOURS: Sebaceous gland adenoma, and lung (tumour type not given)
MALIGNANT/ BENIGN: Benign [?]
BACKGROUND INCIDENCE: No information
TIME OF ONSET: No information
SURVIVAL: No information
DOSE/ RESPONSE: No information (only one dose)

Females
LOAEL: Approximately 0.02 mg/kg bw/day
NOAEL: No information

TUMOURS: Sebaceous gland adenoma, breast: adenocarcinoma.
MALIGNANT/ BENIGN: Benign (sebaceous gland), Malignant (breast) [?]
BACKGROUND INCIDENCE: No information
TIME OF ONSET: No information
SURVIVAL: No information
DOSE/ RESPONSE: No information (only one dose)

REFERENCE SOURCE: EL-MOFTY,MM, SAKR,SA, RIZK,AM AND MOUSSA,EA; CARCINOGENIC EFFECT OF GIBBERELLIN A3 IN SWISS ALBINO MICE; NUTR. CANCER 21(2):183-190, 1994 [HSDB]
RELIABILITY (KLIMISCH SCORE): 3

[The Agency considered that insufficient information is available for this to form that basis of a classification. The Agency also noted that the dose level is extremely low and only one treatment group appears to have been used.]

TYPE OF STUDY: Mice
SPECIES: Mice
STRAIN: No information
NO.ANIMALS/SEX/GROUP: No information
TEST SUBSTANCE: acid (GA3)
DOSE LEVELS: 160-464 mg/kg bw/day
ROUTE: Oral
GLP: No information
TEST GUIDELINES: No information
REMARKS: [CCRIS] GIBBERELLIC ACID WAS FOUND NOT TO BE TUMORIGENIC IN MICE ORALLY ADMIN AT 160-464 MG/KG/DAY. /FROM TABLE

a. Non-neoplastic effects
LOAEL: No information
NOAEL: No information

b. Neoplastic effects
LOAEL: N/A
NOAEL: N/A

TUMOURS: None reported.

MALIGNANT/ BENIGN: N/A
BACKGROUND INCIDENCE: N/A
TIME OF ONSET: N/A
SURVIVAL: N/A
DOSE/ RESPONSE: N/A

REFERENCE SOURCE: Hayes, W. J., Jr. Toxicology of Pesticides Baltimore: Williams & Wilkins, 1975. 191 [HSDB]
RELIABILITY (KLIMISCH SCORE): 4

TYPE OF STUDY:
SPECIES: Egyptian toad
STRAIN: No information
NO.ANIMALS/SEX/GROUP: 50

TEST SUBSTANCE:
DOSE LEVELS: 10 ppm twice weekly for 5 months (a single dose group). [There is no reference to a control group.]
ROUTE: Oral (gavage [?])
GLP: N/A
TEST GUIDELINES: N/A
REMARKS: Force feeding the Egyptian toads (Bufo regularis) with gibberellin A3 (10 ppm) twice a wk for 5 mo induced neoplasms in 8 out of 50 (16%) experimental animals. Primary tumors developed in the liver (hepatocellular carcinomas). Two secondary tumors in the kidneys and another 2 in the ovaries of toads developed due to metastases from the hepatocellular carcinomas. The results show that gibberellin A3 has a carcinogenic effect in the Egyptian toads.

a. Non-neoplastic effects
LOAEL: No information
NOAEL: No information

b. Neoplastic effects
LOAEL: 10 ppm (the dose is unclear)
NOAEL: No information

TUMOURS: Heptaocellular carcinomas (with two secondary tumours in kidneys and ovaries.
MALIGNANT/ BENIGN: Malignant
BACKGROUND INCIDENCE: No information
TIME OF ONSET: No information
SURVIVAL: No information
DOSE/ RESPONSE: No information

REFERENCE SOURCE: el-Mofty MM, Sakr SA; Oncology 45 (1): 61-4 (1988) [HSDB]
RELIABILITY (KLIMISCH SCORE): 4

There is one study in mice with positive findings in male and female mice, but insufficient information on this study is available for a thorough evaluation, even the dose level unclear. There is also one positive finding reported in the Egyptian toad, but this in not an appropriate study for an evaluation of carcinogenicity.

Conclusion on classification: Insufficient data

REPRODUCTIVE/DEVELOPMENTAL TOXICITY

Developmental studies

STUDY TYPE: Developmental study in rats
SPECIES: Rats
STRAIN: Crl: CD (SD) BR

NO/GROUP: 24
DOSE: 0, 10, 100, 1000 mg/kg bw/day (by gavage) on days 6 – 15 of gestation.
TEST SUBSTANCE: acid (GA3, 93.4%) in hydroxypropylmethyl cellulose at 0.2%. Dose volumes were 10 ml/kg.
TEST METHOD: No information
REMARKS: No treatment-related deaths occurred. Approximately half of the fetuses were given visceral examinations and half, skeletal exams. There was no effect on body weight or food consumption with treatment. No developmental toxicity was reported.

DEVELOPMENTAL STUDIES

MATERNAL TOXICITY
NOAEL: 1000 mg/kg bw
LOAEL > 1000 mg/kg bw

FOETAL TOXICITY
NOAEL: 1000 mg/kg bw
LOAEL: > 1000 mg/kg bw (no adverse effects reported).

REFERENCE SOURCE: California Environmental Protection Agency/Department of Pesticide Regulation; Toxicology Data Review Summaries. Available from: http://www.cdpr.ca.gov/docs/toxsums/toxsumlist.htm on Gibberellins as of January 26, 2006.
RELIABILITY (KLIMISCH SCORE): 2

STUDY TYPE: Developmental study in rabbits
SPECIES: Rabbits
STRAIN:
NO/GROUP: 24
DOSE: 0, 100, 300, 1000 mg/kg bw/day (by gavage) on days 6 – 15 of gestation, by gavage.
TEST SUBSTANCE: acid (GA4+GA7)
TEST METHOD: No information
REMARKS: The highest concentration caused increased mortality, abortion rates, clinical signs of toxicity and gross pathological observations. The maternal and developmental NOELs were established at 300 mg/kg/day.

DEVELOPMENTAL STUDIES

MATERNAL TOXICITY
NOAEL: 100 mg/kg bw
LOAEL 300 mg/kg bw based on mortality clinical signs of toxicity and gross pathological findings.

FOETAL TOXICITY
NOAEL: 100 mg/kg bw
LOAEL: 300 mg/kg bw (adverse effects reported was increase abortion rates).

REFERENCE SOURCE: USEPA/Office of Pesticide Programs; Reregistration Eligibility Decision Document - Acid. EPA 738-R-96-005 December 1995. Available from, as of January 26, 2006:
RELIABILITY (KLIMISCH SCORE): 2

STUDY TYPE: Developmental study in rats
SPECIES: Rats
STRAIN: No information
NO/GROUP: No information
DOSE: 0, 100, 1000 mg/kg bw/day for 8 weeks.
TEST SUBSTANCE: acid (GA3)
TEST METHOD: No information
REMARKS: Treatment was without significant clinical, hematological or pathologic evidence of

toxicity. The maternal toxicity NOEL was greater than 1000 mg/kg/day.

DEVELOPMENTAL STUDIES

MATERNAL TOXICITY
NOAEL: 1000 mg/kg bw (claimed that the NOEL was . 1000 mg/kg bw)
LOAEL > 1000 mg/kg bw

FOETAL TOXICITY:

NOAEL: 1000 mg/kg bw
LOAEL: > 1000 mg/kg bw (no adverse effects reported).

REFERENCE SOURCE: MRID 40155201. US EPA RED 1995

RELIABILITY (KLIMISCH SCORE): 2

Reproductive studies

STUDY TYPE: Reproductive toxicity in mice
SPECIES: Mice
STRAIN: No information
NO/SEX/GROUP: No information
DOSE: No information
TEST METHOD: No information
TEST SUBSTANCE: acid (GA3)
REMARKS: The treatment of GA3 on mice caused an increase in the ratio of male offspring in the F1 population, and the total protein amount of liver tissue was significantly decreased compared with the control mice. GA3-2 treatment significantly increased erythrocyte counts. GA3 exposure caused a significant decrease in the mean body weight of male offspring of the F1 generation compared with the control group animals.

REPRODUCTIVE TOXICITY STUDIES

PARENTAL TOXICITY
NOAEL: No dose information given
LOAEL: No dose information given

REPRODUCTIVE EFFECTS
NOAEL: No dose information given
LOAEL: No dose information given
DEVELOPMENTAL TOXICITY
NOAEL: No dose information given
LOAEL: No dose information given

REFERENCE SOURCE: Ozmen M et al; Turk J Biol 19 (4): 357-64 (1995)
RELIABILITY (KLIMISCH SCORE): 4

The Agency notes the data support the view that GA3 is unlikely to be a developmental toxicant, but the data are insufficient data for reproductive toxicity.

Conclusion on classification: Insufficient information

TARGET ORGAN SYSTEMIC TOXICITY

Subchronic toxicity – oral

TYPE OF STUDY: 13 week toxicity study in rats
SPECIES: Rats
STRAIN: No information.

NO.ANIMALS/SEX/GROUP:
TEST SUBSTANCE: acid (GA3) 88.5% purity.
DOSE LEVELS: 0, 1000, 10,000 and 50,000 ppm in diet. (There was an additional 4 week recover period for a group on control and top dose animals.) The dose levels for the treated groups were equivalent to 53-117, 550-1178, or 2994-5786 mg/kg/day (males) and 67-130, 730-1283, or 3872-6241 mg/kg/day (females) respectively.
ROUTE: Oral in diet.
GLP:
TEST GUIDELINES:
REMARKS: The only treatment-related clinical sign of toxicity was a low incidence of soft stools in both sexes receiving the highest dose. Very slightly decreased body weight gains were observed in mid-dose males and high dose animals of both sexes. Slightly increased total food consumption in all treated groups were observed.

Evidence suggestive of a compound-related effect on kidney function included significantly increased blood urea nitrogen levels (BUN) and increased relative kidney weights in female rats in the high-dose group. BUN levels and kidney weights were comparable to controls at the end of a 4-week recovery period, indicating reversibility of renal effects.

Other effects observed in high-dose males included decreased globulin levels at termination of the study and decreased glucose levels (p</= 0.05) at the end of the 4-week recovery period. Increased relative liver weights were observed in males at 50,000 ppm and in females at 10,000 ppm and 50,000 ppm. At the end of the recovery period, increased relative liver weight were still evident in females (11%), but not in males. In the absence of clinical chemistry correlates and gross and microscopic hepatic abnormalities, the liver weight changes are considered compensatory rather than a toxic effect of the test material. Under the conditions of this study, the NOEL is 10,000 ppm; the LOEL is 50,000 ppm, based on the occurrence of soft stools in both sexes, and increased BUN levels, liver and kidney weights in females.

LOAEL: 50,000 ppm (equivalent to 3000- 5800 mg/kg bw/day in males and 3800 – 6200 mg/kg bw/day in females)
NOAEL: 10,000 ppm (equivalent to 550- 1200 mg/kg bw/day in males and 730 – 1300 mg/kg bw/day in females)

REFERENCE SOURCE: USEPA/Office of Pesticide Programs; Reregistration Eligibility Decision Document - Gibberellic Acid. EPA 738-R-96-005 December 1995. Available from, as of January 26, 2006:
RELIABILITY (KLIMISCH SCORE): 2

TYPE OF STUDY: 13 week toxicity study in deer mice
SPECIES: Deer mice
STRAIN: Deer mice
NO.ANIMALS/SEX/GROUP: "Appropriate" [No information]
TEST SUBSTANCE: acid (GA3) 88.5% purity.
DOSE LEVELS: 0, 1000, 10,000 and 50,000 ppm in diet. (There was an additional 4 week recover period for a group on control and top dose animals.) The dose levels for the treated groups were equivalent to 53-117, 550-1178, or 2994-5786 mg/kg/day (males) and 67-130, 730-1283, or 3872-6241 mg/kg/day (females) respectively.
ROUTE: Oral in diet.
GLP:
TEST GUIDELINES:
REMARKS: Outbred deer mice were exposed to the plant growth regulators at appropriate concentrations orally. Mice were challenged by a test dose of Pichinde virus and Modoc virus. Persistence of both viruses in mouse tissues was determined by explanting lung, liver, spleen, kidney, and salivary glands from all mice at 63 to 65 days after inoculation. Virus in blood, brain, and other organs was assayed by a cytochemical method. Immunotoxicity was measured. Age and sex of mice

profoundly influenced many immune parameters. Old male and female mice were significantly heavier, and had significantly lighter thymuses, lower hemolysin titers, and fewer plaque forming cells. Mean number of circulating white blood cells was significantly greater in old mice than in young females. Plant growth stimulators significantly decreased body wt of old females but did not affect young females or old males. Gibberellic acid lengthened the duration of the virus induced viremia. Pichinde virus infection triggered antibody response in the presence of gibberellic acid. It was concluded that gibberellic acid affects the immune function of deer mice, but the effect is dependent on age and sex.

LOAEL: No dose information provided. The report claims an effect on immune response based on challenge testing.
NOAEL: No dose information provided.

REFERENCE SOURCE: Fairbrother A et al; Arch Environ Contam Toxicol 15 (3): 265-75 (1986)
RELIABILITY (KLIMISCH SCORE): 4

Chronic toxicity/carcinogenicity;

See studies above.

The Agency notes that the repeat dose studies carried out, most notably the 13 week study in rats for which sufficient information is available, indicate that the LOAEL value is above the threshold for classification for target organ systemic toxicity.

Conclusion on classification: No classification.

Class 9 Ecotoxicity and environmental fate

Sub-class 9.1 Aquatic ecotoxicity, fate and degradation

The Agency considered the acute and chronic aquatic toxicity of gibberellic acid its bioaccumulative and persistence properties when classifying it under this sub-class.

Aquatic fate and degradation of gibberellic acid and its metabolites
Information on aquatic fate and degradation is summarised in Table A2.6.

Table A2.6: Summary of aquatic fate and degradation of gibberellic acid

Study type	Test results		Test method [reference]
	gibberellic acid	Metabolites	
Abiotic degradation			
Hydrolysis	At 30 oC pH 4: DT_{50} = 9 d pH 7: DT_{50} = 6.8 d pH 9: DT_{50} = 1.9 d		EU assessment, 2008
	Gibberellic acid slowly undergoes hydrolysis in aqueous or aqueous-alcoholic solutions. In alkalis, undergoes a rearrangement to less biologically-active compounds.		Hartley, D. and H. Kidd (eds.). The Agrochemicals Handbook. 2nd ed. Lechworth, Herts, England: The Royal Society of Chemistry, 1987
Photolysis	pH 5: DT_{50} = 10.4 d pH 7.51: DT_{50} = 11.3 d		EU assessment, 2008
Biodegradation (laboratory)			
ND			
Dissipation (field)			
ND			
Bioaccumulative			
Log Kow < 4 therefore the Agency assumes no bioaccumulation			

ND= No data provided

Conclusion
Gibberellic acid is not considered bioaccumulative based on the log Kow and is considered rapidly degradable.

Aquatic toxicity
The toxicity of gibberellic acid to aquatic organisms is summarised in Table A2.7.

Table A2.7: Summary of aquatic toxicity data for Gibberellic acid

Test species	Test type & duration	Test results	Test method [reference]
		Active	
Fish			
Rainbow trout, *Oncorhynchus mykiss*	96 h static	LC_{50}> 112 mg a.i./L	EU assessment, 2008
Cyprinus carpio	96 h semi static	LC_{50}> 100 mg a.i./L	EU assessment, 2008
Invertebrates			
Dapnia magna	48 h static	EC_{50} = 76 mg a.i./L	EU assessment, 2008
Algae/ Aquatic plants			
Pseudokirchneriella subcapitata	72 h static	E_bC_{50} = 17 mg a.i./L (biomass) E_rC_{50} = 25 mg a.i./L (growth)	EU assessment, 2008

Conclusion
Gibberellic acid is classified as 9.1 D due to its toxicity to algae, lack of bioaccumulation and rapid degradability.

Sub-class 9.2 Soil ecotoxicity and terrestrial fate

Classification under this sub-class requires consideration of the persistence of the components of the GIB 32SL in soil, and the toxicity of the GIB 32SL to soil-dwelling invertebrates (e.g. earthworm), soil microbial function and terrestrial plants resulting from soil based exposure.

Data on the adsorption, mobility and field dissipation of the active ingredient is used in the ecological risk assessment for the substance. Refer to Appendix 3.

Terrestrial fate and degradation of gibberellic acid
Information of terrestrial fate and degradation is summarised in Table A2.8.

Table A2.8: Terrestrial fate and degradation of gibberellic acid.

Test type	Test results		Test method [reference]
	Active		
Abiotic degradation	ND		
Biodegradation (Laboratory)	At 20°C Clay soil (OC% 1.4, pH 5.9): DT_{50} =4.25 d Loam soil (OC% 4.79, pH 7.01): DT_{50} =5 d		EU assessment, 2008
Soil accumulation	ND		
Adsorption/desorption	soil	Koc	EU assessment, 2008

	Sandy loam (OC% 1, pH 4.5)	3.92	
	Sandy clay loam (OC% 5.9, pH 7.4)	0.875	
	Silt loam (OC% 6.6, pH 7.0)	1.13	
	Volcanic ash (OC% 3.2, pH 5.4)	29.7	
Mobility/Leaching	ND		

ND= No data provided

Conclusion

Based on these data gibberellic acid is considered to meet the HSNO criteria for degradability in soil <30 days.

Soil toxicity

A summary of the toxicity of gibberellic acid to soil dwelling macro-organisms, soil microbial function and terrestrial plants is provided in Table A2.9.

Table A2.9: Summary of terrestrial toxicity data for gibberellic acid

Test species	**Test type & duration**	**Test results** **Active**	**Test method [reference]**
Soil-dwelling invertebrates			
ND			
Terrestrial plants			
ND			
Soil microbial function			
Nitrogen mineralisation		Applications of GA_3 at concentrations of up to 100 ppm did not influence the content of soil nitrogen substantially.	EU assessment, 2008
Carbon mineralisation		Applications of GA_3 at concentrations of up to 100 ppm lead to significant increases in soil organic carbon content. This did not affect the carbon mineralisation processes in soil.	EU assessment, 2008

ND= No data provided

Conclusion

Due to a lack of data the Agency was not able to classify gibberellic acid.

Sub-class 9.3 Terrestrial vertebrate ecotoxicity

The mammalian toxicity of gibberellic acid has been addressed under sub-class 6. Key endpoints for both mammalian and avian toxicity are summarized in Table A2.10.

Table A2.10: Summary of terrestrial vertebrate toxicity data for gibberellic acid

Test species	Test type & duration	Test results		Test method [reference]
		Active	Metabolites	
Mammals				
Rat	Acute tox	LD_{50} > 5000 mg/kg bw/day		EU assessment, 2008
Mice	Acute tox	LD_{50} > 25,000 mg/kg bw		Gosselin, RE, Smith RP, Hodge HC. Clinical Toxicology of commercial products. 5th ed. Baltimore: Williams and Wilkins, 1984, p.II-351 cited in HSDB, USA
Birds				
Mallard duck	Acute tox	LD_{50} = 2250 mg/kg bw/day		EU assessment, 2008

Conclusion

Based on the information (Table A2.10), gibberellic acid does not trigger the threshold for toxicity to terrestrial vertebrates.

Sub-class 9.4 Terrestrial invertebrate ecotoxicity

A summary of the data on the toxicity of gibberellic acid to honeybees and other non-target terrestrial invertebrates is provided in Table A2.11.

Table A2.11: Summary of terrestrial invertebrate toxicity data for gibberellic acid

Test species	Test type & duration	Test results		Test method [Reference]
		Active	Metabolites	
Honey bee	Acute oral	ND		
Honey bee	Acute contact	LD_{50} > 25 µg/bee		EU assessment, 2008

ND= No data provided

Conclusion

Based on the information (Table A2.11), gibberellic acid does not trigger the threshold for toxicity to terrestrial invertebrates.

Table A2.12: Summary of ecotoxicity classifications for gibberellic acid and GIB 32SL

Sub-class	gibberellic acid	GIB 32SL
9.1 Aquatic ecotoxicity	**9.1D**	**No***
9.2 Soil ecotoxicity	**ND**	**ND**
9.3 Terrestrial vertebrate ecotoxicity	**no**	**no**
9.4 Terrestrial invertebrate ecotoxicity	**no**	**no**

*based on mixture rules
ND= No data