Environmental Protection Authority
Te Mana Rauhī Taiao

DRAFT SCIENCE MEMO

APP203925 – SOLETO

Substance database ID 50010

DECEMBER/ 2020

Standard terms and abbreviations

Abbreviation	Definition
ai	active ingredient
ADE	Acceptable Daily Exposure
ADI	Acceptable Daily Intake
AOEL	Acceptable Operator Exposure Level
BBA	Biologishe Bundersantalt für Land- und Forstwirtschaft
BBCH	Biologische **B**undesanstalt, **B**undessortenamt und **CH**emische Industrie
BCF	BioConcentration Factor
Bw	body weight
CAS #	Chemical Abstract Service Registry Number
cm	centimetres
CoA	Certificate of Analysis
CRfD	Chronic Reference Dose
DDD	Daily Dietary Dose
DT_{50}	Dissipation Time (days) for 50% of the initial residue to be lost
dw	dry weight
E_bC_{50}	EC_{50} with respect to a reduction of biomass
E_yC_{50}	EC_{50} with respect to a reduction of yield (y)
EC	European Commission
EC_{25}	Effective Concentration at which an observable adverse effect is caused in 25 % of the test organisms
EC_{50}	Effective Concentration at which an observable adverse effect is caused in 50 % of the test organisms
EEC	Estimated Environmental Concentration
EEL	Environmental Exposure Limit
EFSA	European Food Safety Authority
E_rC_{50}	EC50 with respect to a reduction of growth rate (r)
ER_{50}	Effective Residue concentration to 50% of test organisms
FAO	Food and Agriculture Organization
g	grams

Abbreviation	Definition
GAP	Good Agricultural Practice
GENEEC	Generic Estimated Environmental Concentration
ha	hectare
HQ	Hazard Quotient
Kd	partition (distribution) coefficient
K_{oc}	organic carbon adsorption coefficient
K_{ow}	octanol water partition coefficient
Kg	Kilogram
L	litres
Lb	pounds
LC_{50}	Lethal Concentration that causes 50% mortality
LD_{50}	Lethal Dose that causes 50% mortality
LOAEC	Lowest Observable Adverse Effect Concentration
LOAEL	Lowest Observable Adverse Effect Level
LOC	Level Of Concern
LOD	Limit Of Detection
LOEC	Lowest Observable Effect Concentration
LOEL	Lowest Observable Effect Level
LR_{50}	Lethal Rate that causes 50% mortality
M	Molar
m^3	cubic metre
MAF	Multiple Application Factor
µm	micrometre (micron)
mg	milligram
µg	microgram
mol	mole(s)
MSDS	Material Safety Data Sheet
NAEL	No Adverse Effect Level
ng	nanogram
NOAEC	No Observed Adverse Effect Concentration

Abbreviation	Definition
NOAEL	No Observed Adverse Effect Level
NOEC	No Observed Effect Concentration
NOED	No Observed Effect Dose
NOEL	No Observed Effect Level
NOER	No Observed Effect Rate
OECD	Organisation for Economic Cooperation and Development
OPPTS	Office of Prevention, Pesticides, and Toxic Substances (US Environmental Protection Agency)
PDE	Potential Daily Exposure
PEC	Predicted Environmental Concentration
PHI	Pre-Harvest Interval
pK_a	Acid dissociation constant (base 10 logarithmic scale)
PNEC	Predicted No Effect Concentration
P_{ow}	Partition coefficient between n-octanol and water
ppb	parts per billion (10^{-9})
PPE	Personal Protective Equipment
ppm	parts per million (10^{-6})
REI	Restricted Entry Interval
RPE	Respiratory Protective Equipment
RQ	Risk Quotient

Executive Summary

The applicant Belchim Crop Protection NV/SA has submitted an application on 18 September 2019 to import or manufacture SOLETO for release. It was given Application Number APP203925 and was formally received on 13 March 2020 as notified Cat C application.

SOLETO contains the active ingredient (ai) metobromuron at 500 g/L, plus other components.

Metobromuron is not approved in Australia, Canada, Japan and the United States. It is approved in Europe.

Metobromuron is of relatively low acute toxicity in mammals and should be classified 6.1E by oral route only. It is not a skin or eye irritant, but is a contact sensitiser and is classified as 6.5B. Metobromuron was found not to be genotoxic, but should be classified as a suspected human carcinogen (6.7B). It does not cause reproductive or developmental toxicity. Results of repeated dose oral toxicity studies in laboratory animals indicate it should be classified for systemic organ toxicity (6.9B).

Metobromuron is also very ecotoxic to the aquatic environment, soil organisms and slightly toxic to terrestrial vertebrates (9.1A, 9.2A and 9.3C), it is however, not toxic to terrestrial invertebrates. .

Mammalian toxicity studies with SOLETO demonstrated it has relatively low acute toxicity in mammals and should be classified 6.1E for acute toxicity by the oral exposure route. It is not a skin or eye irritant, or a contact sensitiser. Based on mixture rules it should be classified for suspected human carcinogenicity (6.7B) and target organ systemic toxicity (6.9B, oral). Based on test data for the formulation, SOLETO should be classified 9.1A. Based on mixture rules and formulation data, SOLETO should also be classified 9.1A and 9.2A, but does not require classification as toxic to terrestrial vertebrates or invertebrates.

Metobromuron is not considered bioaccumulative based on the Log K_{ow} of 2.48 at pH 7.3. No whole fish bioconcentration study was performed.

It is considered that there is potential for significant exposure to people and the environment during the use phase of the lifecycle of SOLETO. As such, quantitative risk assessments have been undertaken to understand the likely exposures to the substance under the use conditions proposed by the applicant, using the endpoint data available and the standard risk assessment methodologies used by the EPA.

It is considered that the risks to human health from the proposed use of SOLETO are acceptable with the use of appropriate Personal Protective Equipment (PPE). No Restricted Entry Intervals (REI) or buffer zones are recommended. The expected concentration in groundwater is well below the level of concern in relation to human drinking water consumption..

It is considered that the risks to the environment from the proposed use of SOLETO are below the level of concern with the proposed controls based on the available data for all areas except for non-target soil macro-organisms (mites, collembola) for which a risk above the level of concern was identified.

A set of controls have been proposed for SOLETO, and are detailed under section 6.

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1. Introduction/Background

1.1. This application is to import or manufacture SOLETO for release.

1.2. SOLETO is intended to be used as a broad spectrum herbicide for potatoes.

1.3. SOLETO contains the active ingredient metobromuron at 500 g/L, plus other components.

1.4. Metobromuron is not approved in Australia, Canada, Japan and the United States. It is approved in Europe.

1.5. More details about the use pattern of SOLETO and the regulatory status of metobromuron can be found in Appendix A.

1.6. It is considered that there is potential for significant exposure to people and the environment during the use phase of the lifecycle of SOLETO. As such, quantitative risk assessments have been undertaken to understand the likely exposures to the substance under the use conditions proposed by the applicant, using the endpoint data available and the standard risk assessment methodologies used by the EPA. Full context related to the risk assessment of SOLETO is given in section 3.

1.7. The applicant has confirmed they have access to the studies conducted with metobromuron and SOLETO. The original study reports have been provided.

1.8. Unless otherwise stated, all endpoint data summarised were fully compliant with the relevant international test methods. For full details of testing undertaken, reference should be made to the relevant sections of the overseas review.

1.9. Physical and Chemical properties of SOLETO can be found in Appendix B.

1.10. Mammalian toxicological properties of SOLETO and metobromuron have been reported in Appendix C.

1.11. Environmental Fate properties of metobromuron have been reported in Appendix D.

1.12. Ecotoxicological properties of SOLETO and metobromuron have been reported in Appendix E.

1.13. Hazard properties and classification determination of SOLETO and metobromuron derived from their properties can be found under 2.Hazardous properties and Appendix F.

1.14. Mammalian toxicological data have subsequently been used to generate human health risk assessment and this is detailed in Appendix G.

1.15. Environmental Fate, Ecotoxicological and other relevant data have subsequently been used to generate environmental risk assessment and this is detailed in Appendix H.

1.16. Relevant study summaries can be found in Appendix J.

2. Hazardous properties

Hazard classification of metobromuron

2.1. The hazard classifications proposed for metobromuron are outlined in Table 1. Full details are provided in Table 27.

Table 1: Proposed classification for metobromuron

Hazard endpoint	EPA Classification
Acute oral toxicity	6.1E
Contact sensitisation	6.5B
Carcinogenicity	6.7B
Target organ systemic toxicity (oral)	6.9B
Aquatic ecotoxicity	9.1A
Soil ecotoxicity	9.2A
Terrestrial vertebrate ecotoxicity	9.3C

2.2. Metobromuron is of relatively low acute toxicity in mammals and should be classified 6.1E by oral route only. It is not a skin or eye irritant, but is a contact sensitiser and is classified as 6.5B. Metobromuron was found not to be genotoxic, but should be classified as a suspected human carcinogen (6.7B). It does not cause reproductive or developmental toxicity. Results of repeated dose oral toxicity studies in laboratory animals indicate it should be classified for systemic organ toxicity (6.9B).

2.3. Metobromuron is also very ecotoxic to the aquatic environment, soil organisms and slightly toxic to terrestrial vertebrates (9.1A, 9.2A and 9.3C), it is however, not toxic to terrestrial invertebrates.

Hazard classification of SOLETO

2.4. The hazard classifications of SOLETO determined by the EPA are given in Table 2. The hazard classifications of SOLETO were determined based on the information provided by the applicant (including toxicity and ecotoxicity studies), information on the individual components of SOLETO, mixture rules and other available information (EC 2012). Table 28 in Appendix F shows the method used for classification and indicates the main component that contributes to each hazard classification.

Table 2: Hazard classification of SOLETO

Hazard	EPA classification
Acute toxicity (oral)	6.1E
Carcinogenicity	6.7B
Target organ or systemic (oral)	6.9B
Aquatic ecotoxicity	9.1A
Soil ecotoxicity	9.2A

Mammalian toxicity studies with SOLETO demonstrated it has relatively low acute toxicity in mammals and should be classified 6.1E for acute toxicity by the oral exposure route. It is not a skin or eye irritant, or a contact sensitiser. Based on mixture rules it should be classified for suspected human carcinogenicity (6.7B) and target organ systemic toxicity (6.9B, oral). Based on test data for the formulation, SOLETO should be classified 9.1A. Based on mixture rules and formulation data, SOLETO should also be classified 9.1A and 9.2A, but does not require classification as toxic to terrestrial vertebrates or invertebrates.

3. Risk assessment context

3.1. It is considered that there is potential for significant exposure to people and the environment during the use phase of the lifecycle of SOLETO. As such, quantitative risk assessments have been undertaken to understand the likely exposures to the substance under the use conditions proposed by the applicant, using the endpoint data available and the standard risk assessment methodologies used by the EPA (EPA 2020).

3.2. During the importation, manufacture, transportation, storage and disposal of this substance, it is estimated that the proposed controls and other legislative requirements will sufficiently mitigate risks to a negligible level. This assessment takes into account the existing EPA Notices around packaging, identification and disposal of hazardous substances. In addition, the Land Transport Rule 45001, Civil Aviation Act 1990, Maritime Transport Act 1994 and New Zealand's Health and Safety at Work (HSW) requirements all have provisions for the safe management of hazardous substances.

4. Human health risk assessment

4.1. The risks from the use of metobromuron are considered as a proxy for the risks of SOLETO on users and operators of the substance, re-entry workers and bystanders. In addition an assessment of human consumption of ground water was undertaken. Full details can be found in Appendix G: Human health risk assessment

4.2. **Operator Exposure:**

Predicted operator exposures to metobromuron are below the Acceptable Operator Exposure Level

(AOEL), provided full PPE (gloves, hood/visor, coveralls, and heavy boots without a respirator) is worn during mixing, loading, and application. Therefore operator exposures are not expected to result in adverse health effects, if PPE is worn.

4.3. **Worker Re-Entry:**

Worker re-entry was not quantitatively assessed as there are no models to assess worker re-entry following the application of a pre-emergent crop herbicide. As there would be minimal need for worker re-entry following use of SOLETO a qualitative assessment was performed. Any re-entry to a field after application would not be associated with significant dermal contact to the sprayed weeds. Predicted exposures to metobromuron for workers re-entering and working in areas where SOLETO has been applied would qualitatively be deemed to be below the AOEL. No re-entry intervals are necessary.

4.4. **Bystanders:**

Estimated bystander exposure from spray drift after application of SOLETO to weeds associated with pre-emergent potatoes is below the AOEL. No buffer zone of is required in protect bystanders.

4.5. **Impurities:**

No impurity limits for metobromuron have been identified by the EU (EC 2012).

4.6. **Overall human health conclusion:**

It is considered that the risks to human health from the proposed use of SOLETO are acceptable with the use of appropriate Personal Protective Equipment (PPE). No Restricted Entry Intervals (REI) or buffer zones are recommended. The expected concentration in groundwater is well below the level of concern in relation to human drinking water consumption.

5. Environmental risk assessment

5.1. The risks to a range of environmental receptors from the use of metobromuron are considered as a proxy for the risks from SOLETO. Full details can be found in Appendix H: Environmental risk assessment

5.2. **Aquatic environment:**

Predicted exposure concentrations, using GENEEC2, of metobromuron, applied as the formulated product SOLETO to potatoes resulted in calculated risk quotients above the level of concern (LOC) for non-threatened and threatened species of fish, aquatic invertebrates, algae and aquatic plants.

5.3. **Groundwater:**

Using the Sci-Grow screening model the predicted concentration in groundwater for metobromuron is above the 0.1 µg/L trigger level set by the European regulators. Groundwater assessments conducted for the same metobromuron use pattern overseas did not identify the same risk to groundwater using their methodology, indicating in this case that the groundwater concentration predicted by Sci-Grow is overly conservative. A human health risk assessment has however been conducted (see Appendix G)

and showed that the risks associated with the drinking of groundwater at the concentrations calculated are well below the level of concern.

5.4. **Sediment:**

No data on toxicity of metobromuron to sediment-dwelling organisms have been provided by the applicant. Metobromuron was observed to partition into the sediment, reaching a maximum of 28.7% AR, however a daphnid reproduction study is available with a chronic endpoint >0.1 mg a.i./L (NOEC of 10 mg a.i./L). Therefore a risk assessment on sediment-dwelling organisms is not required (EFSA 2013). In addition, it was concluded that the proposed controls based on the aquatic risk assessment will provide a level of protection to sediment dwelling organisms. The proposed controls are based on the *Lemna gibba* endpoint which is 32 times lower than the chronic daphnid endpoint.

5.5. **Soil organisms:**

Acute and chronic risks to earthworms following the application of the formulated product SOLETO to potatoes are considered below the level of concern.

Chronic risks were identified as above the level of concern for non-threatened and threatened species of soil mites and collembola for applications to potatoes.

For soil microorganisms risks are below the level of concern for potatoes.

5.6. **Non-target Plants:**

Risk Quotients to non-target plants calculated for metobromuron when applied to pre-emergent potatoes as the formulated product SOLETO are above the level of concern. This is expected as the product is a herbicide. A buffer zone of 10 m increased the TER for non-threatened species resulting in a risk below the LOC. A buffer zone of 50 m was needed to increase the TER for threatened species resulting in a risk below the LOC.

Additional controls have been suggested to address the identified risks.

5.7. **Birds:**

The PT values obtained are thought to be overestimations for pre-emergence crop and are therefore over conservative (EC 2012).

Treated pre-emergent fields will have low food availability and provide no protection to predators. Considering this and the conservative toxicity endpoint, the possibility that birds will forage in other (non-treated) areas, and limited availability of contaminated food, the risks identified for birds (threatened and non-threatened) following application of the formulated product Soleto to pre-emergent potato are therefore likely to be negligible.

5.8. **Pollinators:**

The risks to pollinators are below the level of concern and any risks are negligible.

5.9. **Non-target Arthropods:**

Risks to non-target arthropods are below the level of concern for both off-field and in-field. The identified in-field risks to predatory mites when exposed to fresh residues of SOLETO are not relevant for the pre-emergent application of potatoes as there will be no foliage in the field during application.

Predatory mites are a leaf-dwelling species and therefore exposure will be limited. The following label statement is proposed to be added:
A label statement indicating: “Ensure mechanical removal of weeds, remaining crop and seeds has taken place before application. The substance should only be used after planting and before crop emergence”

5.10. **Overall Ecological risk assessment conclusion:**
It is considered that the risks to the environment from the proposed use of SOLETO are below the level of concern with the proposed controls based on the available data for all areas except for non-target soil macro-organisms (mites, collembola) for which a risk above the level of concern was identified.

6. Proposed controls

6.1. More details about proposed controls are available in Appendix I.

Application rate

6.2. Maximum application rate of 1 application of 2 kg metobromuron/ha per year.

Application method

6.3. SOLETO must not be applied when wind speeds are less than 3 km/hr or more than 20 km/hr as measured at the application site.

6.4. Apply with ground-based equipment and minimum medium droplets, as defined by the American Society of Agricultural and Biological Engineers ASABE Standard (S572) or the British Crop Production Council guideline. This information should be required on the label so that users are aware of this control.

Buffer zones

6.5. To mitigate risks from spray drift and runoff, when applied to bare soil, the substance should not be applied within 5 m of any waterbody. This information should be required on the label so that users are aware of this control.

Additional label statements

6.6. A label statement indicating: “**WARNING**, might impact non-target plants, the substance should not be applied within 10 m downwind of an area containing non-target plants. Additional care is required when sprayed near sensitive terrestrial areas (eg areas with threatened plants or of higher ecological value)”.

6.7. A label statement indicating: “**WARNING**, exposure to SOLETO may injure or kill susceptible agricultural crops and native vegetation. Care should be taken avoid spray to neighbouring vegetation, it is recommended to conduct a site specific risk assessment that considers the potential movement of

spray drift downwind to sensitive areas. This includes assessment of the weather conditions, application equipment, topography and species of plants downwind."

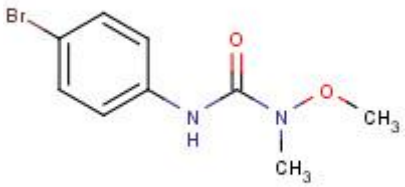
6.8. A label statement indicating: "Ensure mechanical removal of weeds, remaining crop and seeds has taken place before application. The substance should only be used after planting and before crop emergence".

Appendix A: Identity of the active ingredient, use pattern and mode of action

Identity of the active ingredient and metabolites

As this is the first full application under Part 5 of the Hazardous Substances and New Organisms (HSNO) Act 1996 considered for metobromuron, general data are provided in Table 3.

Table 3: Identification of metobromuron

IUPAC name	3-(4-bromophenyl)-1-methoxy-1-methylurea
CAS name	N'-(4- bromophenyl)- N-methoxy-N-methylurea
Molecular formula	$C_9H_{11}BrN_2O_2$
CAS Number	3060-89-7
Molecular weight (g/mol)	259.10
Structural formula	
Purity (minimum)	978 g/kg
Significant impurities/additives (% concentration)	None identified
Other international classification & labelling	The proposed classification from EFSA conclusions (EFSA 2014) are: Car Cat 2 STOT RE 2 Skin Sen 1B Aquatic Acute 1 Aquatic Chronic 1 Not Readily Biodegradable (The dossier has not yet been processed by ECHA.)

Regulatory status

The regulatory history of metobromuron is summarised in Table 4 below.

Table 4: Active ingredient regulatory status

Active ingredient name	Regulatory history in New Zealand	International regulatory history (Australia, Canada, Europe, Japan, USA)
metobromuron	New to New Zealand	Approved in Europe Not approved in Canada, United States, Japan and Australia.

Metobromuron is not approved in Australia, Canada, Japan and the United States. It is approved in Europe.

Impurities and or restrictions on purity or composition

No impurity limits for metobromuron have been identified by the EU (EC 2012).

Use pattern and mode of action

Use pattern

SOLETO is a soluble concentrate containing 500 g/L metobromuron which is diluted in water (200-600 L of water/hectare). The applicant seeks to have SOLETO approved for ground based application.

Application will be at the rate of 3-4 L of product per hectare which is equivalent to 1.5-2 kg/ha of metobromuron, with a maximum frequency of 1 applications per crop cycle (~1/year). More details on the intended uses for SOLETO are given in Table 5.

Mode of action

Metobromuron belongs to the urea class of herbicides and is classified in HRAC Group C2 and inhibits photosynthesis. Its mode of action involves inhibiting photosynthetic electron transfer at photosystem two (PS II).

Table 5: List of intended uses for SOLETO

Crop and/or situation (a)	Use pattern (b)	Pests or group of pests controlled (c)	Mixture		Application				Application rate per treatment			Remarks (l)
			Type (d-f)	Conc of ai (g)	Method and kind (h-i)	Growth stage & season (j)	Number Min max (k)	Interval between applications – days (minimum)	kg ai/hL min max	water L/ha min max	kg ai/ha max	
Potatoes	F	Broad leaved weeds	SC	500 g/L	Broadcast	Pre-emergence	1	NA	0.25-1	200-600	1.5-2	PHI 130 days

a Where relevant, the use situation should be described (eg fumigation of soil)
b Outdoor or field use (F), glasshouse application (G) or indoor application (I).
c eg biting and sucking insects, soil borne insects, foliar fungi, weeds
d eg wettable powder (WP), emulsifiable concentrate (EC), granule (GR), soluble concentrate (SC)
e CropLife international, 2008. Technical Monograph no 2, 6th edition. Catalogue of pesticide formulation types and international coding system
f All abbreviations used must be explained
g g/kg or g/l or others
h Method, eg high volume spraying, low volume spraying, spreading, dusting, drench, aerial, etc
i Kind, eg overall, broadcast, aerial spraying, row, individual plant, between the plant - type of equipment used must be indicated. If spraying include droplet size spectrum
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 Remarks may include: Extent of use/economic importance/restrictions

Appendix B: Physico-chemical properties of SOLETO

The physico-chemical properties of SOLETO are listed in Table 6. All values were referenced from the EC Draft Assessment Report on Metobromuron, Volume 3 – Annex B.2 (EC 2012).

Table 6: Physical and chemical properties of SOLETO

Property	Value	Reference
Colour	Off-white suspension with a 1.7% clear, brown supernatant	(EC 2012) B.2 and Application form
Odour	Faint aromatic	
Physical state	Liquid	
Relative density	1.219 g/ml	
Flash point	>100^{o} C	
pH	7.9	

Appendix C: Mammalian toxicology

Unless otherwise noted, all studies were conducted according to GLP and were fully compliant with the requirements of the international test guidelines followed.

Executive summaries and list of endpoints for SOLETO

The mammalian toxicology data for SOLETO are summarised in Table 7.

Table 7: Summary of mammalian toxicology data for SOLETO

Endpoint (Test Guideline)	Klimisch score	Result	HSNO Classification	Reference
Acute oral toxicity (OECD TG 423, EC B.1)	1	LD_{50} >2000 mg/kg bw	6.1E	Appendix J, Table 57; Study ID: TAO423-PH-10/0026
Acute dermal toxicity (OECD TG 402)	1	LD_{50} >2000 mg/kg bw	No	Appendix J, Table 58; Study ID: TAD-PH-10/0026
Acute inhalation toxicity (OECD TG 403/436)	1	LC_{50} >4.15 mg/L	No	Appendix J, Table 59; Study ID: ST17HC
Skin irritation/corrosion (OECD TG 404)	1	Non-irritating Mean score (24, 48, 72 hr) Erythema: 0.0, Oedema: 0.0	No	Appendix J, Table 60; Study ID: IC-OCDE-PH-10/0026
Eye irritation/corrosion (OECD TG 405)	1	Non-irritating Mean Draize Score (24, 48, 72 hrs) - Cornea -Opacity: 0.0 Conjunctiva -Redness: 0.44 -Chemosis: 0.0 Iris: 0.0	No	Appendix J, Table 61; Study ID: IO-OCDE-PH-10/0026
Contact sensitisation (OECD TG 406, EU B.6)	1	Non-sensitiser	No	Appendix J, Table 62; Study ID: SMK-PH-10/0026

Executive summaries and list of endpoints for metobromuron

All data for metobromuron were sourced from the EC Draft Assessment Report on Metobromuron, Volume 3 – Annex B.6 (EC 2012) unless otherwise stated.

Acute toxicity, skin and eye irritation, contact sensitisation, and genotoxicty data for metobromuron are summarised in Table 8.

Table 8: Summary of acute toxicity, irritation, sensitisation and genotoxicity data for metobromuron

Endpoint (Test Guideline)	Klimisch score	Result	Classification	Reference
Acute oral toxicity mice (Similar to OECD TG 401)	2	LD_{50} = 2098 (1647 – 2672) mg/kg bw	6.1E	(EC 2012), Study ID: Siss 4576
Acute oral toxicity rat (Similar to OECD TG 401)	2	LD_{50} = 2603 (1902 – 3735) mg/kg bw	6.1E	(EC 2012), Study ID: 801171
Acute dermal toxicity (Similar to OECD TG 402)	2	LD_{50} >3000 mg/kg bw	No	(EC 2012) Study ID: Not stated [Sachsse, K. Hurni, H. (1969)]
Acute dermal toxicity (OECD TG 402, EPA OPPTS 870.1200)	1	LD_{50} >2000 mg/kg bw	No	Appendix J, Table 56 Study ID: IET 16-0080
Acute inhalation toxicity (OECD TG 403, EU B.2)	1	LC_{50} >1.6 mg/L	No	(EC 2012), Study ID: 961120
Skin irritation/corrosion (Similar to OECD TG 404)	2	Non-irritating (study used non-guideline methods)	No	(EC 2012), Study ID: 801173
Eye irritation/corrosion (Similar to OECD TG 405)	2	Mean Draize Score (24, 48, 72 hrs) - Cornea -Opacity: 0.0 Conjunctiva -Redness: 0.11 -Chemosis: 0.0 Iris: 0.0	No	(EC 2012), Study ID: 801174
Contact sensitisation (OECD TG 406, EU B.6)	1	Positive for sensitisation	6.5B	(EC 2012), Study ID: 961121

Endpoint (Test Guideline)	Klimisch score	Result	Classification	Reference
Mutagenicity (3 studies) – *In Vitro* Reverse mutation assay in bacteria: (OECD TG 471, EC B.13/14) and Chromosomal aberration test in human peripheral blood lymphocytes: (OECD TG 473, EC B.10) and Forward mutation assay in mammalian cells: (OECD TG 476, EC B.17)	1	Negative (+/-S9)	No	(EC 2012), Study ID: 25910, 25911, and 25912,
Mutagenicity (1 study) – *In Vivo* Micronucleus test in rat bone marrow: (OECD TG 474, EC B.12)	1	Negative	No	(EC 2012), Study ID: 25913

Results of the repeated dose toxicity studies with metobromuron are summarised in Table 9.

Table 9: Summary of repeated dose studies with metobromuron

Study type	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day	Key effect	Reference
1-year oral toxicity: rats (Replaced with a 12 month interim sacrifice from the 2 year carcinogenicity study) (OECD TG 453)	3.1M/3.7F	9.6M/11.84F	Haematological (methaemoglobinaemia, regenerative anaemia), increased organ weight (spleen weight), and haemosiderin deposition (spleen, liver)	(EC 2012), Study ID: 70CO329/8116
1-year oral toxicity: mice (Replaced with a 12 month interim sacrifice from the 2 year carcinogenicity study) (OECD TG 451)	3M/F	12M/F	Haematological effects (Increased Heinz bodies)	(EC 2012), Study ID: 75SO188/8219
1-year oral toxicity: dogs (Similar to OECD TG 452 and EC B.30)	1.59M/1.71F	7.88M/8.49F	Haematological (methaemoglobinaemia, regenerative anaemia), increased relative spleen weight, and histological alterations (spleen, liver, kidneys, and bone marrow)	(EC 2012), Study ID: 45SO329/8117
18-month dietary chronic toxicity/carcinogenicity study: mice (Replaced with a 24 month carcinogenicity study) (Similar to OECD TG 451 EC B.32)	12M/F (highest dose tested)	>12M/F	No evidence of carcinogenicity	(EC 2012), Study ID: 75SO188/8219
2-year chronic toxicity/carcinogenicity: rat (OECD 453)	2.6M/3.4F	7.9M/9.9F	Increase in mammary gland tumours (fibrosarcoma) in females and pheochromocytomas in males	(EC 2012), Study ID: 70CO329/8116
Developmental toxicity: rats (OECD TG 414, EC B.31	Offspring: 30 Maternal: 10	Offspring: 90 Maternal: 30	Offspring: Delayed physiological growth, no teratogenic potential Maternal: Mortality in the high dose and decreased weight gain and food consumption	(EC 2012), Study ID: 810179

Study type	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day	Key effect	Reference
Developmental toxicity: rabbits (OECD TG 414, EC B.31)	Offspring: 30 Maternal: 30	Offspring: >100 (highest dose tested) Maternal: 100	Offspring: No teratogenic potential Maternal: Mortality with embryo toxicity and decreased weight gain and food consumption	(EC 2012), Study ID: 38R0329/8124
2-generation reproductive toxicity: rats (OECD 416, EC B.35)	Reproduction: 16.03M/20.89 F (highest dose tested) Parental: 1.38M/1.66F	Reproduction:NA Parental: 4.53M/5.56F	No reproductive toxicity. Parental toxicity consisted of methaemoglobinaemia and splenic haemosiderin deposition	(EC 2012), Study ID: 74RO188/8253

Beagle dogs are known to have a deficiency in methaemoglobin reductase in their erythrocytes. Accordingly, this deficiency is likely to be responsible for their increased sensitivity towards oxidant induced methaemoglobinaemia and a lower NOAEL compared to what was observed in the rodent studies. Therefore, the NOAEL's utilized in the EPA risk assessment were based on the results observed in the rodent species whose values were very similar to each other, and likely more reflective of human vulnerability than the dog.

Toxicokinetics and dermal absorption studies with metobromuron are summarised in Table 10.

Table 10: Summary of toxicokinetics and dermal absorption studies with metobromuron

Study type	Results
Toxicokinetics (EC 2012), Study ID: 4507, E5449, 35/90, and 36/90	Metobromuron is rapidly and almost completely absorbed from the intestinal tract in both sexes (>80%) and is rapidly eliminated (>75% in first 24 hours). The main route of elimination being the urine (>70%) followed by the biliary route and faeces. Seven days following administration, tissue residues are low except for whole blood where it is concentrated in the erythrocytes (56-90% of radio-activity was associated with haemoglobin). Metobromuron is completely metabolised (no parent compound was detected) and the metabolic pathways appear to be independent of the dose (0.5 and 50 mg/kg), route (oral and iv), pre-treatment (multiple and single dose) and sex of the animals. A similar metabolite profile was found in both sexes. The dominating metabolic pathway of metobromuron is N-demethylation and N-demethoxylation, phenyl ring hydroxylation, and conjugation with sulphuric or acetic acid and glutathione.
In vitro dermal absorption OECD 428 (EC 2012), Study ID: JV2115	The results of an *in vitro* study assessing the dermal absorption potential of metobromuron through human skin as both a formulation concentrate and as a 50X aqueous dilution indicated it was poorly absorbed. Specifically, the absorption rate for the formula concentrate was 0.48 ± 0.07% and for the “in use” field dilution it was 6.31 ± 0.83%.

General conclusion about mammalian toxicology of metobromuron

Acute toxicity, irritation and sensitisation

Metobromuron is of relatively low acute toxicity in mammals and should be classified 6.1E for acute toxicity by oral exposure. Metobromuron is not a skin or eye irritant but was shown to be a contact sensitiser and should be classified 6.5B.

Mutagenicity

Metobromuron did not show evidence of genotoxicity in three *in vitro* studies or in one *in vivo* study and should not be classified.

Carcinogenicity

No evidence of carcinogenicity was noted in mice. In rats, evidence of carcinogenicity was observed based on an increase in mammary gland fibrocarcinomas in females and an increase in pheochromocytomas in males. The tumour increase in females was not statistically significant relative to controls and its incidence rate of 6% was just slightly above the historical control range of 4%. Similarly, the incidence rate of pheochromocytomas in males (12%) was also not statistically significant relative to controls (6%). The background incidence rate of for pheochromocytomas in control animals for the years associated with this study (1983-1986) was 4% so even control animals were above that. When the historical control data are expanded for the years 1983 – 2000 the control incidence rate goes up to 8%. This is still lower than the rate observed in the high dose group. The report does not identify whether the pheochromocytomas are benign or malignant and the historical control incidence rate of benign pheochromocytomas is up to 38%.

A review in Critical Reviews in Toxicology (Greim, Hartwig et al. 2009) suggested that this tumour type is believed to have a low relevance to humans; and that pheochromocytomas occur with relatively higher frequency in male rats, especially when the following conditions are involved: hypoxia, uncoupling of oxidative phosphorylation, disturbance in calcium homeostasis, and disturbance of the hypothalamic endocrine axis. The fact that the animals suffered from a methaemoglobinaemia would indicate a mild hypoxia was likely present and may have contributed to the slight increase.

The EPA notes that the magnitude of the incidence of the tumour types observed in either sex of rat were never of statistical significance and were only slightly above historical control values. There is a suggestion that in males the tumour type is of limited human relevance. However, the EPA notes that neither the applicant nor EFSA proposed this mode of action for pheochromcytomas as reason to not apply the carcinogenicity classification. The EPA notes that even if the mode of action is valid it has not been clearly demonstrated as applicable in this instance, and relates to only one of the tumour types identified. Therefore the carcinogenicity classification 6.7B has been proposed.

Reproductive and developmental toxicity

No evidence of developmental toxicity (rat, rabbit) or reproductive toxicity (rat, 2 generation) was observed in any study.

Target organ toxicity

Metobromuron appears to target red blood cells (RBCs) inducing a mild methaemoglinaemia that ultimately leads to lysis of RBCs and deposits of haemosiderin (iron and haemoglobin) in the spleen and liver. There is a compensatory regeneration of RBCs. The effect was noted to readily reverse upon treatment cessation.

Toxicokinetics and dermal absorption

Metobromuron is rapidly and almost completely absorbed from the intestinal tract in both sexes and is rapidly eliminated mainly in the urine. Tissue residues are low except for whole blood where it is concentrated in the erythrocytes and is associated with haemoglobin. Metobromuron is completely metabolised with no parent compound detected in the excreta. The metabolite profile is similar in both sexes. The dominating metabolic pathway of metobromuron is N-demethylation and N-demethoxylation, phenyl ring hydroxylation, and conjugation with sulphuric or acetic acid and glutathione.

The results of an *in vitro* dermal absorption study indicated metobromuron was poorly absorbed. Specifically, the absorption rate for the formula concentrate was 0.48 ± 0.07% and for the “in use” field dilution was 6.31 ± 0.83%.

Appendix D: Environmental fate

Executive summaries and list of endpoints

All studies on the environmental fate of metobromuron provided by the applicant have been reviewed. Unless otherwise noted, all studies were conducted according to GLP and were fully compliant with all requirements of the standard international test methods used. These studies are used to understand how metobromuron behaves and moves through the environment. Data from these studies have been used in relevant areas of the risk assessment to parameterise the models, predict the environmental concentrations of metobromuron in the environment, following use of SOLETO and thus, the likely exposure of environmental receptors.

In this case, the EPA has reviewed the submitted studies, and the summaries of these studies, which have also been reviewed as part of the European review of metobromuron (EC 2012, EFSA 2014). Where the EPA has not agreed with the European review of the environmental fate study or had additional comments, a brief study summary has been included in Appendix J. When the EPA fully agrees with the review in the European assessment, no summary has been made as the summary is available in the publicly available DAR (EC 2012).

The environmental fate endpoints and conclusions for metobromuron are presented under the following sub-sections.

Residues relevant to the environment

In laboratory and field degradation studies in soil and water, three major metabolites of metobromuron (ie, those found at ≥10% active radioactivity (AR) at any sample interval) were identified: desmethoxy-metobromuron, desbromo-metobromuron and HHAC-027. No data on the persistency of metabolites was provided. The major metabolites are listed in Table 11.

Table 11: Major metabolites of metobromuron

Metabolite code	Chemical name (IUPAC)	Molecular weight (g/mol)	Chemical formula	Max. % formed[1]				Reference
				Soil	Sediment	Water	Total sediment/ water	
R2, CGA 18 236, HHAC-026, desmethoxy-metobromuron	1-(4-bromophenyl)-3-methylurea	229.1	$C_8H_8BRN_2O$	ND	23.5%[2]	12.8%[2]	36.3%[2]	EU DAR (EC 2012) Report No. C91703
				14.9%	ND	ND	ND	EU DAR (EC 2012) Report No. C96890
R6, HHAC-022, desbromo-metobromuron	1-methoxy-1-methyl-3-phenylurea	180.2	$C_9H_{12}N_2O_2$	ND	ND	35.0%	ND	EU DAR (EC 2012) Report No. C96912
R3, CGA 18 237, HHAC-027	4-bromophenylurea	215.1	$C_7H_7BrN_2O$	ND	13.6%[2]	10.0%[2]	23.7%[2]	EU DAR (EC 2012) Report No. C91703

[1] Only major metabolites defined as per the HSNO Act ("metabolites formed in amounts of equal to or more than 10% of the applied amount of substance and any time-point evaluated during the degradation studies in the appropriate compartment under consideration (soil or water)") have been listed. Only the maximum percent formed of each of these metabolites is reported in this table. Metabolites listed may have been identified in other compartments but since this is not relevant to the environmental risk assessment as they did not meet the "major metabolite" criteria, the values were not reported here.

[2] Worst-case values reported.

As is discussed in Appendix E, none of the major metabolites identified are considered to be ecotoxicologically relevant based on the data provided by the applicant. The tested metabolites of metobromuron are of similar toxicity, or are less toxic than the parent. The risk profile of the metabolites is considered similar or lower than that of the parent. As such, any controls proposed to mitigate risks identified for the parent compound are considered sufficient to protect the environment from any possible risks from the major metabolites.

Degradation and fate of metobromuron and its metabolites in aquatic environments

Information on the degradation and fate of metobromuron in the aquatic environment is summarised in Table 12. No studies reporting endpoints for the metabolites of metobromuron were submitted by the applicant. Information on bioaccumulation potential is listed in Table 13.

Table 12: Degradation and fate of metobromuron in aquatic environments

Test type	Value or conclusion for metobromuron	Reference
Ready biodegradation	Not classified as readily biodegradable	EU DAR (EC 2012)
Aqueous photolysis half-life (DT_{50})	5.6 days (continuous radiation), this is equivalent to **12.6 days** at 50°N summer sunlight and 12.1 days at 30-40°N summer sunlight	EU DAR (EC 2012) Report No. C96912
Degradation in aerobic water/sediment (DT_{50})	*River system* 14.5 days - water phase (DFOP, best fit) 33.2 days - whole system Max % of AR in sediment - 28.7% *Pond system* 11.3 days - water phase (DFOP, best fit) **34.5** days - whole system Max % of AR in sediment - 28.1%	EU DAR (EC 2012) Report No. C91703
Water solubility at 20°C [mg/L]	**328**	EU DAR (EC 2012)
Hydrolysis half-life (DT_{50})	pH 4: 20°C - stable; 50°C - 31.5 days; 70°C - 1.6 days pH 7: 20°C - stable; 50°C - 27.2 days; 70°C - 1.6 days pH 9: 20°C - stable; 50°C - 32.6 days; 70°C - 1.6 days	EU DAR (EC 2012) Report No. C96923

Table 13: Bioaccumulation potential of metobromuron

Test type	Metobromuron	Reference
Partition coefficient octanol/water [Log Pow]	2.48 at pH 7.3[1]	EU DAR (EC 2012)
Fish bioconcentration (whole fish)	Not triggered based on Log Pow	N/A

[1] Metobromuron is considered to be lipophilic (Log K_{ow} >2), which has implications for the soil toxicity endpoints as described in Appendix E

Degradation and fate of metobromuron and its metabolites in soil

Information on the degradation and fate of metobromuron and its metabolite(s) in the soil environment is summarised in Table 14 and Table 15.

Table 14: Degradation and fate of metobromuron in soil

Test type	Metobromuron	Reference
Degradation under laboratory conditions		
Calculated 80th percentile aerobic soil DT_{50}	42.2 days (non-normalised)[1]	-
Aerobic half-life in soil (DT_{50lab})	*Silt loam* - 24.6 days *Clay* - 28.4 days *Loamy sand* - 49.7 days *Sandy loam* - 40.3 days	EU DAR (EC 2012) Report No. C77551
	Silt - 32 days	EU DAR (EC 2012) Report No. C3126 0289
	27.5 & 29.5 days [Note values are not included in the 80th percentile calculation, not considered reliable]	EU DAR (EC 2012) Report No. C3126 0057[2]
	Sandy clay loam 19.4 days - 25°C & 75% field capacity 25.0 days - 25°C & 33% field capacity 44.1 days - 10°C & 75% field capacity [Note values are not included in the 80th percentile calculation, not considered reliable]	EU DAR (EC 2012) European Journal of Agronomy 16 (2002) 321-238[2]
Anaerobic degradation in soil (DT_{50lab})	*Silt loam* - 73.7 days	EU DAR (EC 2012) Report No. C96890
Soil photolysis half-life (DT_{50})	*Sandy loam* 57.3 days, equivalent to 86 days of latitude 30°N summer sunlight	EU DAR (EC 2012) Report No. 315382

Test type	Metobromuron	Reference
Degradation under field conditions		
Aerobic half-life in soil ($DT_{50field}$)[1]	*Sandy loam*[3] - 18.3 days Applied to bare soil at 2500 g ai/ha as formulated product at one trial site in Switzerland. Due to poor homogeneity of application, top 0-3 cm layer was taken, mixed and redistributed evenly across soil surface. The majority of radioactivity was located in the top 0-10 cm layer. Losses due to volatilisation are deemed minimal as the top layer was incorporated. From day 63 onwards the unextracted residues accounted for more than 80%. The unextracted residues from day 90 sample were analysed by TLC and the major fraction represented the metabolite CGA 18238 (15.3%).	EU DAR (EC 2012) Report No. 93GN21PR1
Aerobic half-life in soil ($DT_{50field}$)[1]	*Silt loam* - *4*.1 days (Germany) *Loam* - **73.3 days** (France) Applied to bare soil at 2000 g ai/ha as formulated product at two trial sites in Germany and France. Immediately after application the test item was incorporated into the top 3-5 cm of soil. Loses due to volatilisation are deemed minimal as the top layer was incorporated. DFOP deemed best fit for German trial site. SFO deemed best fit for French trial site, day 28 excluded as outlier.	EU DAR (EC 2012) Report No. OZ/10/010
Aerobic half-life in soil ($DT_{50field}$)[1]	*Sandy clay loam* - 71.1 days (Spain) *Clay* - 32.9 days (France) Applied to bare soil at 2000 g ai/ha as formulated product at two trial sites in Spain and France. Immediately after application the test item was incorporated into the top 3-5 cm of soil. Loses due to volatilisation are deemed minimal as the top layer was incorporated. SFO deemed best fit for Spanish trial site, day 0 excluded as outlier. SFO deemed best fit for French trial site, day 7 excluded as outlier.	EU DAR (EC 2012) Report No. OZ/10/011
Mobility in soil		
Sorption to soil (K_d/K_{oc})[4]	K_d = **2.9 mL/g** (range 2.9 to 15.0 mL/g, n=4)[5] K_{oc} = **114 mL/g** (range 114 to 596 mL/g, n=4)[5]	EU DAR (EC 2012) Report No. C77540
Lysimeter study	Metobromuron considered immobile in test soil (sandy loam) under natural field conditions.	EU DAR (EC 2012) Report No. 274634

[1] Calculated upper 80% percentile DT_{50} of 24.6, 28.4, 40.3, 49.7 & 32 days for metobromuron for use in the quantitative risk assessment. Note that in this specific case, the longest field DT_{50} was selected for use in the modelling for conservatism, since in both field studies one of the DT_{50} values in each case was determined to be greater than that measured in the lab (>70 days).
[2] Study not accepted to derive endpoints [EU DAR (EC 2012)].
[3] EU DAR (EC 2012) classifies this soil as clay (USDA) as the study does not state which classification system this is based.

[4] Lowest value from a non-sand soil used for risk assessment (K_d/K_{oc} values measured in soils classified as “sand”, “coarse sand”, “fine sand” or “loamy sand” are excluded as per the GENEEC2 guidance).
[5] Note that five soil types were tested in total but the “loamy sand” was disregarded as it is a sandy soil as per footnote “4” above

Table 15: Degradation and fate of metobromuron metabolites desmethoxy-metobromuron in soil

Test type	Desmethoxy-metobromuron	Reference
Degradation under laboratory conditions		
Calculated 80th percentile aerobic soil DT_{50}[1]	**45.4 days (**non-normalised)	-
Aerobic half-life in soil (DT_{50lab})	*Sandy* loam - 36 days *Clay* - 49 days *Silt loam* - 40 days	EU DAR (EC 2012) Report No. 41005347
Mobility in soil		
Sorption to soil (K_d/K_{oc})[2]	K_d = 2.21 mL/g (range 2.21 to 3.66 mL/g, n=3) K_{oc} = 154 mL/g (range 154 to 242 mL/g, n=3)	EU DAR (EC 2012) Report No. 41005346

[1] Calculated upper 80% percentile DT_{50} of 36, 49 & 40 days for desmethoxy-metobromuron for use in the quantitative risk assessment.
[2] Lowest value from a non-sand soil used for risk assessment (K_d/K_{oc} values measured in soils classified as “sand”, “coarse sand”, “fine sand” or “loamy sand” are excluded as per the GENEEC2 guidance).

Two additional studies were provided by the applicant (Guth, 1972 & 1982). These studies did not provide enough information to generate K_d/K_{oc} values. As such, they have not been reported, and will not be used to generate any endpoints.

General conclusion about environmental fate

Metobromuron

Persistence and behaviour in the aquatic environment

The active ingredient metobromuron is not considered readily biodegradable.

Photolysis and hydrolysis are not considered significant degradation pathways of metobromuron (DT_{50} of 57.3 days, and stable at 20°C, respectively).

With a total system water/sediment DT_{50} of 34.5 days (worst-case, n=2), metobromuron meets the “Not readily biodegradable/persistent” criterion in accordance with the risk assessment methodology (DT_{50} (whole system) 16 days - 2 months). Metobromuron dissipated relatively rapidly from the water phase, with $DT_{50water}$ values of 14.5 and 11.3 days in the river and pond systems, respectively. Metobromuron reached a maximum % of AR of 28.7% (river) in sediment at day 14 which reduced to <5% in river sediment at day 99 and <10% in pond sediment at day 134. No DT_{50} was calculated for the sediment compartment.

A DT_{50} was not calculated for the sediment compartment in the studies provided by the applicant, although a maximum of 29.0% of AR (worst-case, n=2) partitioned into the sediment phase. This suggests that dissipation to sediment is a significant mechanism for the decline of metobromuron in the aqueous phase.

In aquatic environment major metabolites were formed: desmethoxy-metobromuron and HHAC-027. The DT_{50} values in water/sediment systems of these metabolites were not calculated but reached maximum % of AR of 36.3% and 23.7% (whole system) for desmethoxy-metobromuron and HHAC-027, respectively. These metabolites are discussed in more detail under the “Metabolites” heading below.

Persistence and behaviour in the soil environment

In laboratory soils, metobromuron meets the “Persistent” criterion (DT_{50lab} 30 days to 6 months) in accordance with the EPA risk assessment methodology (80th percentile DT_{50} of 42.2 days, range 24.6 to 49.7 days, n=5). Metobromuron was also considered persistent under field conditions, with a worst-case $DT_{50field}$ of 73.3 days (range 4.1 to 73.3 days). In the two field studies, at one of the sites in each study (two sites were studied in each), the $DT_{50field}$ values were determined to be 71.1 days (sandy clay loam, Spain), and 73.3 days (loam, France). This is longer than the DT_{50} values determined in the laboratory studies, which is unusual, and no reason for this difference has been identified. As such, in this specific case, it was decided to use the longest field DT_{50} value for use in the environmental modelling for conservatism.

As the DT_{50} values in laboratory and field soils are <6 months, it is not considered necessary to assess the accumulation of metobromuron in soil.

In anaerobic laboratory soils, metobromuron degraded with a DT_{50} of 73.7 days (very similar to the longest aerobic lab DT_{50} value). This study also identified a major metabolite as desmethoxy-metobromuron (14.9% AR) in anaerobic soil.

In the laboratory, soil photolysis DT_{50} values were determined to be 57.3 days, equivalent to 86 days of latitude 30 °N summer sunlight. Overall, soil photolysis is not considered to be a major route of degradation for metobromuron.

In the soil environment one major metabolites was formed (and this was under anerobic conditions): desmethoxy-metobromuron (max. 14.9% of AR), and is discussed in more detail under the “Metabolites” heading below.

Mobility in soil

Metobromuron is considered to have high mobility in soil according to the McCall classification system (McCall P.J., Laskowski D.A. et al. 1981) based on a lowest non-sand soil K_{oc} = 114 mL/g (range 114 to 596 mL/g, n=4). Substances with K_{oc} values 100-150 mL/g are classified as high mobility in soil. In the terrestrial field dissipation study (93GN21PR1) only the upper 0-10 cm soil layer was analysed specifically for metobromuron and metabolites due to the low amount of total radioactivity in soil below 10 cm. Levels of metobromuron above the Limit of Quantitation (LOQ) were measured down to the 40-50 cm horizon in the terrestrial field dissipation studies (OZ/10/010 & OZ/10/011). In most instances detectable residues at the lower horizons were low (around the LOQ). A lysimeter study provided by the applicant considered metobromuron to be immobile in the test soil under natural field conditions. The leachates analysed after two years detected <1% AR suggesting contamination of the ground water by normal use can be excluded.

The low K_{oc} values generated in laboratory studies indicate high mobility of metobromuron in soil however the field studies (soil dissipation and lysimeter) provided by the applicant suggest a limited potential for leaching.

Potential for bioaccumulation

Metobromuron is not considered bioaccumulative based on the Log K_{ow} of 2.48 at pH 7.3. No whole fish bioconcentration study was performed.

Data gaps and uncertainties

No data gaps or uncertainties were identified.

Major metabolite desmethoxy-metobromuron

Persistence and behaviour in the aquatic environment

No aquatic DT_{50} was calculated for the metabolite desmethoxy-metobromuron. However the percentage of applied radioactivity was reported for water, sediment and whole system in river and pond systems. As such, although the persistence of desmethoxy-metobromuron cannot be assessed, the data reveal the metabolite does partition into the sediment phase over time (max. 23.5% AR – sediment, max. 12.9% AR – water).

The behaviour of metabolite desmethoxy-metobromuron in the aquatic environment will be assessed in conjunction with the aquatic ecotoxicity endpoints in Appendix E, in order to determine whether it is necessary to include metabolite desmethoxy-metobromuron within the aquatic and/or sediment risk assessment.

Persistence and behaviour in the soil environment

In laboratory soils metabolite desmethoxy-metobromuron (max. 14.9% AR) meets the “Persistent” criterion in accordance with our risk assessment methodology (DT_{50lab} 30 days to 6 months) with a calculated 80th percentile DT_{50lab} of 45.4 days (range 36 to 49 days, n = 3). This is the similar to the parent, metobromuron.

In conclusion, major metabolite desmethoxy-metobromuron is considered persistent in laboratory soils. The ecotoxicity of major metabolite desmethoxy-metobromuron will be considered in Appendix E, in conjunction with the persistence and behaviour information, to determine whether the environmental risk of this metabolite is required to be addressed.

Mobility in soil

Metabolite desmethoxy-metobromuron is of medium mobility in soil according to the McCall classification system (McCall and Laskowski *et al*. 1981) based on a lowest non-sand soil K_{oc} of 154 mL/g (range 154 to 242 mL/g, n=3). Substances with a K_{oc} of 150 to 500 mL/g are considered of medium. Although metabolite desmethoxy-metobromuron is more mobile in soil than the parent metobromuron however the terrestrial field dissipation study (93GN21PR1) reported any metabolites that formed during the study remained below 5% AR (maximum 4.4%), suggesting a limited potential for leaching in the field. As such, no quantitative groundwater modelling is considered necessary.

Other metabolites of metobromuron

Two other metabolites of metobromuron were identified in the aquatic environment with a max. >10% AR (desbromo-metobromuron and HHAC-027). However no environmental fate studies were provided by the applicant, therefore it is not possible to evaluate their persistence and behaviour in aquatic and soil environments.

The ecotoxicity of these metabolites will be considered in Appendix E to determine whether the environmental risk of these metabolites is required to be addressed.

Appendix E: Ecotoxicity

Executive summaries and list of endpoints

Unless otherwise noted, all ecotoxicity laboratory studies were conducted in accordance with GLP and were fully compliant with all requirements of the standard international test methods.

All studies on the toxicity of metobromuron and its major metabolites provided by the applicant on environmental receptors have been reviewed. These studies are used to describe the key impacts of metobromuron or SOLETO on the different environmental compartments. The data from the studies have been used for classifying the active ingredient and in relevant areas of the risk assessment.

In this case, the EPA has reviewed the studies and the summaries of these studies provided as part of the European review of metobromuron (EC 2012, EFSA 2014). Where the EPA has not agreed with the European review of the ecotoxicity study or had additional comments, a study summary has been included in Appendix J. When the EPA fully agrees with the review in the European assessment, no summary has been made as the summary is available in the publicly available DAR (EC 2012).

The ecotoxicity endpoints and conclusions for metobromuron are presented under the following sub-sections.

Aquatic toxicity

Table 16 contains the acute and chronic aquatic toxicity test results for the active ingredient metobromuron.
Table 17 contains the acute and chronic aquatic toxicity test results for metobromuron metabolites
Table 18 contains the acute and chronic aquatic toxicity test results for the formulated product SOLETO.
Values in bold are those used for the risk assessment. Underlined values are those used to determine the classification.

Table 16: Summary of aquatic toxicity data for metobromuron

Test species	Test type and duration	Endpoint value	Reference
Fish	**Acute**		
Rainbow trout, *Oncorhynchus mykiss*	96-hr LC_{50}	43 mg ai/L (nominal)	EU DAR (EC 2012); Report No. C3126 0035
Common carp, *Cyprinus carpio*		43 mg ai/L (nominal)	EU DAR (EC 2012); Report No. C3126 0036
Fish	**Chronic**		
Rainbow trout, *Oncorhynchus mykiss*	28-d semi-static, NOEC	**0.50 mg ai/L** (geometric mean)	EU DAR (EC 2012); Report No. 60201231

Test species	Test type and duration	Endpoint value	Reference
Invertebrates	**Acute**		
Daphnia magna	48-hr EC_{50}	44.1 mg ai/L (nominal)	EU DAR (EC 2012); Report No. C3126 0037
Invertebrates	**Chronic**		
Daphnia magna	21-d reproduction, NOEC	**10 mg ai/L** (nominal)	EU DAR (EC 2012); Report No. C3126 0390
Algae and aquatic macrophytes			
Green alga, *Pseudokirchneriella subcapitata*	72-hr E_rC_{50} (growth rate)	0.63 mg ai/L (nominal)	EU DAR (EC 2012); Report No. 55101210
Cyanobacterium, *Anabaena flos-aquae*	72-hr E_rC_{50} (growth rate)	1.09 mg ai/L (nominal)	EU DAR (EC 2012); Report No. 55102210
Duckweed, *Lemna gibba*	7-d E_rC_{50} (growth rate)	*Dry weight* 0.31 mg ai/L (nominal)	EU DAR (EC 2012); Report No. 55103240

Table 17: Summary of aquatic toxicity data for metabolites

Test species	Test type and duration	Endpoint value	Reference
Metabolite desmethoxy-metobromuron			
Algae and aquatic macrophytes			
Green alga, *Pseudokirchneriella subcapitata*	72-hr E_rC_{50} (growth rate)	0.43 mg metabolite/L (mean measured)	EU DAR (EC 2012); Report No. 60191210
Duckweed, *Lemna gibba*	7-d E_rC_{50} (growth rate)	*Dry weight* 0.63 mg metabolite/L (nominal)	EU DAR (EC 2012); Report No. 60192240
Metabolite 4-bromophenylurea			
Algae and aquatic macrophytes			
Green alga, *Pseudokirchneriella subcapitata*	72-hr E_rC_{50} (growth rate)	>100 mg metabolite/L (nominal)	EU DAR (EC 2012); Report No. 60451210
Duckweed, *Lemna gibba*	7-d E_rC_{50} (growth rate)	*Dry weight* >100 mg metabolite/L (nominal)	EU DAR (EC 2012); Report No. 60452240
Metabolite desbromo-metobromuron			
Algae and aquatic macrophytes			
Green alga, *Pseudokirchneriella subcapitata*	72-hr E_rC_{50} (growth rate)	2.0 mg metabolite/L (nominal)	EU DAR (EC 2012); Report No. 62021210
Duckweed, *Lemna gibba*	7-d E_rC_{50} (growth rate)	*Dry weight* 1.28 mg metabolite/L (nominal)	EU DAR (EC 2012); Report No. 62022240

The applicant provided four additional metabolite studies, two each for 3-(4-hydroxyphenyl)-1-methoxy-1-methylurea (green alga: Report No. 63571210, duckweed: Report No. 63572240), and 1-(4-hydroxyphenyl)-3-methylurea (green alga: Report No. 63581210, duckweed: Report No. 63582240). Since the max. % AR was <10% for both of these metabolites [EU DAR (EC 2012); Report No. C96912] and therefore neither of these metabolites are considered major, these studies have not been not been included here.

Table 18: Summary of aquatic toxicity data for SOLETO

Test species	Test type and duration	Endpoint value	Reference
Fish	**Acute**		
Rainbow trout, *Oncorhynchus mykiss*	96-hr LC_{50}	**>100 mg formulation/L, equivalent to >42.6 mg ai/L (nominal)**	EU DAR (EC 2012); Report No. 55095230
Invertebrates	**Acute**		
Daphnia magna	48-hr EC_{50}	**>100 mg formulation/L, equivalent to >42.6 mg ai/L (nominal)**	EU DAR (EC 2012); Report No. 55094220
Algae and aquatic macrophytes			
Green alga, *Pseudokirchneriella subcapitata*	72-hr E_rC_{50} (growth rate)	1.39 mg formulation/L, **equivalent to 0.59 mg ai/L** (nominal)	EU DAR (EC 2012); Report No. 55091210
Cyanobacterium, *Anabaena flos-aquae*	72-hr E_rC_{50} (growth rate)	10.6 mg formulation/L, equivalent to 4.51 mg ai/L (nominal)	EU DAR (EC 2012); Report No. 55092210
Duckweed, *Lemna gibba*	7-d E_rC_{50} (growth rate) NOAEC (recovery)	*Dry weight* E_rC_{50} - 0.73 mg formulation/L, **equivalent to 0.31 mg ai/L** NOAEC after 2 weeks - 5 mg substance/L, equivalent to 2.1 mg ai/L (nominal)	EU DAR (EC 2012); Report No. 55093240
Parrot's feather, *Myriophyllum aquaticum*	7-d E_rC_{50} (growth rate)	*Dry weight* No dose response for dry weight (growth rate and yield). Unable to determine E_rC_{50}. NOEC 1.59 mg formulation/L, equivalent to 0.27 mg ai/L)	EU DAR (EC 2012); Report No. 55093240

Metabolites

Major metabolites 4-bromophenylurea and desbromo-metobromuron show less toxicity to *Pseudokirchneriella subcapitata* and *Lemna gibba* than the active ingredient metobromuron in the aquatic environment. Major metabolite desmethoxy-metobromuron was more toxic to the green algae *Pseudokirchneriella subcapitata* than active ingredient metobromuron (72-hr E_rC_{50} 0.43 mg metabolite/L versus 0.63 mg ai/L), but less toxic to the aquatic macrophyte *Lemna gibba*.

No information was provided in regard to the persistence of these metabolites in the aquatic environment.

The major metabolites of metobromuron have similar or less toxicity to the tested aquatic species compared to the parent metobromuro, with the exception of major metabolite desmethoxy-metobromuron and toxicity to the green algae *Pseudokirchneriella subcapitata.* Since no risks were identified for the green algae *Pseudokirchneriella subcapitata* at the screening stage of the aquatic risk assessment for the parent, it is not considered necessary to assess risks to green algae from major metabolite desmethoxy-metobromuron. Once the equivalent application rate for the metabolite has applied, the slightly higher toxicity observed for green algae is very unlikely to result in a risk quotient above the level of concern. The risk profile of the metabolites is considered similar or lower than that of the parent therefore, and the risk assessment for the parent compound is considered to also appropriately protect the aquatic environment from any potential risks from the major metabolites.

In conclusion, based on this assessment, the major aquatic metabolites of metobromuron will not be further assessed; the controls managing the risks from the parent substance are considered to manage the risks from these metabolites.

Formulation

Expressed as the active ingredient, the end-use product SOLETO shows less toxicity to the cyanobacterium *Anabaena flos-aquae* (4.1 times less toxicity), similar toxicity to the rainbow trout *Oncorhynchus mykiss* (equivalent toxicity), aquatic invertebrate *Daphnia magna* (equivalent toxicity), and duckweed *Lemna gibba* (identical toxicity endpoint), and showed very slightly higher toxicity to the green algae *Pseudokirchneriella subcapitata* (0.59 mg ai/L versus 0.63 mg ai/L, or 1.07 times higher toxicity) than the individual active ingredient metobromuron.

Uncertainties and data gaps

A possible data gap has been identified for the assessment of sediment-dwelling organisms as the maximum % of AR in the sediment study provided by the applicant [EU DAR (EC 2012): Report No. C91703] was 28.7% at day 14. This reduced to <10% within 6 months suggesting metobromuron is not persistent in sediment. No DT_{50} for the sediment compartment was calculated in the water/sediment study.

General conclusion about aquatic toxicity

Metobromuron triggers a 9.1A hazard classification (very ecotoxic in the aquatic environment) based on the 72-hour E_rC_{50} of 0.63 mg ai/L determined for the green algae *Pseudokirchneriella subcapitata* [EU DAR (EC 2012); Report No. 55101210], which is the most sensitive endpoint.

The end-use product SOLETO triggers a 9.1A hazard classification (ecotoxic in the aquatic environment) based on the 7-day E_rC_{50} of 0.73 mg formulation/L determined for the duckweed *Lemna gibba* [EU DAR (EC 2012); Report No. 55093240], which is the most sensitive endpoint.

Soil toxicity

Table 19 contains the acute and chronic soil toxicity test results for the active ingredient metobromuron.
Table 20 contains the acute and chronic soil toxicity test results for the relevant metabolites of metobromuron.
Table 21 contains the acute and chronic soil toxicity test results for the formulated product SOLETO.
Values in **bold** are those used for the risk assessment. Underlined values are those used to determine the classification.

Table 19: Summary of soil toxicity data for metobromuron

Test species	Test type and duration	Endpoint value	Reference
Earthworm, *Eisenia fetida*	Acute, 14-d LC_{50}	**233.5 mg ai/kg soil dw**[1] [uncorrected value 467 mg ai/kg soil dw]	EU DAR (EC 2012); Report No. C3126-0292

[1] Original toxicity endpoints from the artificial soil tests have been divided by 2 to account for different soil characteristics and the possibility of reduced bioavailability for soil organisms of lipophilic substances (Log P_{ow} >2) as per the EFSA Technical Report (EFSA 2015)

Table 20: Summary of soil toxicity data for major metabolite desmethoxy-metobromuron

Test species	Test type and duration	Endpoint value	Reference
Earthworm, *Eisenia fetida*	Acute, 14-d LC_{50}	>1000 mg/kg soil dw	EU DAR (EC 2012); Report No. 60193021
Soil microbial function			
Soil microflora	Nitrogen mineralisation, 28 days	Did not cause adverse effects on nitrogen content (mineral nitrogen) up to a rate of 3.15 mg/kg dry weight	EU DAR (EC 2012); Report No. 60194080
	Carbon mineralisation, 28 days	Did not cause adverse effects on carbon transformation up to a rate of 3.15 mg/kg dry weight	

Table 21: Summary of soil toxicity data for SOLETO

Test species	Test type and duration	Uncorrected endpoint value	Corrected endpoint value[1]	Reference
Earthworm, *Eisenia fetida*	Reproduction, NOEC	281.4 mg formulation/kg soil dw, equivalent to 119.8 mg ai/kg soil dw	140.7 mg formulation/kg soil dw, equivalent to **59.9 mg ai/kg soil dw**	EU DAR (EC 2012); Report No. 54822022
Springtail, *Folsomia candida*	LC_{50}/EC_{50} (14-days)	>95 mg formulation/kg soil dw, equivalent to 40.4 mg ai/kg soil dw	>47.5 mg formulation/kg soil dw, equivalent to 20.2 mg ai/kg soil dw	EU DAR (EC 2012); Report No. 55098016
	NOEC, mortality (14-days)	>95 mg formulation/kg soil dw, equivalent to 40.4 mg ai/kg soil dw	>47.5 mg formulation/kg soil dw, equivalent to 20.2 mg ai/kg soil dw	
	NOEC, reproduction (14-days)	55.6 mg formulation/kg soil dw, equivalent to 23.7 mg ai/kg soil dw	27.8 mg formulation/kg soil dw, equivalent to **11.85 mg ai/kg soil dw**	
Soil mite, *Hypoaspis aculeifer*	LC_{50}/EC_{50} (14-days)	>95 mg formulation/kg soil dw, equivalent to 40.4 mg ai/kg soil dw	>47.5 mg formulation/kg soil dw, equivalent to 20.2 mg ai/kg soil dw	EU DAR (EC 2012); Report No. 55097089
	NOEC, mortality (14-days)	>95 mg formulation/kg soil dw, equivalent to 40.4 mg ai/kg soil dw	>47.5 mg formulation/kg soil dw, equivalent to 20.2 mg ai/kg soil dw	
	NOEC, reproduction (14-days)	55.6 mg formulation/kg soil dw, equivalent to 23.7 mg ai/kg soil dw	27.8 mg formulation/kg soil dw, equivalent to **11.85 mg ai/kg soil dw**	
Terrestrial plants				
Six dicot and four monocot crop species	Vegetative vigour, 21 days Lowest ER_{50}	*Fresh weight* **0.19 L substance/ha, equivalent to 97.34 g ai/ha** (Sugar beet, *Beta vulgaris*)	N/A	EU DAR (EC 2012); Report No. ACE-10-002
	Lowest NOER	*Fresh weight*	N/A	

Test species	Test type and duration	Uncorrected endpoint value	Corrected endpoint value[1]	Reference
		0.0307 L formulation/ha, equivalent to 15.73 g ai/ha (Spinach, *Spinacia oleraceae*)		
Six dicot and four monocot crop species	Seedling emergence, 21 days Lowest ER_{50}	*Fresh weight* 0.11 L formulation/ha, equivalent to **56.35 g ai/ha** (onion, *Allium cepa*)	N/A	EU DAR (EC 2012); Report No. ACE-10-001
	Lowest NOER	*Fresh weight* 0.0123 L formulation/ha, equivalent to **6.30 g ai/ha** (onion, *Allium cepa*)	N/A	
Soil microbial function				
Soil microbial function	Nitrogen mineralisation, 28 days	Did not cause adverse effects on nitrogen content (mineral nitrogen) up to a rate of 6.59 mg formulation/kg dry weight, equivalent to 2.73 mg ai/kg dry soil[2]. **Tolerable adverse effects (<25%) on nitrogen content (mineral nitrogen) up to a rate of 65.87 mg formulation/kg dry weight, equivalent to 27.32 mg ai/kg dry soil[2]**	N/A	EU DAR (EC 2012); Report No. 54823080
	Carbon mineralisation, 28 days	**Did not cause adverse effects on carbon transformation up to a rate of 65.87 mg formulation/kg dry weight, equivalent to 27.32 mg ai/kg dry soil[2]**	N/A	

[1] Original toxicity endpoints from the artificial soil tests have been divided by 2 to account for different soil characteristics and the possibility of reduced bioavailability for soil organisms of lipophilic substances (Log P_{ow} >2) as per the EFSA Technical Report (EFSA 2015)
[2] Based on the density reported in the "Concentrations tested" section in EU DAR (EC 2012) Report No. 54823080.

Metabolites

Results from a range of ecotoxicity studies on earthworms and soil microbes (see Table 18) show that the metabolite desmethoxy-metobromuron (from metobromuron) shows less toxicity compared with the parent substance (metobromuron). Desmethoxy-metobromuron was shown to be slightly more persistent than metobromuron based on a calculated 80th percentile DT_{50lab} of 45.4 days.

Formulation

Toxicity to soil organisms of the formulated product SOLETO cannot be directly compared with that of the pure active ingredient metobromuron since data are not available for the same test species. This is with exception to soil microflora which indicated no increase in toxicity when using the formulated product.

Uncertainties and data gaps

No data gaps or uncertainties were identified.

General conclusion about soil toxicity

The active ingredient metobromuron does not trigger the HSNO thresholds for toxicity to soil organisms based on active ingredient data (earthworms) provided by the applicant.
As Soleto is a herbicide, the toxicity of Soleto to non-target plants has been used to classify the hazard of metobromuron in the soil environment. When the content of metobromuron in Soleto is considered, a 9.2A hazard classification (very ecotoxic in the soil environment) is triggered.
This is based on the lowest EC_{50} of 56.35 g ai/ha, equivalent to 0.075 mg ai/ka dw, for onion, *Allium cepa* [EU DAR (EC 2012); Report No. ACE-10-001], which is the most sensitive endpoint. This hazard classification is expected for a herbicide.

The end-use product Soleto triggers a 9.2A hazard classification (very ecotoxic in the soil environment) based on the lowest EC_{50} of 0.11 L formulation/ha, equivalent to 0.177 mg formulation/kg dw, for onion, *Allium cepa* [EU DAR (EC 2012); Report No. ACE-10-001], which is the most sensitive endpoint.

Terrestrial vertebrate toxicity

For effects on terrestrial vertebrates other than birds, refer to the mammalian toxicity section.

Table 22 contains the acute and chronic avian toxicity test results for the active ingredient metobromuron. Values in **bold** are those used for the risk assessment. Underlined values are those used to determine the classification.

Table 22: Summary of terrestrial vertebrate toxicity data for metobromuron

Test species	Test type and duration	Endpoint values	Reference
Japanese quails *Coturnix coturnix japonica*	Acute oral LD_{50}	**1429 mg ai/kg bw**	EU DAR (EC 2012); Report No. C3126 0030
	8-d dietary LC_{50}	>274.1 mg ai/kg bw/d	EU DAR (EC 2012); Report No. C3126 0031
Bobwhite quail, *Colinus virginianus*	Reproductive 1 generation, 22 weeks NOEL	22.1 mg ai/kg bw/d (males) **21.6 mg ai/kg bw/d (females)**	EU DAR (EC 2012); Report No. GHQ0001

Uncertainties and data gaps

No data were generated for the end-use product SOLETO but a waiver was provided by the applicant justifying assessing the risk to birds based on the toxicity of the individual active substance. Therefore no data gaps or uncertainties were identified.

General conclusion about ecotoxicity to terrestrial vertebrates

The active ingredient metobromuron triggers a 9.3C hazard classification based on the acute oral LD_{50} of 1429 mg ai/kg bw determined for the Japanese quail *Coturnix coturnix japonica* [(EC 2012): Report No. C3126 0030], which is the most sensitive endpoint.

The end-use product SOLETO does not trigger a 9.3 hazard classification based on mixture rules.

Terrestrial Invertebrates toxicity

Pollinators

Acute toxicity

Table 23 contains the acute toxicity test results for the active ingredient metobromuron for pollinators.

Table 24 contains the acute toxicity test results for the end-use product SOLETO for pollinators.

Table 23: Summary of pollinator toxicity data for metobromuron

Test species	Test type and duration	Endpoint value	Reference
Honeybee, *Apis mellifera (adult)*	Acute oral, 48-hr LD_{50}	>86 µg ai/bee	Appendix J; Table 63 Report No. 20140150
	Acute contact, LC_{50}	>100 µg ai/bee	
Honeybee, *Apis mellifera* (larval)	LD_{50} (7-day repeat exposure)	22.43 µg ai/bee	Appendix J; Table 64; Report No. 20140152
	NOED (7-day repeat exposure)	**6.25 µg ai/bee**	

It is noted that metobromuron showed some toxicity in the honey bee larvae study.

Table 24: Summary of pollinator toxicity data for SOLETO

Test species	Test type and duration	Endpoint value	Reference
Honeybee, *Apis mellifera* (adult)	Acute oral, 48-hr LD_{50}	**119.1 µg formulation/bee, equivalent to 50.68 µg ai/bee**	EU DAR (EC 2012); Report No. 54815035
	Acute contact, LC_{50}	**>200 µg formulation/bee, equivalent to >85.10 µg ai/bee**	

Field studies

The endpoints resulting from the acute oral and contact studies did not trigger the requirement for any higher tier pollinator field studies to be performed.

Uncertainties and data gaps

No data gaps identified.

Non-target arthropods

Tier I – Laboratory studies

Table 25 contains the Tier I laboratory studies conducted with SOLETO on non-target arthropods.

Table 25: Summary of Tier I laboratory toxicity data on non-target arthropods for SOLETO

Test species	Test type and duration	Endpoint value	Reference
Parasitic wasp, *Aphidius rhopalosiphi*	48-hr LR_{50} Laboratory glass plate	**>8000 mL formulation/ha, equivalent to >4098.4 g ai/ha**	EU DAR (EC 2012); Report No. 54816001
Predatory Mite, *Typhlodromus pyri*	48-hr LR_{50} (mortality) Laboratory glass plate	**99.9 mL formulation/ha, equivalent to 51.18 mg ai/ha**	EU DAR (EC 2012); Report No. 54817063

Tier II – Extended laboratory studies

Table 26 contains the higher tier studies conducted with SOLETO on non-target arthropods.

Table 26: Summary of higher tier toxicity data on non-target arthropods for SOLETO

Test species	Test type and duration	Endpoint values	Reference
Extended Laboratory			
Predatory mite, *Typhlodromus pyri*	7-day LR_{50} (dose response test)	LR_{50} 130 mL formulation/ha, equivalent to 66.6 mg ai/ha	EU DAR (EC 2012); Report No. 54828062
	7-day NOER (dose response test)	**127 mL formulation/ha, equivalent to 65.1 g ai/ha**	
Predatory mite, *Typhlodromus pyri*	7-day LR_{50} - fresh residues (aged residue test)	**>4000 mL formulation/ha, equivalent to >2049.2 g ai/ha**	EU DAR (EC 2012); Report No. 55096060
	7-day NOER - fresh residues (aged residue test)	<4000 mL formulation/ha, equivalent to >2049.2 g ai/ha[1]	
	7-day LR_{50} - aged residues, 7 days (aged residue test)	>4000 mL formulation/ha, equivalent to >2049.2 g ai/ha	
	7-day NOER - aged residues, 7 days (aged residue test)	4000 mL formulation/ha, equivalent to >2049.2 g ai/ha	
Rove beetles, *Aleochara bilineata*	28-day NOER	**4000 mL formulation/ha, equivalent to >2049.2 g ai/ha**	EU DAR (EC 2012); Report No. 54818071
Wolf spider, *Pardosa spec.*	14-day LR_{50}	**>4000 mL formulation/ha, equivalent to >2049.2 g ai/ha**	EU DAR (EC 2012); Report No. 54819066

[1] Limit test conducted at 4 L formulation/ha. Significant effect on mortality and reproduction at application rate when predatory mites are exposed to freshly dried residues. Mortality (corr) at 4 L formulation/ha was 40.6% at day 0, and 15.1% at day 7. Effect on reproduction at 4 Lformulation/ha was 39.3% at day 0 and 16.8% at day 7.

Some toxicity was demonstrated in the laboratory glass plate study performed with *Typhlodromus pyri*. Tier II studies were also conducted for the formulation SOLETO. The predatory mites were still sensitive to SOLETO with a 48-hr LR_{50} of 99.9 mL product/ha when exposed to freshly dried residues on apple leaves. This sensitivity was also apparent in the first bioassay of the aged residue study. Sensitivity was less when predatory mites were exposed to SOLETO residues 7 days after application at 4 L product/ha. No significant effect on mortality (based on corrected mortality), or reproduction were observed at 4 L product/ha.

The applicant also provided two additional Tier II studies for rove beetles and wolf spiders. No significant effects were observed at the highest rate tested (4 L formulation/ha) for rove beetles. Only one application rate (4 L formulation/ha) was tested for wolf spiders. A statistically significant effect on mortality was reported (26.5%), therefore the LR_{50} is >4 L formulation/ha.

Semi-field studies

The data provided by the applicant for non-target arthropods did not trigger the requirement for any semi-field studies.

Field studies

The data provided by the applicant for non-target arthropods did not trigger the requirement for any field studies.

Uncertainties and data gaps

No data gaps identified.

General conclusion in terms of classification for terrestrial invertebrate toxicity

The active ingredient metobromuron does not trigger the HSNO thresholds for toxicity to terrestrial invertebrates based on the data available.

The end-use product SOLETO does not trigger the HSNO thresholds for toxicity to terrestrial invertebrates based on the data available.

Appendix F: Hazard classification of metobromuron and SOLETO

The hazard classifications of metobromuron and SOLETO are listed in Table 27 and Table 28 respectively.

Table 27: EPA classifications of the active ingredient metobromuron

Hazard Class/Subclass			Classification	Method of classification		Remarks
				Test results	Read across	
Physical/Chemical properties						
Class 1 Explosiveness			No	☒	☐	EU DAR (EC 2012)
Class 2, 3 & 4 Flammability			No	☒	☐	EU DAR (EC 2012)
Class 5 Oxidisers/Organic Peroxides			No	☒	☐	EU DAR (EC 2012)
Subclass 8.1 Metallic corrosiveness			No	☒	☐	EU DAR (EC 2012)
Toxic properties						
Subclass 6.1	Acute toxicity	oral	6.1E	☒	☐	LD_{50} = 2603 mg/kg bw (rat) LD_{50} = 2098 mg/kg bw (mouse)
		dermal	No	☒	☐	LD_{50} > 3000 mg/kg bw
		inhalation	No	☒	☐	LC_{50} >1.6 mg/L (highest obtainable concentration)

Hazard Class/Subclass		Classification	Method of classification		Remarks
			Test results	Read across	
	Aspiration hazard	No	☒	☐	Active ingredient is a solid
Subclass 6.3/8.2 Skin irritancy/corrosion		No	☒	☐	No evidence of irritation in a non-guideline study.
Subclass 6.4/8.3 Eye irritancy/corrosion		No	☒	☐	Mean Draize score below threshold for classification
Subclass 6.5A Respiratory sensitisation		ND	☐	☐	No test guidelines are available to assess respiratory sensitisation.
Subclass 6.5B Contact sensitisation		6.5B	☒	☐	Positive sensitisation result
Subclass 6.6 Mutagenicity		No	☒	☐	*In vitro* and *in vivo* tests are negative
Subclass 6.7 Carcinogenicity		6.7B	☒	☐	Studies in rat demonstrated a small increase in two types of tumours one in females and one in males which cannot be discounted as being of human relevance (see Appendix C).
Subclass 6.8 Reproductive/ developmental toxicity		No	☒	☐	No evidence of toxicity was observed in offspring in the developmental or the 2-generation reproductive toxicity studies
Subclass 6.8 Reproductive/ developmental toxicity (*via* lactation)		No	☒	☐	No evidence of toxicity was observed in offspring in the 2-generation reproductive study

Hazard Class/Subclass		Classification	Method of classification		Remarks
			Test results	Read across	
Subclass 6.9 Target organ systemic toxicity	oral	6.9B	☒	☐	The LOAEL from all the repeated dose oral toxicity studies were below the 100 mg/kg bw/d threshold value for classification
	dermal	ND	☐	☐	
	inhalation	ND	☐	☐	
Ecotoxic properties					
Subclass 9.1 Aquatic ecotoxicity		9.1A	☒	☐	7-day E_rC_{50} 0.31 mg ai/L, duckweed *Lemna gibba*
Subclass 9.2 Soil ecotoxicity		9.2A	☒	☐	Seedling emergence EC_{50} of 56.35 g a.i./ha, equivalent to 0.075 mg ai/kg dw, for onion, *Allium cepa*
Subclass 9.3 Terrestrial vertebrate ecotoxicity		9.3C	☒	☐	Acute oral LD_{50} of 1429 mg ai/kg bw, Japanese quail *Coturnix coturnix japonica*
Subclass 9.4 Terrestrial invertebrate ecotoxicity		No	☒	☐	

NA: Not Applicable.

ND: No Data or poor quality data [according to Klimisch criteria (Klimisch, Andreae et al. 1997)]. There is a lack of data for one or more components.

No: Not classified based on actual relevant data available for the substance. The data are conclusive and indicate the threshold for classification is not triggered.

Metobromuron is of relatively low acute toxicity in mammals and should be classified 6.1E by oral route only. It is not a skin or eye irritant, but is a contact sensitiser and is classified as 6.5B. Metobromuron was found not to be genotoxic, but should be classified as a suspected human carcinogen (6.7B). It does

not cause reproductive or developmental toxicity. Results of repeated dose oral toxicity studies in laboratory animals indicate it should be classified for systemic organ toxicity (6.9B). Metobromuron is also very ecotoxic to the aquatic environment, soil organisms and slightly toxic to terrestrial vertebrates (9.1A, 9.2A and 9.3C), it is however, not toxic to terrestrial invertebrates.

Table 28: Applicant and EPA classifications of SOLETO[1]

Hazard Class/Subclass			Mixture classification by:		Method of classification			Remarks
			Applicant	EPA	Mixture data	Read across	Mixture rules	
Physical/Chemical properties								
Class 1 Explosiveness			No	No	☐	☐	☒	SOLETO is an aqueous-based solution
Class 2, 3 & 4 Flammability			No	No	☐	☐	☒	SOLETO is an aqueous-based solution
Class 5 Oxidisers/Organic Peroxides			No	ND	☐	☐	☐	
Subclass 8.1 Metallic corrosiveness			No	ND	☐	☐	☐	
Toxic properties								
Subclass 6.1	Acute toxicity	oral	**No**	**6.1E**	☒	☐	☐	Although the LD_{50} was >2000 mg/kg bw animals showed signs of toxicity
		dermal	No	No	☒	☐	☐	LD_{50} > 2000 mg/kg bw

[1] Use of mixture rules may not adequately take into account interactions between different components in some circumstances and must be considered of lower reliability than substance (formulation) data.

Hazard Class/Subclass			Mixture classification by:		Method of classification			Remarks
			Applicant	EPA	Mixture data	Read across	Mixture rules	
		inhalation	No	No	☒	☐	☐	LC_{50} >4.15 mg/L
	Aspiration hazard		No	No	☐	☐	☐	Substance is an aqueous-based solution
Subclass 6.3/8.2 Skin irritancy/corrosion			No	No	☒	☐	☐	Mean Draize score below threshold for classification
Subclass 6.4/8.3 Eye irritancy/corrosion			No	No	☒	☐	☐	Mean Draize score below threshold for classification
Subclass 6.5A Respiratory sensitisation			**No**	**ND**	☐	☐	☐	No test guidelines are available to assess respiratory sensitisation.
Subclass 6.5B Contact sensitisation			No	No	☒	☐	☐	Negative sensitisation result
Subclass 6.6 Mutagenicity			**No**	**ND**	☐	☐	☒	ND is due to data missing from several very minor non-active components. The significance of this data absence is believed to be minimal.
Subclass 6.7 Carcinogenicity			**6.7**	**6.7B**	☐	☐	☒	Based on metobromuron
Subclass 6.8 Reproductive/ developmental toxicity			**No**	**ND**	☐	☐	☒	ND is due to data missing from several very minor non-active components. The significance of this

Hazard Class/Subclass		Mixture classification by:		Method of classification			Remarks
		Applicant	EPA	Mixture data	Read across	Mixture rules	
							data absence is believed to be minimal.
Subclass 6.8 Reproductive/ developmental toxicity (*via* lactation)		**No**	**ND**	☐	☐	☒	ND is due to data missing from several very minor non-active components. The significance of this data absence is believed to be minimal.
Subclass 6.9 Target organ systemic toxicity	oral	6.9B	6.9B	☐	☐	☒	Based on metobromuron
	dermal	**No**	**ND**	☐	☐	☒	There is an absence of repeated dose dermal toxicity data from almost all components.
	inhalation	**No**	**ND**	☐	☐	☒	There is an absence of repeated dose inhalation toxicity data from almost all components.
Ecotoxic properties							
Subclass 9.1 Aquatic ecotoxicity		9.1A	9.1A	☒	☐	☐	7-day E_rC_{50} 0.73 mg formulation/L, duckweed *Lemna gibba*
Subclass 9.2 Soil ecotoxicity		9.2A	9.2A	☒	☐	☐	Seedling emergence EC_{50} of 0.11 L formulation/ha, equivalent to 0.177 mg formulation/kg dw, for onion, *Allium cepa*

Hazard Class/Subclass	Mixture classification by:		Method of classification			Remarks
	Applicant	EPA	Mixture data	Read across	Mixture rules	
Subclass 9.3 Terrestrial vertebrate ecotoxicity	No	ND	☐	☐	☒	
Subclass 9.4 Terrestrial invertebrate ecotoxicity	No	No	☒	☐	☐	

NA: Not Applicable. For instance testing for a specific endpoint may be omitted if it is technically not possible to conduct the study as a consequence of the properties of the substance: eg very volatile, highly reactive or unstable substances cannot be used, mixing of the substance with water may cause danger of fire or explosion or the radio-labelling of the substance required in certain studies may not be possible.

ND: No Data or poor quality data [according to Klimisch criteria (Klimisch, Andreae et al. 1997)]. There is a lack of data for one or more components.

No: Not classified based on actual relevant data available for the substance or all of its components. The data are conclusive and indicate the threshold for classification is not triggered.

Mammalian toxicity studies with SOLETO demonstrated it has relatively low acute toxicity in mammals and should be classified 6.1E for acute toxicity by the oral exposure route. It is not a skin or eye irritant, or a contact sensitiser. Based on mixture rules it should be classified for suspected human carcinogenicity (6.7B) and target organ systemic toxicity (6.9B, oral). Based on test data for the formulation, SOLETO should be classified 9.1A. Based on mixture rules and formulation data, SOLETO should also be classified 9.1A and 9.2A, but does not require classification as toxic to terrestrial vertebrates or invertebrates.

The EPA classification of SOLETO differed from that of the applicant as the applicant classifying several end points as “No” whereas the EPA used ND in the absence of data on many of the minor inactive components.

Appendix G: Human health risk assessment

Quantitative risk assessment

The operator exposure assessment is based on a modification of the approach used by European regulators, taking into account New Zealand specific factors. The model is based on the results of actual measurements carried out in the field and has an established history of providing reliable and reproducible results.

The re-entry worker exposure assessment is based on a modification of the approach used by European regulators and the US-EPA. The parameters for the modelling are based on empirical data relating to measurements of dermal exposure of workers from contact with residues on foliage for various activities and the amount of foliar residues that are dislodgeable.

The bystander exposure assessment is based on a modification of the approaches used by European regulators and the US-EPA. Spray drift deposition from ground based application is estimated using the AgDrift model using the curves produced by the Australian Pesticides and Veterinary Medicines Authority [APVMA, (APVMA 2010)]. The parameters are based on empirical data. Spray drift deposition from aerial application is estimated using the AGDISP model along with appropriate New Zealand input parameters.

Full details of the methodology can be found in the EPA risk assessment methodology document (EPA 2020).

To assess risks the predicted systemic exposures to the active ingredient(s) are compared with an acceptable operator exposure limit (AOEL) for the active ingredient and a risk quotient (RQ) is calculated. RQ values greater than one indicate that predicted exposures are greater than the AOEL and potentially of concern. RQ values below one indicate that predicted exposures are less than the AOEL and are not expected to result in adverse effects.

Input values for the human health risk assessment

Reference doses for metobromuron established by internationally reputable regulatory authorities are summarised in Table 29.

Table 29: Reference doses established by regulators for metobromuron

Available international Reference doses	Key systemic effect	NOAEL (LOAEL) mg/kg bw/d	Uncertainty factors	Reference value mg/kg bw/d	EPA modifications	Remarks
ADI - (EFSA 2014)	Increased Heinz bodies, extramedullary haematopoiesis in mice at 1 year.	0.8	100	0.008	None	The EPA disagrees that the NOAEL for the study in mice is 0.8 mg/kg bw/day. The EPA selected next highest dose (3 mg/kg bw/day) which is the 1 year chronic toxicity NOAEL. This is also the 2 year NOAEL for tumours in rats (after rounding).

The relevant toxicity studies that were considered to derive an acceptable operator exposure level (AOEL) for metobromuron are summarised in Table 30. The AOEL derived by EFSA was based on the results of a one year study in dogs. Beagle dogs are known to have a deficiency of methaemoglobin reductase in their erythrocytes. Due to this biological sensitivity it is likely responsible for the lower NOAEL (based on methaemoglobinaemia) compared to what was observed in the rodent studies. Accordingly, the NOAEL's utilized in the EPA risk assessment for establishing an AOEL were based on rodent data. For both rats and mice, the NOAEL is 0.03 mg/kg bw/day (after rounding).

Table 30: Summary of studies relevant for establishing an AOEL

Key systemic effect	NOAEL mg/kg bw/day	Uncertainty factors	Absorption factor	AOEL mg/kg bw/day	Justification
Haematological effects (1 year dog study)	1.6	100	1.0	0.016	EFSA derivation of the AOEL based on dogs. EPA considers over precautionary.
Haematological (methaemoglinaemia, regenerative anaemia), increased organ weight	3.1	100	1	0.030	A one year interim sacrifice of rats as part of the carcinogenicity study

Key systemic effect	NOAEL mg/kg bw/day	Uncertainty factors	Absorption factor	AOEL mg/kg bw/day	Justification
(spleen weight), and haemosiderin deposition (spleen, liver) – rats 1 year chronic toxicity phase					
Haematological effects (Increased Heinz bodies) – mouse 1 year chronic toxicity phase	3.0	100	1	0.031	A one year interim sacrifice of mice as part of the carcinogenicity study

Other input values for the exposure assessment are summarised in Table 31.

The results of an *in vitro* dermal absorption study for SOLETO indicated the absorption rate for the formula concentrate was 0.48 ± 0.07% and for the “in use” field dilution was 6.31 ± 0.83%.

Table 31: Input values for human exposure modelling

Physical form	Concentration of metobromuron (g/L)	Maximum application rate g ai/ha	Dermal absorption (%)		AOEL mg/kg bw/day
			Concentrate	Spray	
liquid	500	2000	0.48	6.3	0.03

Operator exposure assessment

The results of the operator exposure assessment are shown in Table 32.

Table 32: Output of operator mixing, loading and application exposure assessment for metobromuron

Exposure Scenario	Estimated operator exposure (mg/kg bw/d)	Risk Quotient
Boom		
No personal protective equipment (PPE)[2] during mixing, loading and application	0.2023	6.74
Gloves only during mixing and loading	0.1875	6.25
Gloves only during application	0.1716	5.72
Full PPE during mixing, loading and application (excluding respirator)	0.0148	0.49
Full PPE during mixing, loading and application (including FP1, P1 and similar respirator achieving 75 % inhalation exposure reduction)	0.0131	0.44
Full PPE during mixing, loading and application (including FP2, P2 and similar respirator achieving 90 % inhalation exposure reduction)	0.0127	0.42

[2] ‘Full PPE’ includes: gloves, hood/visor, coveralls, and heavy boots during application and gloves during mixing and loading.

Predicted operator exposures to metobromuron are below the Acceptable Operator Exposure Level (AOEL), provided full PPE (gloves, hood/visor, coveralls, and heavy boots without a respirator) is worn during mixing, loading, and application. Therefore operator exposures are not expected to result in adverse health effects, if PPE is worn.

Re-entry worker exposure assessment

Worker re-entry was not quantitatively assessed as there are no models to assess worker re-entry following the application of a pre-emergent crop herbicide. As there would be minimal need for worker re-entry following use of SOLETO a qualitative assessment was performed. Any re-entry to a field after application would not be associated with significant dermal contact to the sprayed weeds. Predicted exposures to metobromuron for workers re-entering and working in areas where SOLETO has been applied would qualitatively be deemed to be below the AOEL. No re-entry intervals are necessary.

Quantitative bystander risk assessment

It is considered that the main potential source of exposure to the general public for substances of this type (other than via food residues which will be considered as part of the registration of this substance under the Agricultural Compounds and Veterinary Medicines (ACVM) Act 1997) is via spray drift. In terms of bystander exposure, toddlers are regarded as the most sensitive sub-population and are regarded as having the greatest exposures. For these reasons, the risk of bystander exposure is assessed in this sub-population. The AOEL calculated for the operator and re-entry worker exposure assessments has been used for the bystander assessment, as the use of an oral chronic reference dose (CRfD) is usually likely to be over precautionary.

The results of the bystander exposure assessment are summarised in Table 33.

Table 33: Output of the bystander exposure assessment for metobromuron

Exposure Scenario	Estimated exposure of 15 kg toddler exposed through contact to surfaces 8 m from an application area (µg/kg bw/d)	Risk Quotient	Buffer zone needed to reduce toddler exposure to the AOEL
Boom			
High boom, fine droplets	4.02	0.1340	0
High boom, coarse droplets	0.64	0.0213	0
Low boom, fine droplets	1.36	0.0452	0
Low boom, coarse droplets	0.32	0.0108	0

Estimated bystander exposure from spray drift after application of SOLETO to weeds associated with pre-emergent potatoes is below the AOEL. No buffer zone of is required in protect bystanders.

Exposure via groundwater

The ecotoxicity assessment identified that the PEC_{gw} (peak environmental concentration in ground water) in the EPA's calculation is 1.46 µg/L which exceeds the EU trigger concentration of 0.1 µg/L. Therefore this concentration was assessed in comparison to the human health PDE (Drinking Water) to ensure that this concentration would not present a human health concern if the ground water were used for human consumption. The PDE (Drinking Water) is 0.006 mg/kg bw/day. For an adult of 70 kg the appropriate maximum acceptable concentration (MAV) in drinking water is given by the following calculation assuming the daily drinking water consumption for the 70 kg adult is 2 litres per day:

(0.006 x 70)/2 = 0.21 mg/L

It is appropriate to compare this value (210 µg/L) with the PEC_{gw} of 1.46 µg/L. The conclusion is that the likely ground water concentration of metobromuron is well below the level of concern in relation to human drinking water consumption.

Conclusions of the human health risk assessment

It is considered that the risks to human health from the proposed use of SOLETO are acceptable with the use of appropriate Personal Protective Equipment (PPE). No Restricted Entry Intervals (REI) or buffer zones are recommended. The expected concentration in groundwater is well below the level of concern in relation to human drinking water consumption.

Appendix H: Environmental risk assessment

Aquatic risk assessment

The basis for the aquatic risk assessment is a comparison of the Expected Environmental Concentrations (EEC) with toxicity endpoints to which safety factors have been applied. The EEC is divided by the toxicity endpoint to calculate a risk quotient (RQ) value. The methodology for the aquatic risk assessment, including the level of concern (LOC) ascribed to specific RQ values, is described in detail in the EPA standard risk assessment methodology (EPA 2020).

Calculation of expected environmental concentrations

The parameters used in GENEEC2 modelling are listed in Table 34.

Table 34: Input parameters for GENEEC2 analysis for the active ingredient metobromuron

Parameter	Value
Crop(s)	Potato
Application rate (kg ai/ha)	2.0
Application frequency	1
Application interval (days)	N/A
Kd (mL/g)	2.21
Aerobic soil DT_{50} (days)	73.3 (longest field value, worst-case approach)
Pesticide wetted in?	No
Methods of application	High ground boom sprayer (medium droplet size)
'No spray' zone	0
Water solubility (ppm)	328
Hydrolysis (DT_{50} in days)	Stable at 20ºC
Aerobic aquatic $DT_{50\ whole\ system}$(days)	34.5
Aqueous photolysis DT_{50} (days)	12.6

Output from the GENEEC2 model

RUN No. 1 FOR Metobromuron ON Potato * INPUT VALUES *

RATE (#/AC) ONE(MULT)	No.APPS & INTERVAL	SOIL Kd	SOLUBIL (PPM)	APPL TYPE (%DRIFT)	NO-SPRAY ZONE(FT)	INCORP (IN)
1.781(1.781)	1 1	2.2	328.0	GRHIME(1.2)	0.0	0.0

FIELD AND STANDARD POND HALFLIFE VALUES (DAYS)

METABOLIC (FIELD)	DAYS UNTIL RAIN/RUNOFF	HYDROLYSIS (POND)	PHOTOLYSIS (POND-EFF)	METABOLIC (POND)	COMBINED (POND)
73.30	2	0.00	12.60- 1562.40	34.50	33.75

GENERIC EECs (IN MILLIGRAMS/LITER (PPM)) Version 2.0 Aug 1, 2001

PEAK GEEC	MAX 4 DAY AVG GEEC	MAX 21 DAY AVG GEEC	MAX 60 DAY AVG GEEC	MAX 90 DAY AVG GEEC
328.00	328.00	328.00	328.00	328.00

The maximum (peak) Estimated Environmental Concentrations (EEC) for the active ingredient metobromuron following application of the formulated product SOLETO to potatoes as estimated by GENEEC2 is 328 mg/L.

Calculated risk quotients

The calculated acute risk quotients for each trophic level considering the above EEC and lowest relevant toxicity figures are presented in Table 35. The calculated chronic risk quotients are presented in Table 36.

Table 35: Acute risk quotients derived from the GENEEC2 model and toxicity data

Species	Peak EEC from GENEEC2 (mg/L)	LC_{50} or EC_{50} (mg/L)	Acute RQ	Conclusion
Fish, *Oncorhynchus mykiss*	328	>42.6[1]	<7.70	**Above the LOC for threatened/non-threatened species**
Crustacea, *Daphnia magna*	328	>42.6[1]	<7.70	**Above the LOC for threatened/non-threatened species**
Algae, *Pseudokirchneriella subcapitata*	328	0.59[1]	555.93	**Above the LOC for non-threatened species[2]**
Aquatic plants, *Lemna gibba*	328	0.31[1]	1058.06	**Above LOC for threatened/ non-threatened species**

[1] Values calculated using ai content in formulation
[2] No threatened species of algae are identified in New Zealand

Table 36: Chronic risk quotients derived from the GENEEC2 model and toxicity data

Species	Relevant EEC from GENEEC2 (mg/L)[1]	NOEC (mg/L)	Chronic RQ	Conclusion
Fish, *Oncorhynchus mykiss*	328	0.50	656	**Above the LOC for threatened/non-threatened species**
Crustacea, *Daphnia magna*	328	>10	<32.8	**Above the LOC for threatened/non-threatened species**

[1] In both cases the 21-day Expected Environmental Concentration (EEC) was closest to the exposure duration of the study selected for risk assessment purposes

Using GENEEC2 to model the application of the formulated product SOLETO to potatoes, calculated acute and chronic risk quotients are above the LOC for non-threatened and threatened species of fish, aquatic invertebrates, alga and aquatic plants.

Refinement of the aquatic risk assessment

Predicted exposures are above the LOC for chronic risks to non-threatened and threatened species (fish, crustacea, algae and aquatic plants) metobromuron following application of SOLETO for the application to potatoes. Further modelling was performed as risks were identified to consider whether buffer zones may be able to mitigate risks from spray drift and runoff.

Spray drift

The Agdrift model was used to calculate the required downwind buffer zone to protect the aquatic environment from adverse effects of the substance due to spray drift using high boom [see Table 37 and relevant spray drift scenarios (APVMA 2010)].

Exact buffer zones are impractical and too precise to be applied in the real world. Therefore, the buffer zone distance is rounded so it can be visualized and remembered by end-users.

Table 37: Input parameters and calculation of spray drift buffer zone for the refined risk assessment of metobromuron

Input parameters	Potato
Application rate (g ai/ha)	2000
Number of applications (max)	1
Application interval	N/A
Application method	High ground boom sprayer (medium droplet size)
Koc (mL/g)	117
$DT_{50\ soil}$	73.3 days (longest field value, worst-case approach)
$DT_{50\ whole\ system}$	34.5 days
Toxicity endpoint (mg/L)	0.31 (*Lemna gibba* test conducted with the formulation)
Assessment factor	20
Buffer zone (m) - model	2
Buffer zone (m) – control	5

A downwind buffer zone of 5 m is recommended for the use of Soleto containing metobromuron on bare soil to mitigate the risks to aquatic organisms.

Runoff

The REXTOX model was also used to calculate the required buffer zone to protect the aquatic environment from adverse effects of the substance due to runoff (see Table 38).

Table 38: Input parameters and calculation of runoff buffer zone for the refined risk assessment

Input parameters	Potato
Application rate (g ai/ha)	2000
K_d (mL/kg)	2.21
$DT_{50\ soil}$ (days)	73.3 (longest field value, worst-case approach)
Crop interception	0
Slope	4%[1]
Toxicity endpoint (mg/L)	0.31 (*Lemna gibba* test conducted with the formulation)
Assessment factor	20
Buffer zone (m) – model	4
Buffer zone (m) – control	5

[1] A 4% slope has been considered as realistic worst-case value for applications to potatoes in the absence of any quantitative data in regard to slopes and potato growing. Slopes of 2 to 4% are considered "intermediate case" in terms of slope steepness in the "Generic guidance for FOCUS surface water scenarios" (FOCUS 2015). It is expected that for the majority of the time, potatoes would not be grown on steeper slopes (>4%).

A buffer zone of 5 m is recommended for the use of Soleto containing metobromuron on bare soil to mitigate the risks due to runoff to aquatic organisms.

Uncertainties and data gaps

No data gaps identified.

Conclusions of the aquatic risk assessment

Predicted exposure concentrations, using GENEEC2, of metobromuron, applied as the formulated product SOLETO to potatoes resulted in calculated risk quotients above the level of concern (LOC) for non-threatened and threatened species of fish, aquatic invertebrates, algae and aquatic plants.

Due to the specific nature of the application method, the following controls are proposed:

Use restrictions

- The maximum application rate is 2.0 kg metobromuron/ha, maximum 1 application/year
- Apply with minimum medium droplets, as defined by the American Society of Agricultural and Biological Engineers ASABE Standard (S572) or the British Crop Production Council guideline. This information should be required on the label so that users are aware of this control
- A label statement indicating: "**DO NOT** apply when wind speeds are less than 3 km/hr or more than 20 km/hr as measured at the application site".

Buffer zones

- To mitigate risks from spray drift and runoff, when applied to bare soil, the substance should not be applied within 5 m of any waterbody. This information should be required on the label so that users are aware of this control.

Groundwater risk assessment

The predicted concentration of the active ingredient metobromuron in groundwater, calculated using the Sci-Grow model, is shown in Table 39. The concentration is initially compared to the EU limit for the maximum permissible concentration of pesticide active ingredients and their relevant metabolites of 0.1 µg/L.

Table 39: Input parameters for Sci-Grow analysis and resulting PEC values

Input parameters	Values
Application rate (kg ai/ha)	2.0
Application rate (lb ai/acre)[1]	1.78
Number of applications	1
K_{oc}[2]	114 mL/g
Aerobic soil DT_{50} (days)	73.3 (longest field value, worst-case approach)
PEC_{gw} (µg/L)	1.46

[1] The application rate is conversion from kg ai/ha to lb/acre (the units required to be entered into the model) by multiplying it by 0.892

[2] Lowest value non-sandy soil used for risk assessment (K_d/K_{oc} values measured in soils classified as “sand”, “coarse sand”, “fine sand” or “loamy sand” are excluded as per the GENEECE2 guidance)

The predicted concentration in groundwater (PECgw) for metobromuron is above the 0.1 µg/L threshold. The low K_{oc} values generated in laboratory studies used in the Sci-Grow model indicate high mobility of metobromuron in soil however the field studies (soil dissipation and lysimeter) provided by the applicant suggest a limited potential for leaching. This data suggests contamination of the groundwater by normal use is not likely.

Furthermore, it is important to note here that EFSA identified no risks or concerns in regard to groundwater contamination (ie all generated PECgw values were below 0.1 µg/L) in their assessment of metobromuron. EFSA modelled the same use pattern for metobromuron (2000 g ai/ha, applied once to potatoes) but used their groundwater risk assessment methodology. The Sci-Grow model is a screening tool. As such, although a risk to groundwater is identified for metobromuron using the Sci-Grow screening model, the groundwater concentrations generated by Sci-Grow are a very conservative estimate. This is because the model is based on groundwater monitoring studies which were conducted by applying pesticides at maximum allowed rates and frequency to vulnerable sites

(ie shallow aquifers, sandy, permeable soils, and substantial rainfall and/or irrigation to maximize leaching).

A risk assessment has been conducted in Appendix G to assess the risks associated with the exposure of metobromuron through groundwater. The conclusions being that the likely ground water concentration of metobromuron is well below the level of concern in relation to human drinking water consumption.

Conclusions of the groundwater risk assessment

Using the Sci-Grow screening model the predicted concentration in groundwater for metobromuron is above the 0.1 µg/L trigger level set by the European regulators. Groundwater assessments conducted for the same metobromuron use pattern overseas did not identify the same risk to groundwater using their methodology, indicating in this case that the groundwater concentration predicted by Sci-Grow is overly conservative. A human health risk assessment has however been conducted (see Appendix G) and showed that the risks associated with the drinking of groundwater at the concentrations calculated are well below the level of concern.

Sediment risk assessment

No data on toxicity of metobromuron to sediment-dwelling organisms have been provided by the applicant. Metobromuron was observed to partition into the sediment, reaching a maximum of 28.7% AR, however a daphnid reproduction study is available with a chronic endpoint >0.1 mg a.i./L (NOEC of 10 mg a.i./L). Therefore a risk assessment on sediment-dwelling organisms is not required (EFSA 2013). In addition, it was concluded that the proposed controls based on the aquatic risk assessment will provide a level of protection to sediment dwelling organisms. The proposed controls are based on the *Lemna gibba* endpoint which is 32 times lower than the chronic daphnid endpoint.

Terrestrial risk assessment

The terrestrial risk assessment considers the risks to soil organisms, terrestrial plants, birds, bees, and non-target arthropods.

The methodology for the terrestrial risk assessment is described in the EPA standard risk assessment methodology (EPA 2020).

Soil macro-organisms

The soil organism risk assessment is based on a comparison of the PEC with toxicity values for the substance. The toxicity value is divided by the PEC to give a Toxicity Exposure Ratio (TER). The different levels of concern assigned to specific TER values are listed in the EPA standard risk assessment methodology (EPA 2020).

The results of the acute risk assessment for soil organisms are summarised in Table 40. Results of the chronic risk assessment are summarised in Table 41.

Table 40: Acute TER values for soil organisms

Species	LC_{50} (mg/kg soil)	Drift (%)	PEC (mg/kg soil)	TER acute	Conclusion
Scenario – 2000 g ai/ha, one application – "in-field"					
Earthworm, *Eisenia fetida*	233.5[1]	NA	2.67	87.56	Below LOC for non-threatened species. **Above LOC for threatened species**.
Scenario – 2000 g/ha, one application – "off-field"					
Earthworm, *Eisenia fetida*	233.5[1]	2.77	0.07	3161.10	Below LOC for threatened/non-threatened species

[1] Original toxicity endpoints from the artificial soil tests have been divided by 2 to account for different soil characteristics and the possibility of reduced bioavailability for soil organisms of lipophilic substances (Log Kow >2) as per the EFSA Technical Report (EFSA 2015)

Table 41: Chronic TER values for soil organisms

Species	NOEC (mg/kg soil)	Drift (%)	PEC (mg/kg soil)	TER chronic	Conclusion
Scenario – 2000 g ai/ha, one application – "in-field"					
Earthworm, *Eisenia fetida*	59.9[1,2]	NA	2.67	22.46	Below LOC for non-threatened species. **Above LOC for threatened species**
Springtail, *Folsomia candida*	11.85[1,2]	NA	2.67	4.44	**Above LOC for threatened/non-threatened species**
Soil mite, *Hypoaspis aculeifer*	11.85[1,2]	NA	2.67	4.44	**Above LOC for threatened/non-threatened species**
Scenario – 2000 g/ha, one application – "off-field"					
Earthworm, *Eisenia fetida*	59.9[1,2]	2.77	0.074	810.92	Below LOC for threatened/non-threatened species.
Springtail, *Folsomia candida*	11.85[1,2]	2.77	0.074	160.42	Below LOC for threatened/non-threatened species.
Soil mite, *Hypoaspis aculeifer*	11.85[1,2]	2.77	0.074	160.42	Below LOC for threatened/non-threatened species.

[1] Values calculated using ai content in formulation.
[2] Original toxicity endpoints from the artificial soil tests have been divided by 2 to account for different soil characteristics and the possibility of reduced bioavailability for soil organisms of lipophilic substances (Log Kow >2) as per the EFSA Technical Report (EFSA 2015)

For earthworms, both acute and chronic risks were identified for threatened species of earthworms in-field, following application of the active ingredient metobromuron to potatoes.
However, it is considered that threatened earthworm species are unlikely to be present in-field.

It is important to note that there are 179 taxa or earthworms in New Zealand with only one species reported as "at risk - declining" (*Deinodrilus gorgon*) and 31 reported as "at risk - naturally uncommon" (Department Of Conservation (DOC) 2014). Despite a potentially large distribution area for this earthworm species on the West Coast, the best documented natural habitat is not threatened by agriculture but rather by on-going and future mining activities on the Stockton and Denniston Plateaus. Furthermore, *Deinodrilus gorgon* is reported have a total area of occupancy ≤1000 ha (10 km^2) in New Zealand. The other 31 species ranked as "naturally uncommon" are predominantly endemic to New Zealand. These 32 earthworm species are confined to a specific forestry areas or occur within naturally small and widely scattered populations, where this distribution is not the result of human disturbance.

Therefore, in-field risks to threatened species of earthworms are considered below the level of concern.

Chronic risks were identified for both non-threatened and threatened species of soil mites and collembolan as the calculated TER does not meet the acceptable level of concern (non-threatened species TER>5, threatened species TER>50; see Appendix L):

- For non-threatened species, the chronic TER is very close to level of concern (1.1x higher to be >5, and mean no identified chronic risk).
- For threatened species however, the TER is further from the level of concern (11.3x higher to be >50, and mean no identified chronic risk).

These risks were only associated to the in-field scenario as no risks above the level of concern were identified to these organisms off-field.

The applicant suggests the NOEC is conservative and that no-observed effect is probably closer to the highest concentration tested. They calculated the EC_{10} for each study which supported this. The EPA would use the lowest value when presented with a NOEC and an EC_{10} to ensure sufficient level of protection to the New Zealand environment. The EPA also believes that regression analysis is not applicable to these studies due to their design (ie only five concentrations when eight to 12 are required for the determination of an EC_x (OECD 2016b, OECD 2016a) and the lack of dose response. As such, the use of a EC_{10} value to refine the assessment to non-target soil organisms has not been accepted.

Soil micro-organisms

Based on nominal concentrations, under conditions anticipated in the field, metobromuron can be considered as having no long-term influence on nitrogen and carbon transformation in soil at rates up to 28.03 mg/kg dw soil (up to 20.49 kg ai/ha). Deviations in nitrogen and carbon transformation activity after 28 days (between treatment and control) were less than 25% for all parameters examined. The current application rate is lower and therefore risks are considered below the level of concern.

Conclusions of the soil organism risk assessment

Acute and chronic risks to earthworms following the application of the formulated product SOLETO to potatoes are considered below the level of concern.

Chronic risks were identified as above the level of concern for non-threatened and threatened species of soil mites and collembola for applications to potatoes.

For soil microorganisms risks are below the level of concern for potatoes

Non-target plant risk assessment

The non-target plant risk assessment is based on a comparison of the PEC with toxicity values for SOLETO. Depending on the type of data provided, for non-threatened plants a TER or an RQ is calculated (a TER is used when an EC_{50} is available, an RQ is used when an EC_{25} is available). For threatened non-target plants an RQ is calculated by comparing the PEC with a NOEC. The different levels of concern assigned to specific TER/RQ values are listed in the EPA standard risk assessment methodology (EPA 2020).

RQ/TER values for non-threatened non-target plants are shown in Table 42. TER values for threatened non-target plants are shown in Table 43. No crop interception was incorporated in the risk assessment.

Exact buffer zones are impractical and too precise to be applied in the real world. Therefore, the buffer zone distance is rounded so it can be visualized and remembered by end-users.

Table 42: RQ/TER value for non-target plant – edge of field

Scenarios	Exposure (g ai/ha) * drift factor	ER_{50} (g ai/ha)	TER	Conclusion
2.0 kg ai/ha – 0 m buffer zone (drift factor 2.77%)				
Vegetative vigour, 21 days	55.4	56.35	1.02	**Above LOC for non-threatened species**
Seedling emergence, 21 days	55.4	97.34	1.76	**Above LOC for non-threatened species**
2.0 kg ai/ha – 5 m buffer zone (drift factor 0.57%)				
Vegetative vigour, 21 days	11.4	56.35	4.94	**Above LOC for non-threatened species**
Seedling emergence, 21 days	11.4	97.34	8.54	Below LOC for non-threatened species
2.0 kg ai/ha – 10 m buffer zone (drift factor 0.29%)				
Vegetative vigour, 21 days	5.8	56.35	9.72	Below LOC for non-threatened species
Seedling emergence, 21 days	5.8	97.34	16.78	Below LOC for non-threatened species

Table 43: TER value for threatened non-target plant

Scenarios	Exposure (g ai/ha) * drift factor	NOER (g ai/ha)	TER	Conclusion
2.0 kg ai/ha - vegetative vigour (lowest NOER)				
0 m buffer zone (drift factor 2.77%)	55.4	6.3	0.11	**Above LOC for threatened species**
10 m buffer zone (drift factor 2.77%)	5.8	6.3	1.09	**Above LOC for threatened species**
40 m buffer zone (drift factor 2.77%)	1.4	6.3	4.50	**Above LOC for threatened species**
50 m buffer zone (drift factor 2.77%)	1.2	6.3	5.25	Below LOC for threatened species

Conclusion for non-target plant risk assessment

Risk Quotients to non-target plants calculated for metobromuron when applied to pre-emergent potatoes as the formulated product SOLETO are above the level of concern based on fresh weight as the endpoint. The main reported symptoms shown by effected plants in the vegetative vigour study was stunting. Significant chlorosis (≥20% of surviving plants) was observed in *Brassica napus*,

Cucumis sativa and *Sinapis alba* up to a maximum of 40% of surviving plants. Fresh weight was used as a more reliable endpoint which is in line with the endpoints generated for visual injury.

The level of risk to non-target plants is expected as the product is a herbicide. A buffer zone of 10m was necessary to protect non-threatened species of plants (ie for the TER to be acceptable). A buffer zone of 50 m was necessary to protect threatened species of plants (ie for the TER to be acceptable).

Additional care is required when sprayed near sensitive terrestrial areas, and this is captured in the proposed controls outlined below.

The following variations on the controls are proposed to reduce exposures below the level of concern:

Controls

- A label statement indicating: "**WARNING**, might impact non-target plants, the substance should not be applied within 10 m downwind of an area containing non-target plants. Additional care is required when sprayed near sensitive terrestrial areas (eg areas with threatened plants or of higher ecological value)".
- A label statement indicating: "**WARNING**, exposure to SOLETO may injure or kill susceptible agricultural crops and native vegetation. Care should be taken avoid spray to neighbouring vegetation, it is recommended to conduct a site specific risk assessment that considers the potential movement of spray drift downwind to sensitive areas. This includes assessment of the weather conditions, application equipment, topography and species of plants downwind."
- A label statement indicating: "**DO NOT** apply when wind speeds are less than 3 km/hr or more than 20 km/hr as measured at the application site".

Bird risk assessment

The bird risk assessment is based on a comparison of the PEC with toxicity values for the substance. The toxicity value is divided by the PEC to give a Toxicity Exposure Ratio (TER). The different levels of concern assigned to specific TER values are listed in the EPA standard risk assessment methodology (EPA 2020).

Based on the proposed use pattern for pre-emergent potatoes the foliar spay scenario is considered inappropriate as the leaves will not be sprayed. A soil scenario was considered to realistically reflect the exposure of the birds to the substance SOLETO.

The "Bare soil" scenario was considered the most appropriate (in combination with the most conservative NOAEL) for the proposed application methods since it represents all arable crops at BBCH <10. It is not considered appropriate to use the "Potato" or "Leafy vegetables" scenario because the first growth stage is BBCH 10, which is when the plant emerges.

Screening assessment

Predicted exposure to metobromuron under the bird acute dietary and reproduction screening assessments is shown in Table 44.

Table 44: Exposure of birds for acute and reproduction screening assessments

Screening type[1]	Indicator species[2]	Application rate (kg ai/ha)	Short-cut value (90th%)[3]	TWA[4]	MAF (90th %)[5]	No of applications	TER
Metobromuron							
Acute	Small omnivorous bird	2.0	24.7	-	1	1	28.9
Reproduction	Small omnivorous bird	2.0	11.4	0.53	1	1	1.8

[1] EFSA (EFSA 2009), Table 5 p27
[2] EFSA (EFSA 2009), Table 6 p28
[3] 90th %ile short-cut value used for the acute assessment, mean value used for the reproduction assessment. EFSA (EFSA 2009), Table 6 p28
[4] The exposure assessment of the reproduction assessment uses time-weighted average (TWA) exposure estimates over 1, 2, 3 or 21 days for different phases of the assessment. 1 d = 1.0; 2 days = 0.93; 3 days = 0.9; 21 days = 0.53. EFSA (EFSA 2009), Table 11 p34.
[5] 90th %ile MAF value used for the acute assessment, mean value used for the reproduction assessment. EFSA (EFSA 2009), Table 7 p29

Conclusions of the bird screening risk assessment

For applications to potatoes, the screening risk assessment indicates an acute risk below the level of concern to non-threatened and threatened birds from metobromuron. The reproductive screening assessment indicates a chronic risk above the level of concern to threatened and non-threatened birds.

As chronic risks were identified, a Tier 1 risk assessment was performed for applications of SOLETO to potatoes.

Tier 1 assessment

Tier 1 uses the same general approach as the screening assessment but requires more specific exposure scenarios. More details are provided in the EPA standard risk assessment methodology (EPA 2020).

For each generic focal species the toxicity exposure ratio (TER) has been determined, and these are presented in Table 45.

The toxicity figures are the same than those considered in the screening assessment.

The indicator species mentioned in Table 45 are not real species but have to be considered as representative of groups of birds of the same size and same feeding behaviour.

Table 45: TER values for chronic risk assessment – Tier 1 assessment (standard approach using worst-case endpoint)

Crops & BBCH class	Focal species	Short-cut value[2] (90th %)	Toxicity endpoint (mg/kg bw)	TER ratio	Conclusion
Application to potatoes, 1 x 2.0 kg ai/ha					
Bare soil (BBCH <10)	Small granivorous bird "finch" small seeds 100% weeds	11.4	21.6	1.8	**Above the level of concern for non-threatened and threatened species**
	Small omnivorous bird "lark" combination (invertebrates without interception) 50% weed seeds, 50% ground arthropods	5.9	21.6	3.5	**Above the level of concern for non-threatened and threatened species**
	Small insectivorous bird "wagtail" ground invertebrates without interception 100% soil-dwelling invertebrates	8.2	21.6	2.5	**Above the level of concern for non-threatened and threatened species**

Conclusion for bird risk assessment (Tier 1)

The chronic Tier 1 risk assessment indicates risks above the level of concern to both threatened and non-threatened birds following application of the formulated product SOLETO to potatoes.

Refinement

The chronic Tier 1 risk assessment indicates potential risks above the level of concern to both threatened and non-threatened birds following application of the formulated product SOLETO to potatoes.

The chronic risk to non-threatened and threatened birds identified at Tier 1 may potentially overestimate the actual risk however, and this is discussed in more detail in the following paragraphs.

General consideration regarding the endpoint

The chronic avian endpoint used in the risk assessment was a NOEL of 240 ppm (equivalent to 21.6 mg ai/kg bw/d) obtained for the bobwhite quail (*Colinus virginianus*). The NOEL was based on a significant difference observed in number of eggs laid when compared to the control. In the study a significant difference was also observed for body weight and food consumption at 384 ppm suggesting an avoidance reaction of the birds. There is evidence in EU DAR (EC 2012) that a reduction in food intake may have an effect on the number of eggs laid per female. It is therefore potentially more ecologically relevant to look at the number of 14 day survivors per female and initial

chick weight. Taking this into consideration the NOEL can be refined to 384 ppm (34.2 mg ai/kg bw/d).

The NOEL endpoint has therefore been refined from 21.6 to 34.2 mg ai/kg bw/d and for each generic focal species the toxicity exposure ratio (TER) has been determined using the refined chronic toxicity endpoint. The refined Tier II TERs are presented in Table 46.

Table 46 values for chronic risk assessment – Tier 1 assessment (refined endpoint approach)

Crops & BBCH class	Focal species	Short-cut value[2] (90th %)	Toxicity endpoint (mg/kg bw)	TER ratio	Conclusion
Application to potatoes, 1 x 2.0 kg ai/ha					
Bare soil (BBCH <10)	Small granivorous bird "finch" small seeds 100% weeds	11.4	34.2	2.8	**Above the level of concern for non-threatened and threatened species**
	Small insectivorous bird "wagtail" ground invertebrates without interception 100% soil-dwelling invertebrates	5.9	34.2	5.5	Below the level of concern for non-threatened species **Above the level of concern for threatened species**
	Small omnivorous bird "lark" combination (invertebrates without interception) 50% weed seeds, 50% ground arthropods	8.2	34.2	3.9	**Above the level of concern for non-threatened and threatened species**

The refinement of the reproductive endpoint resulted in risks below the level of concern for non-threatened omnivorous birds. Risks are still above the level of concern for granivorous and insectivorous birds (non-threatened & threatened species) and threatened species of small omnivorous birds.

Generic focal species and foraging behaviour

For the "bare soil" scenario there are three generic focal species:

1. Small granivorous bird "finch" [feeding on small seeds, 100% weed seeds]
2. Small insectivorous bird "wagtail" [feeling on ground invertebrates without interception, 100% soil dwelling invertebrates]
3. Small omnivorous bird "lark" [feeding on combination of ground invertebrates without interception, 50% seeds, 50% ground arthropods]

For these generic focal species, the EFSA Risk Assessment for birds assumes that 100% of their diet is obtained from the treated field, and that 100% of their diet is contaminated. This is a highly conservative assumption. Using the refined reproductive endpoint the acceptable proportion of the birds diet obtained from outside the treated area is estimated.

Based on the EFSA Risk Assessment for Birds and Mammals guidance (EFSA 2009), for the TER to be acceptable for non-threatened bird species following applications to potatoes, the “finch” and “lark” would have to obtain up to 57% and 78% of their diet, respectively from the treated area.
For the TER to be acceptable for threatened species of birds following applications to potatoes the “finch”, “wagtail” and “lark” would have to obtain up to 28%, 54% and 39% of their diet, respectively from the treated area.
Radio-tracking data for focal species found in arable areas in the UK has provided information on the proportion of time an individual may spend foraging in a treated area (Finch, Payne et al. 2006). The study assessed the behaviour of three focal species; linnet or “finch” (small granivorous bird), yellowhammer [small (predominantly) insectivorous bird] and skylark (small omnivorous bird) in beet/potato fields. The mean PT values for all birds and all months were considered conservative enough for the chronic risk assessment of Soleto to bare soil. These values are also based on arable fields containing crops that would be more attractive to birds and are therefore higher than expected for bare soil.

The PT values in the radio-tracking studies are lower than the values required to achieve an acceptable TER for non-threatened and threatened species of bird (see above). This indicates that focal species of non-threatened and threatened birds would not forage in treated areas for long enough that would result in a risk. It is important to note that this information observed the activity of UK birds in this situation and at this point in time insufficient information is available to know how this data compares to New Zealand species of bird. It is assumed that these birds and their behaviour in this agricultural setting would be comparable to New Zealand species.

Food contamination

Due to the intended use for Soleto as a pre-emergence herbicide, the food availability on treated fields is very limited. The soils of the potato fields are depleted of potential food items for birds as previously harvested crops are incorporated into the soil. Therefore plant matter, including weed seeds, are not easily accessible to birds. The availability of insects is also limited due to the low availability of food resources and the missing habitat structure for insects on the bare soil.

If birds were to feed on bare soil, the area would not meet their nutritional demands. As such, if contaminated food was consumed, it would make a small proportion to their overall diet. Furthermore, in regard to potatoes, according to an EU DAR published for the active ingredient penflufen (EC 2011) for which an assessment was performed for applications to potatoes, it was concluded that potato fields are not a particularly attractive habitat for feeding birds. Birds do not generally dig up and

consume planted potatoes, and as such for the majority of avian species there is minimal risk from the direct consumption of treated tubers therefore. Potato foliage is also known to be unpalatable to birds.

Conclusion

The PT values obtained are thought to be overestimations for pre-emergence crop and are therefore over conservative (EC 2012).

Treated pre-emergent fields will have low food availability and provide no protection to predators. Considering this and the conservative toxicity endpoint, the possibility that birds will forage in other (non-treated) areas, and limited availability of contaminated food, the risks identified for birds (threatened and non-threatened) following application of the formulated product Soleto to pre-emergent potato are therefore likely to be negligible.

Secondary poisoning

Given the criteria under the HSNO Act metobromuron is not considered to be bioaccumulative (log P_{ow} < 4). Therefore, no risk assessment via secondary poisoning is performed.

Conclusions for bird risk assessment

For applications to potatoes, the screening risk assessment indicates an acute risk below the level of concern to non-threatened and threatened birds from metobromuron following use of Soleto. The reproductive screening assessment indicates a chronic risk above the level of concern to threatened and non-threatened birds. The chronic Tier 1 risk assessment indicates potential risks above the level of concern to both threatened and non-threatened birds following application of the formulated product Soleto to potatoes. After refinement and consideration of the conservative toxicity endpoint, the possibility that birds will forage in other (non-treated) areas, and limited availability of contaminated food, the risks identified for birds (threatened and non-threatened) following application of the formulated product Soleto to pre-emergent potatoes are therefore likely to be negligible. The risk from secondary poisoning is considered to be low.

Pollinator risk assessment

The basis for the pollinator risk assessment is a comparison of the environmental exposure concentration (EEC) with toxicity endpoints to which safety factors have been applied. The EEC is divided by the toxicity endpoint to calculate a risk quotient (RQ) value. The methodology for the pollinator risk assessment, including the level of concern (LOC) ascribed to specific RQ values, is

described in detail in the EPA standard risk assessment methodology (EPA 2020). The results of the bee risk assessment are shown in Table 47.

Table 47: Bee exposure estimates and RQ values

Use scenario	Application rate (kg ai/ha)	EEC (µg ai/bee)	Toxicity endpoint value (µg ai/bee)	RQ[1]	Conclusion
Acute - Honey bees (adult) - oral					
Bare soil (BBCH <10)	2.0	0.06	50.68	0.0012	Below the LOC for threatened/non-threatened species
Acute - Honey bees (adult) - contact					
Bare soil (BBCH <10)	2.0	ND	85.1	N/A[2]	N/A[1]
Acute - Honey bees (larva) - oral					
Bare soil (BBCH <10)	2.0	0.03	6.25	0.0041	Below the LOC for threatened/non-threatened species

[1] "Soil application" used as application method in model as the application will be to bare soil.
[2] Contact exposure is not applicable as the application is to bare soil.

Conclusions of the pollinator risk assessment

The risks to pollinators are below the level of concern and any risks are negligible.

Non-target arthropod risk assessment

The non-target arthropod risk assessment is a comparison of the predicted environmental concentration (PEC) with toxicity endpoints to which safety factors have been applied. The PEC is divided by the toxicity endpoint to calculate a hazard quotient (HQ) value. The methodology for the non-target arthropods risk assessment, including the level of concern (LOC) ascribed to specific HQ values, is described in detail in the EPA standard risk assessment methodology (EPA 2020).

Tier I non-target arthropod risk assessment

Results of the Tier I in-field and off-field non-target arthropod risk assessment are shown in Table 48 and Table 49, respectively.

Table 48: In-field HQ values for non-target arthropods

Species	LR_{50} (g ai/h)	Application rate (g ai/ha)	MAF	Hazard Quotient	Conclusion
Parasitic wasp, *Aphidius rhopalosiphi*	>4098.4	2000	1	<0.49	Below the LOC
Predatory Mite, *Typhlodromus pyri*	51.18	2000	1	38.61	**Above the LOC**

Table 49: Off-field HQ values for non-target arthropods (drift factor = 2.77%)

Species	LR_{50} (g ai/ha)	Application rate (g ai/ha)	MAF	Hazard Quotient	Conclusion
Parasitic wasp, *Aphidius rhopalosiphi*	>4098.4	2000	1	<0.01	Below the LOC
Predatory Mite, *Typhlodromus pyri*	51.18	2000	1	1.07	Below the LOC

Tier I conclusion

Risks to predatory wasps are considered to be below the level of concern in-field as well as off-field.

The in-field risk for the predatory mite is above the level of concern. The off-field risk was below the level of concern.

Tier II non-target arthropod risk assessment

Risks were identified as above the level of concern in-field from use of SOLETO at Tier I. As such, risks to non-target arthropods have been assessed at Tier II, using the endpoints derived from the extended laboratory studies for the predatory mite, *Typhlodromus pyri*, as well as the two additional species, rove beetles, *Aleochara bilineata* and wolf spider, *Pardosa spec.* following the recommendations by the ESCORT2 guidance (Workshop, Candolfi *et al*.). The results are presented in

Table 50 and Table 51.

Table 50: In-field HQ values for non-target arthropods

Species	LR_{50}/NOER (g ai/h)	Application rate (g ai/ha)	MAF	Hazard Quotient	Conclusion
Extended Laboratory					
Predatory Mite, *Typhlodromus pyri*[1]	65.1	2000	1	30.72	**Above the LOC**
Rove beetles, *Aleochara bilineata*	>2049.2	2000	1	<0.98	Below the LOC
Wolf spider, *Pardosa spec.*	>2049.2	2000	1	<0.98	Below the LOC
Aged Residue					
Predatory Mite, *Typhlodromus pyri*	*Aged*[1] >2049.2	2000	1	<0.98	Below the LOC

[1] Aged residue study using apple leaves with aged residues (7 days) of Soleto (4 L substance/ha).

Table 51: Off-field HQ values for non-target arthropods (drift factor = 2.77%)

Species	LR_{50}/NOER (g ai/h)	Application rate (g ai/ha)	MAF	Hazard Quotient	Conclusion
Extended Laboratory					
Predatory Mite, *Typhlodromus pyri* [1]	65.1	2000	1	0.85	Below the LOC
Rove beetles, *Aleochara bilineata*	2049.2	2000	1	0.03	Below the LOC
Wolf spider, *Pardosa spec.*	>2049.2	2000	1	<0.03	Below the LOC
Aged Residue					
Predatory Mite, *Typhlodromus pyri*	*Aged*[1] 2049.2	2000	1	0.03	Below the LOC

[1] Aged residue study using apple leaves with aged residues (7 days) of Soleto (4 L substance/ha).

Tier II conclusion

For the predatory mite, in-field risks are still above the level of concern when exposed to fresh residues on apple leaves. The in-field risks were below the level of concern when the predatory mites were exposed to aged residues (7 day) on apple leaves. The off-field risk was below the level of concern.

Although the in-field risks to predatory mites when exposed to fresh residues of SOLETO are still above the level of concern at Tier II (15.4x higher), this exposure scenario is not considered

appropriate for pre-emergence application of potatoes as there will be no foliage in the field during application, and predatory mites are a leaf-dwelling species.

Risks to rove beetles, known to occur in any type of habitat, are considered to be below the level of concern in-field as well as off-field.

The risks to wolf spiders, known to be soil dwellers, are below the level of concern in-field as well as off-field. Only one application rate (2000 g ai/ha) was tested on the wolf spider and a statistically significant difference in mortality was observed when compared to the control. However this mortality rate was <50% and an LR_{50} could not be calculated and be assumed it is greater than the highest application rate (4 L substance/ha), this results in a risk below the level of concern.

Conclusion for non-target arthropod risk assessments

Off-field risks to non-target arthropods are below the level of concern. In-field risks were only above the level of concern for predatory mites when the residues were fresh on the leaves. Aged residues (7 days old) were not toxic to predatory mites up to 4.0 L formulation/ha.

The Applicant provided information on application of metobromuron and the preparation to the soil prior to application. The cultivation of potatoes is a highly mechanised process. The ploughing phase brings nutrients to the soil surface while also burying weeds, any remains of the previous crop and seeds allowing them to break down in the soil. Application of metobromuron takes place between planting and the emergence of potato plants to avoid emergence and growth of weeds.

This information suggests that there will be limited habitat for predatory mites at the time of application and therefore exposure will be limited. The off-field risk and aged residue study also suggests that populations of *T. pyri* in areas surrounding the treated field can recolonize the treated area once there is sufficient habitat.

Therefore risks to non-target arthropods are negligible when the soil is prepared in this way prior to application.

Controls

- A label statement indicating: “Ensure mechanical removal of weeds, remaining crop and seeds has taken place before application. The substance should only be used after planting and before crop emergence.”

Conclusions of the ecological risk assessment

The EPA assessed the potential risk to be triggered by the use of Soleto following the instructions captured in the proposed label and GAP table.

Aquatic and sediment risk assessment

Predicted exposure concentrations, using GENEEC2, of metobromuron, applied as the formulated product SOLETO to potatoes resulted in calculated risk quotients above the level of concern (LOC) for non-threatened and threatened species of fish, aquatic invertebrates, algae and aquatic plants.

Due to the specific nature of the application method, the following controls are proposed:

Use restrictions

- The maximum application rate for potatoes is 2.0 kg metobromuron/ha, maximum 1 application/year
- When applied as a low-boom ground spray (max one application per year of 2.0 kg ai/ha), the substance should not be applied within 5 m of any waterbody
- A label statement indicating: "**DO NOT** apply when wind speeds are less than 3 km/hr or more than 20 km/hr as measured at the application site".

Groundwater:

Using the Sci-Grow screening model the predicted concentration in groundwater for metobromuron is above the 0.1 µg/L trigger level set by the European regulators. Groundwater assessments conducted for the same metobromuron use pattern overseas did not identify the same risk to groundwater using their methodology, indicating in this case that the groundwater concentration predicted by Sci-Grow is overly conservative. A human health risk assessment has however been conducted (see Appendix G) and showed that the risks associated with the drinking of groundwater at the concentrations calculated are well below the level of concern.

Soil organisms:

Acute and chronic risks to earthworms following the application of the formulated product SOLETO to potatoes are considered below the level of concern.
Chronic risks were identified as above the level of concern for non-threatened and threatened species of soil mites and collembola for applications to potatoes.
For soil microorganisms risks are below the level of concern for potatoes.

Non-target plants:

Risk Quotients to non-target plants calculated for metobromuron when applied to pre-emergent potatoes as the formulated product SOLETO are above the level of concern. This is expected as the product is a herbicide. A buffer zone of 10 m increased the TER for non-threatened species resulting in a risk below the LOC. A buffer zone of 50 m was needed to increase the TER for threatened species resulting in a risk below the LOC.

Additional care is required when sprayed near sensitive terrestrial areas, and this is captured in the proposed controls outlined below.

The following variations on the controls are proposed to reduce exposures below the level of concern:

Controls

- A label statement indicating: "**WARNING**, might impact non-target plants, the substance should not be applied within 10 m of a downwind of an area containing non-target plants. Additional care is required when sprayed near sensitive terrestrial areas (eg areas with threatened plants or of higher ecological value)".
- A label statement indicating: "**WARNING**, exposure to Soleto may injure or kill susceptible agricultural crops and native vegetation. Care should be taken avoid spray to neighbouring vegetation, it is recommended to conduct a site specific risk assessment that considers the potential movement of spray drift downwind to sensitive areas. This includes assessment of the weather conditions, application equipment, topography and species of plants downwind."

A label statement indicating: "**DO NOT** apply when wind speeds are less than 3 km/hr or more than 20 km/hr as measured at the application site".

Birds:

For applications to potatoes, the screening risk assessment indicates an acute risk below the level of concern to non-threatened and threatened birds from metobromuron following use of Soleto. The reproductive screening assessment indicates a chronic risk above the level of concern to threatened and non-threatened birds. The chronic Tier 1 risk assessment indicates potential risks above the level of concern to both threatened and non-threatened birds following application of the formulated product Soleto to potatoes. After refinement and consideration of the conservative toxicity endpoint, the possibility that birds will forage in other (non-treated) areas, and limited availability of contaminated food, the risks identified for birds (threatened and non-threatened) following application of the formulated product Soleto to pre-emergent potatoes are therefore likely to be negligible. The risk from secondary poisoning is considered to be low.

Pollinators:

The risks to pollinators are below the level of concern and any risks are negligible.

Non-target arthropods:

Risks to non-target arthropods are below the level of concern for both off-field and in-field. The identified in-field risks to predatory mites when exposed to fresh residues of SOLETO are not relevant for the pre-emergent application of potatoes as there will be no foliage in the field during application. Predatory mites are a leaf-dwelling species and therefore exposure will be limited.

Controls

- A label statement indicating: “Ensure mechanical removal of weeds, remaining crop and seeds has taken place before application. The substance should only be used after planting and before crop emergence”.

Overall conclusions

It is considered that the risks to the environment from the proposed use of SOLETO are below the level of concern with the proposed controls based on the available data for all areas except for non-target soil macro-organisms (mites, collembola) for which a risk above the level of concern was identified.

Appendix I: Proposed controls

Exposure thresholds

Exposure thresholds proposed for metobromuron are shown in Table 52. Acceptable Daily Exposure (ADE) and Potential Daily Exposure (PDE) values are not controls as such, but are health based exposure guidance values which can be used to inform risk assessments as well as the setting of controls, such as Maximum Residue Levels under the ACVM Act.

EPA staff have reviewed health based exposure guidance values established by overseas regulators (shown in Table 52) to inform the selection of ADE and PDE values for metobromuron.

Table 52: Using an existing ADE, ADI, CRfD or DN(M)EL for metobromuron

Available international toxicological thresholds	Key Systemic effect	NOAEL (mg/kg bw/d)	Uncertainty factors	Value (mg/kg bw/d)	Modifications	Remarks
ADI – EFSA	Increased Heinz bodies, extramedullary haematopoiesis	0.8	100	0.008	None	The EPA disagrees that the NOAEL for this study is 0.8 mg/kg bw/day.
ADE - EPA	Mice: Haematological effects (Increased Heinz bodies) Rats: Haematological (methaemoglobinaemia, regenerative anaemia), increased organ weight (spleen weight), and haemosiderin deposition (spleen, liver). Increase in tumours in males and females (2 year NOAEL rounded to 3.0)	3.0	100	0.03	None	The EPA selected next highest dose of 3 mg/kg bw/day as the NOAEL based on both the 1 year interim chronic toxicity data and the 2 year tumour data in rats.

Based on the assessment of the available data, the following Acceptable Daily Exposure (ADE) and Potential Daily Exposure (PDE) values have been provided (see Table 53).

Table 53: exposure thresholds for metobromuron

ADE	PDE	ARfD	TEL
0.030 mg/kg bw/day (EPA)	$PDE_{(Food)}$ = 0.021 mg/kg bw/day $PDE_{(Drinking\ water)}$ = 0.006 mg/kg bw/day $PDE_{(Other)}$ = 0.003 mg/kg bw/day	Not set at this time	Not set at this time

Ecotoxicity controls

Application restrictions

A maximum application rate is proposed to be set for SOLETO, as shown in Table 54.

Table 54: Maximum application rate for SOLETO

Active component	Maximum application rate
Metobromuron	2000 g ai/ha, maximum 1 application/year

Application method

SOLETO must not be applied when wind speeds are less than 3 km/hr or more than 20 km/hr as measured at the application site.

Apply with ground-based equipment and minimum medium droplets, as defined by the American Society of Agricultural and Biological Engineers ASABE Standard (S572) or the British Crop Production Council guideline. This information should be required on the label so that users are aware of this control.

Buffer zones

The person in charge of the application of this substance and any person applying this substance must ensure that the substance is not applied within a specified distance of a waterbody or of a downwind sensitive area containing non-target plants.

For this substance the buffer zones as mentioned in Table 55 are proposed, according to the relevant application method and scenario:

Table 55: Proposed buffer zones for SOLETO

Application method	Sensitive area	Required buffer zone (m)
Ground-based	Waterbody	5

Additional label statements

In order to protect non-target plants, the following label statements are proposed:

- A label statement indicating: "**WARNING**, might impact non-target plants, the substance should not be applied within 10 m of a downwind of an area containing non-target plants. Additional care is required when sprayed near sensitive terrestrial areas (eg areas with threatened plants or of higher ecological value)".

- A label statement indicating: "**WARNING**, exposure to Soleto may injure or kill susceptible agricultural crops and native vegetation. Care should be taken avoid spray to neighbouring vegetation, it is recommended to conduct a site specific risk assessment that considers the

potential movement of spray drift downwind to sensitive areas. This includes assessment of the weather conditions, application equipment, topography and species of plants downwind.

In order to protect non-target arthropods, the following label statement is proposed:

- A label statement indicating: “Ensure mechanical removal of weeds, remaining crop and seeds has taken place before application. The substance should only be used after planting and before crop emergence”.

Appendix J: Study summaries

Manufacturer code name for metobromuron technical grade active ingredient is SL-1201.

Manufacturer code name for SOLETO is BCP 222H (Code No.: PH-10/0026).

Mammalian Toxicity

Mammalian toxicity studies on metobromuron/SOLETO have been reviewed. These studies are used to describe potential risks to human health. The effects on mammals in these studies are used as proxies for the impact on humans. Data from the studies have been used for classifying the active ingredient and the formulated substance and for derivation of appropriate health-based criteria which are used in risk assessment. The summary of the studies is provided in Table 56 to Table 62.

Metobromuron

Acute toxicity [6.1]

All studies on the active were summarised in the DAR except the dermal toxicity study summarised below.

Table 56: Acute Dermal Toxicity [6.1 (dermal)]

Type of study	Acute dermal toxicity in rats
Flag	Key study
Test Substance	Metobromuron Technical (alias name: SL-1201) Lot No.: 1401011; Purity: 98.83%
Endpoint	Mortality (LD_{50})
Value	LD_{50} >2000 mg/kg bw
Reference	[redacted] (2017). Metobromuron Technical: Acute Dermal Toxicity Study in Rats, [redacted]
Klimisch Score	1
Amendments/Deviations	None of significance
GLP	Yes
Test Guideline/s	OECD TG 402; EPA OPPTS 870.1200
Species	Rat
Strain	Sprague-Dawley [Crl:CD(SD)].
No/Sex/Group	5M/5F
Dose Levels	2000 mg/kg bw
Exposure Type	Dermal, applied neat (dampened with water) under a gauze and an occlusive wrap for 24 hours
Study Summary	There was no death in any animals during the observation period. There were no clinical signs of toxicity in any animals during the observation period. All animals gained body weights (Day 7 and 14) after application of test substance. No macroscopic abnormality was noted in any animal at necropsy at the end of the 14 day observation period.
Additional Comments	No additional comments
Conclusion	The LD_{50} is >2000 mg/kg bw. Although mortality and clinical signs of toxicity were noted in the oral toxicity study would warrant a 6.1E classification, the fact that the material has such a low dermal penetration value (~0.5%) the substance should not be classified.

SOLETO

Acute toxicity [6.1]

Table 57: Acute Oral Toxicity [6.1 (oral)]

Type of study	Acute oral toxicity in rats
Flag	Key study
Test Substance	BCP 222H (Code No.: PH-10/0026), Batch No.: 064909, Purity: 512.3 g/L
Endpoint	Mortality (LD_{50})
Value	LD_{50} >2000 mg/kg bw
Reference	[redacted] (2010). BCP 222H Evaluation of Acute Oral Toxicity in Rats: Acute toxic class method. [redacted]
Klimisch Score	1
Amendments/Deviations	None of significance
GLP	Yes
Test Guideline/s	OECD TG 423, EC B.1
Species	Rat
Strain	Sprague-Dawley [SPF:Caw].
No/Sex/Group	6F
Dose Levels	2000 mg/kg bw
Exposure Type	Oral gavage
Study Summary	There was one death noted at approximately 24 hours. Macroscopic examination revealed a “white thinning of the stomach and a thickening of the forestomach). Clinical signs were only noted during Day 1 of the test and consisted of the following: decreases in spontaneous activity (6/6), Peyer’s reflex (3/6) and righting reflex (1/6), changes in muscle tone (2/6), bradypnea (2/6), mydrias (1/6), piloerection (2/6), and increased lachrymation (1/6). All animals gained body weight in a normal manner. At necropsy, no treatment related macroscopic abnormalities were noted in any animal (5/6).
Additional Comments	No additional comments
Conclusion	The LD_{50} is >2000 mg/kg bw and the test article is classified as 6.1E due to the observed clinical signs of toxicity and single mortality.

Table 58: Acute Dermal Toxicity [6.1 (dermal)]

Type of study	Acute dermal toxicity in rats
Flag	Key study
Test Substance	BCP 222H (Code No.: PH-10/0026), Batch No.: 064909, Purity: 512.3 g/L
Endpoint	Mortality (LD_{50})
Value	LD_{50} >2000 mg/kg bw
Reference	[redacted] (2010). BCP 222H Evaluation of Acute Dermal Toxicity in Rats. [redacted]
Klimisch Score	1
Amendments/Deviations	None of significance
GLP	Yes
Test Guideline/s	OECD TG 402; EU B.3
Species	Rat
Strain	Sprague-Dawley [SPF:Caw].
No/Sex/Group	5/sex
Dose Levels	2000 mg/kg bw
Exposure Type	Dermal, applied neat under a gauze wrap for 24 hours
Study Summary	There was no death in any animals during the observation period. There were no clinical signs of toxicity in any animals during the observation period. All animals gained body weight in a normal manner. No macroscopic abnormality was noted in any animal at necropsy at the end of the 14 day observation period.
Additional Comments	No additional comments
Conclusion	The LD_{50} is >2000 mg/kg bw and the substance should not be classified.

Table 59: Acute Inhalation Toxicity [6.1 (inhalation)]

Type of study	Acute inhalation (nose-only) toxicity in rats
Flag	Key study
Test Substance	BCP 222H, Batch No.: 643244, Purity: 491 ± 16.0 g/L
Endpoint	Mortality (LC_{50})
Value	LC_{50} >4.15 mg/L
Reference	[redacted] (2017). BCP222H: Acute (Four-Hour) Inhalation Study in Rats. [redacted]
Klimisch Score	1
Amendments/Deviations	None of significance
GLP	Yes
Test Guideline/s	OECD TG 436
Species	Rat
Strain	RccHan™;WIST
No/Sex/Group	3/sex
Dose Levels	4.15 ± 0.34 mg/L, MMAD: 4.7 µm, GSD: 1.96 µm
Exposure Type	Nose only, 4 hours
Study summary	There were no unscheduled deaths. Chin rubbing was observed in one male and two females immediately after exposure. This resolved in all animals 2 hours after the exposure. Hunched posture was observed in one male 1 hour after exposure, and had resolved by the initial check on Day 2. On the day following exposure slight body weight losses were evident in all animals. Growth was observed at the next weighing occasion (Day 4) for all males and two females. On Day 8, growth was observed for all animals and continued for the remainder of the observation period. No macroscopic abnormalities were observed.
Additional Comments	The mean achieved MMAD value was above the ideal range of 1 to 4 µm. However, the particle size distribution was such that approximately 72% of particles were less than 7 µm. Therefore, the aerosol was considered respirable and the results acceptable.
Conclusion	Under the conditions of this study the LC_{50} (4-hour) of BCP222H (500 g/L metobromuron) is >4.15 mg/L, the maximum attainable concentration and the substance should not be classified.

Skin irritation [6.3/8.2]

Table 60: Skin Irritation [6.3/8.2]

Type of study	Acute dermal irritation in rabbits
Flag	Key study
Test Substance	BCP 222H (Code No.: PH-10/0026) CoA: Patoran FL , Batch No.: 064909, Purity: 512.3 g/L
Endpoint	Mean Draize Score (24, 48, and 72 hours) for erythema and oedema
Value	Erythema: 0.0, Oedema: 0.0
Reference	[redacted] (2010). BCP 222H Assessment of Acute Dermal Irritation. [redacted]
Klimisch Score	1
Amendments/Deviations	None of significance
GLP	Yes
Test Guideline/s	OECD TG 404, EC B.4
Species	Rabbit
Strain	New Zealand White
No/Sex/Group	3F
Dose Levels	0.5 ml
Exposure Type	Dermal, applied neat under a gauze and semi-occlusive wrap for 4 hours
Study Summary	No evidence of dermal irritation was observed.
Additional Comments	No additional comments
Conclusion	No evidence of irritation was observed. The test article is not classifiable.

Eye irritation [6.4/8.3]

Table 61: Eye Irritation [6.4/8.3]

Type of study	Acute eye irritation in rabbits
Flag	Key study
Test Substance	BCP 222H (Code No.: PH-10/0026) CoA: Patoran FL , Batch No.: 064909, Purity: 512.3 g/L
Endpoint	Irritation assessed as a mean Draize score from the 24, 48, and 72 hour observation time points
Value	Mean Draize Score: Cornea Opacity 0.0 Conjunctiva Redness 0.44 Chemosis 0.0 Iris 0.0
Reference	[redacted] (2010). BCP 222H Assessment of Acute Eye Irritation, [redacted]
Klimisch Score	1
Amendments/Deviations	None of significance
GLP	Yes
Test Guideline/s	OECD TG 405, EC B.5
Species	Rabbit
Strain	New Zealand White
No/Sex/Group	3M
Dose Levels	0.1 g
Exposure Type	Ocular instillation into the conjunctival sac
Study Summary	The conjunctival reactions observed during the study were slight to moderate and were associated with a slight chemosis that dissipated within 24 hours. All effects in all animals were reversed by the Day 3 observation time period.
Additional Comments	No additional comments
Conclusion	The test substance was mildly irritating but not classifiable.

Contact sensitisation [6.5]

Table 62: Contact Sensitisation [6.5]

Type of study	Dermal sensitisation
Flag	Key study
Test Substance	BCP 222H (Code No.: PH-10/0026) CoA: Patoran FL , Batch No.: 064909, Purity: 512.3 g/L
Endpoint	Dermal skin reaction (erythema and oedema)
Value	Non-sensitiser: Erythema 0/11, Oedema 0/11
Reference	[redacted]2010). BCP 222H Assessment of Sensitising Properties on Albino Guinea Pigs. Maximisation test according to Magnusson and Kligman. [redacted]
Klimisch Score	1
Amendments/Deviations	None of significance
GLP	Yes
Test Guideline/s	OECD TG 406, EC B.6
Species	Guinea pig
Strain	Dunkin-Hartley
No/Sex/Group	6F:negative control, 11F: treated
Dose Levels	Intradermal induction: 25%, Topical induction: 100%, Challenge: 50 and 100%
Exposure Type	Day 0: Intradermal injection, Day 7 and 20: Topical application
Study Summary	Initial studies were conducted to determine non-necrotizing and non-irritating concentrations for use in the main study. Following intradermal induction on Day 0 and topical induction on Day 7 animals were challenged by topical application with an observational assessment of the dermal reaction at 24 and 48 hours. No macroscopic cutaneous reactions were observed at either time point with either challenge concentration in any animal.
Additional Comments	No additional comments
Conclusion	The test substance is not a sensitiser and not classifiable.

Environmental fate studies

All studies on the environmental fate of metobromuron provided by the applicant have been reviewed. These studies are used to understand how metobromuron behaves and moves through the environment. Data from these studies have been used in relevant areas of the risk assessment to parameterise the models, predict environmental concentrations of metobromuron in the environment following use of SOLETO and thus, the likely exposure of environmental receptors.

In this case, the EPA has reviewed the studies and the summaries of these studies provided as part of the European review of metobromuron (EFSA 2014). When the EPA fully agrees with the review in the European assessment, no summary has been made as the summary is available in the publicly available Draft Assessment Report (EC 2012).

Ecotoxicity study summaries

All studies on the toxicity of metobromuron provided by the applicant on environmental receptors have been reviewed. These studies are used to describe the key impacts of metobromuron or SOLETO on the different environmental compartments. The data from the studies have been used for classifying the active ingredient and in relevant areas of the risk assessment.

In this case, the EPA has reviewed the studies and the summaries of these studies provided as part of the European review of metobromuron (EFSA 2014). Where the EPA has not agreed with the European review of the ecotoxicity study or had additional comments these are described below. When the EPA fully agrees with the review in the European assessment, no summary has been made as the summary is available in the publicly available Draft Assessment Report (EC 2012).

Two additional ecotoxicity study has been performed for the active ingredient metobromuron. A summary of these studies is provided in Table 63 and Table 64.

Table 63: Acute toxicity to *Apis mellifera*: active ingredient [key study]

Study type	Acute toxicity to the adult honey bee (*Apis mellifera*)
Species	*Apis mellifera*
Flag	Key study
Test Substance	Active ingredient: metobromuron
Endpoint	LD_{50} & LC_{50}
Value	Oral >86 µg ai/bee Contact >100 µg ai/bee
Reference	Kimmel (2015). Metobromuron: Acute Oral and Contact Toxicity to Honey bee (*Apis mellifera* L.) under Laboratory Conditions. Laboratory number: 20140150.
Klimisch Score	1
Amendments/Deviations	None
GLP	Yes
Test Guideline/s	OECD 213 & OECD 214
Dose Levels	100 µg ai/bee
Validity criteria met	The study is considered to be valid since mortality was < 10% for oral and contact controls. The oral 24 h-LD_{50} of the reference item was within the range 0.10 - 0.35 µg reference item/bee and the contact 24 h-LD_{50} of the reference item was within the range 0.10 - 0.30 µg reference item/bee. This confirmed that the honey bees used were viable and that the test was valid.
Study Summary	Following a non-GLP range-finding pre-test, a limit test was conducted to assess the effect of metobromuron on the acute oral and contact toxicity to Honey bee (*Apis mellifera*). Mortality and behavioural abnormalities were determined at 4, 24 and 48 hours. As the mortality did not increase more than 10% between 24 and 48 hours, the test was not prolonged to 72 and 96 hours *Oral* Honey bees were starved for 3 hours prior to treatment. Bees were provided the test/reference solutions in a 50% (w/v) sugar solution. The target dose for metobromuron was 100 µg ai/bee. The weight of the vials including the treatment solutions was recorded before and after offering the diet to calculate the total food consumption and the effective treatment dose per bee. The mean food consumption in the test item treatment was 17 µL/bee, resulting in an actual dose of 86 µL ai/bee. Mortality of 3.8% was determined for the final doses tested of 86 µg test item ai/bee with no behavioural abnormalities.

	Contact Each honeybee was treated on the dorsal side of the thorax with 1 µL test solution Mortality of 6.3% was determined for the final doses tested of 100 µg ai/bee with no behavioural abnormalities.
Comments	The slightly lower food ingestion in the test item treatment replicates may be interpreted as repellent effect for the test item.
Conclusion	*Oral* Following 48 hours of acute oral exposure to adult honey bees the LD_{50} was determined to be >86 µg ai/bee. *Contact* Following 48 hours of acute contact exposure to adult honey bees the LD_{50} was determined to be >100 µg ai/bee.

Table 64: Acute toxicity to *Apis mellifera*: active ingredient [key study]

Study type	Toxicity to the larval honey bee (*Apis mellifera*) following repeat exposure
Species	*Apis mellifera*
Flag	Key study
Test Substance	Active ingredient: metobromuron
Endpoint	LD_{50} & NOEC
Value	LD_{50} = 22.43 µg ai/larva NOEC = 6.25 µg ai/larva
Reference	Odemer (2015). Metobromuron: Toxicity to Honey bee (*Apis mellifera* L.) Larva After Repeated Exposure Under *In Vitro* Laboratory Conditions. Laboratory number: 20140152.
Klimisch Score	1
Amendments/Deviations	None
GLP	Yes
Test Guideline/s	OECD 237 & draft OECD "Honey Bee (*Apis mellifera*) Larval Toxicity Test, Repeated Exposure" (2014)
Target Dose Levels	6.25, 12.50, 25, 50 and 100 µg ai/larva (cumulative dose)
Validity criteria met	The study is considered to be valid since mortality was < 15% from D3 to D7 in the controls. D7-LD_{50} of the reference item >50%. This confirmed that the honey bees used were viable and that the test was valid.
Study Summary	Following a non-GLP range-finding pre-test, a dose response test using 1st instar (L1) larvae was conducted. Larvae were grafted from combs from three different honey bee colonies on D1. They were fed with the test solution which was incorporated into the larval diet on D3, D4, D5 and D6 for a repeat exposure. Test termination was on D7. Mortality and behavioural abnormalities were determined on D4, D5, D6 and D7. An assessment on food consumption was conducted on D7.

	Metobromuron (µg ai/larva)				
	6.25	12.5	25	50	100
Cumulative mortality on D7 (%)	25.0	52.8*	44.4*	77.8*	91.7*
Corrected mortality on D7 (%)[1]	15.6	46.9	37.5	75.0	90.6

[1] Corrected with the solvent control mortality (11.1%) and calculated with the formula of Abbott

* Statistically significantlt higher than the solvent control (Step-down Cochran-Armitage Test, α = 0.05)

No behavioural abnormalities were observed.

A statistically significant difference for food consumption was observed in the two highest doses when compared to the control.

	The mean recoveries of metobromuron in the test solutions ranged from 98.0 to 109.7% throughout the tests. The results are corresponding to nominal values.
Comments	None.
Conclusion	The LD_{50} for metobromuron on D7 for honey bee larvae after repeat exposure was determined to be 22.43 µg ai/larva (corresponding to 0.160 µg ai/µL diet. The NOED was determined to be 6.25 µg ai/larva (corresponding to 0.045 µg ai/µL diet).

Appendix K: References

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Appendix L: Levels of concern used by the EPA

Levels of concern used by the EPA	
Aquatic (fish, invertebrates, algae, aquatic plants) – non-threatened	
Acute RQ	< 0.1
Chronic RQ	≥ 1
Aquatic (fish, invertebrates, aquatic plants) threatened species	
Acute RQ	≥ 0.05
Chronic RQ	≥ 0.1
Non-threatened plants (terrestrial)	
Acute RQ /TER	RQ ≥ 1 calculated on the basis of EC_{25} or TER ≥ 5 calculated on the basis of EC_{50}
Threatened plants species (terrestrial)	
Acute RQ	≥ 1 calculated on the basis of the NOEC or EC_{05}
Non-threatened earthworm/ birds	
Acute TER	< 10
Chronic TER	< 5
Threatened bird species	
Acute TER	< 20
Chronic TER	< 10
Threatened soil organisms species	
Acute TER	< 100
Chronic TER	< 50
Bees	
Acute RQ oral/contact	> 0.4
Chronic RQ	> 1
Terrestrial invertebrates	
Hazard Quotient (HQ) in-field/off-field	≥ 2