INFOTOX (Pty) Ltd

2001/000870/07

Retrieval and scientific interpretation of ecotoxicological information

PostNet Suite 112 Private Bag X25723 Monumentpark 0105 SOUTH AFRICA

Tel: 27(12) 346 4668 Fax: 086 513 5478 Cell: 082 416 5864

e-mail: Info@infotox.co.za www.infotox.co.za

Project conducted on behalf of Wentek Chemicals (Pty) Ltd

Toxicological Risk Assessment for the Purpose of Derogation of SILENT (L9545) Substance of Concern: Glufosinate Ammonium

Report No 038-2024 Rev 2.0

Compiled by
WCA van Niekerk PhD ; Environmental Toxicologist QEP (USA);
Pr Sci Nat (Environmental Science)

Internal review by
MH Fourie PhD (Reproductive Biology) MSc (Epidemiology)
Pr Sci Nat (Toxicological Science)

7 October 2024

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WCA van Niekerk PhD QEP (USA) Pr Sci Nat (Environmental Science)
Managing Director

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Internal review:

MH Fourie PhD (Reproductive Biology) MSc (Epidemiology) Pr Sci Nat (Toxicological Science)

Expertise and Declaration of Independence

This report was prepared by INFOTOX (Pty) Ltd ("INFOTOX"). Established in 1991, INFOTOX is a professional scientific company, highly focused in the discipline of ecotoxicological risk assessment. Both occupational and environmental human health risks, as well as risks to ecological receptors, are addressed.

Dr Willie van Niekerk, Managing Director of INFOTOX, has BSc, Hons BSc and MSc degrees from the University of Potchefstroom and a PhD from the University of South Africa. He is a Qualified Environmental Professional (QEP), certified by the Institute of Professional Environmental Practice (IPEP) in the USA (No 07960160), and a registered Professional Natural Scientist (Pr Sci Nat, Environmental Science, No 400284/04). Dr Van Niekerk has specialised in chemical toxicology and human health risk assessments, but he has experience in many other areas in the disciplines of analytical and environmental sciences.

Dr Marlene Fourie has BSc and Hons BSc degrees from the University of Stellenbosch and MSc and PhD degrees from the University of Pretoria. Her field of specialisation is reproductive biology/toxicology. Dr Fourie also has an MSc-degree in epidemiology from the University of Pretoria. Following positions as Medical Natural Scientist at the Andrology Unit, Department of Urology, University of Pretoria and the Pretoria Academic Hospital from 1987 to 2001, she joined INFOTOX as a Medical Biological Scientist. Dr Fourie has conducted many health risk assessments and projects relating to the health status of communities. She is registered as a Professional Natural Scientist (Pr Sci Nat, Toxicological Science, No 400190/14).

Dricky Simpson has a higher diploma in Quality Assurance as well as in Medical Technology. Dricky worked in pathology laboratories and she has done research in human toxicology and pharmacology. She also has experience in animal toxicology and pharmacology. During the last fifteen years as Director of INFOTOX she worked in human health risk assessment for a wide range of industries.

This specialist report was compiled for Wentek Chemicals (Pty) Ltd. We do hereby declare that we are financially and otherwise independent of Wentek Chemicals (Pty) Ltd.

Signed on behalf of INFOTOX (Pty) Ltd, duly authorized in the capacity of Managing Director:

Willem Christiaan Abraham van Niekerk

7 October 2024

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List of Abbreviations

AEL	Acceptable exposure level
CDC	Centers for Disease Control and Prevention
CMR	Carcinogenicity, mutagenicity, and reproductive toxicity
DNT	Developmental neurotoxicity
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemical's
ECHA	European Chemicals Agency
EDSP	Endocrine Disruptor Screening Program
EEC	Estimated environmental concentration
EFSA	European Food Safety Authority
EIIS	Ecological Incident Information System
FFDCA	Federal Food, Drug, and Cosmetic Act
FQPA SF	FQPA Safety Factor
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
HEC	Human equivalent concentration
HED	Human equivalent dose
HHRA	Human health risk assessment
HIARC	Hazard Identification Assessment Review Committee
IDS	Incident Data System
IPCS	International Programme on Chemical Safety
LDT	Lowest dose tested
LOAELs	Lowest-observed-adverse-effect levels
LOC	Level of concern
MOE	Margin of exposure
MRIDs	Master Record Identifiers
NIOSH	National Institute for Occupational Safety
NOAELs	No-observed-adverse-effect levels
NRC	US National Research Council
OC	Organic carbon
OECD	Organisation for Economic Co-operation and Development
OPP	USEPA Office of Pesticide Programs
PAD	Population adjusted dose (a = acute, c = chronic)
PAN	Pesticide Action Network
PND	Postnatal day
POD	Point of departure
PPDB	Pesticide Properties DataBase
RfC	Reference concentration
RfD	Reference dose
RQ	Risk quotient
SENSOR	Health Sentinel Event Notification System for Occupational Risk-Pesticides
STOT RE	Specific target organ toxicity (repeated exposure)

TRA	Targeted Risk Assessment
TSCA	Toxic Substances Control Act
UF	Uncertainty factors
UFA	Uncertainty in extrapolating animal data to humans
UFH	Variation in susceptibility among the members of the human population
UFL	Uncertainty in extrapolating from a LOAEL rather than from a NOAEL
USEPA	United States Environmental Protection Agency
WOE	Weight-of-evidence

List of Terms

Aerobic metabolism	Metabolism, including the production of cellular energy, with the consumption of oxygen
Carcinogenicity	Substance that causes cancer
Derogation	An exemption from or relaxation of the consideration of this product for removal from the market due to it being considered a CMR product of concern.
Developmental toxicity	Any developmental malformation of the foetus, caused by a toxic substance. that is caused by the toxicity of a chemical or pathogen
Dicotyledonous (dicot)	Dicots are a group of plants that have two cotyledons or seed leaves after germination, generally referred to as broad-leaved plants, typically bearing flowers with petals in multiples of four or five.
Dose-response assessment	Addresses the relationship between levels of uptake of a substance and the degree of manifestation of adverse effects
Environmental Fate	Behaviour in or movement of a chemical substance after having been released to the environment. The behaviour in or movements through the environmental compartments of air, soil and water, and the preferred final destiny compartment(s) are described.
Epidemiology	Study of the determinants, occurrence, and distribution of health and disease in a defined population
Exposure assessment	Identification of environmental pathways, potentially exposed groups, routes of direct and indirect exposure, and estimates of concentrations and duration of exposure.
Foliar	On or of the leaves of a plant
Half-life	The time needed for the removal of 50% of the original concentration of a substance in the environment
Hazard assessment	The identification of the chemical constituents of potential concern and the hazards it poses by these chemicals
Monocotyledonous (monocot)	Monocots are a group of plants that have one cotyledon or seed leaf after germination, typically flower-bearing herbaceous plants or grasses.
Mutagenicity	Property of chemical agents to induce genetic mutation
Pathways of exposure	The sequence of environmental compartments of air, soil, water, and/or sediment, through which a substance may be distributed or spread in the environment.
Receptors	People exposed to the substance of interest
Registrar	Registrar of the fertilisers, farm feed, agricultural remedies and stock remedies Act, 1947 (Act 36 of 1947) in the Department of Agriculture, Land Reform and Rural Development
Reproductive toxicity	A substance or agent that can cause adverse effects on the reproductive system, causing the inability to reproduce offspring
Risk characterisation	Integration of the components described above. The risk characterisation will also provide a review of documented human exposure incidents
Routes of exposure	Inhalation, ingestion, and dermal contact
Surrogate	A chemical with properties, including potential toxicity, that are likely to be similar to another substance of interest for which little information about the properties and/or toxicity are known. “Transferring” the known properties of the surrogate to that of the uncharacterised substance is known as the “bridging principle”, or “read-across” for the purposes of hazard and risk assessment.
Synthetase	Enzyme catalysing the joining of two molecules, with concomitant energy expenditure
Target organ toxicity	The effects on the organ impacted by a hazardous substance
Uncertainty review	Identifies the nature and, when possible, the magnitude of the uncertainty and variability inherent in the characterisation of risks

Executive Summary

This document is an independent risk assessment report supporting an application for derogation allowing the restricted use of the registered herbicide SILENT, with Act No. 36 of 1947 registration number L9545.

SILENT is identified as a substance of concern due to its classification as a reproductive hazard category 1B (H360FD) according to the Globally Harmonized System of Classification and Labelling of Chemicals ("GHS"). The classification is due to the ingredient glufosinate ammonium, which is classified in GHS as reproductive toxicity category 1B.

Prepared for: Wentek Chemicals (Pty) Ltd
Product name: SILENT
Act No. 36 of 1947 registration number: L9545

Intended product use:

- A non-selective, non-residual, partly systemic contact herbicide formulated as a water-soluble concentrate, for the control of certain broadleaf weeds, grasses and sedges in crops as indicated, as well as at industrial sites and unplanted areas.
- The product is for use in large-scale agricultural crop production enterprises.
- The product is not intended for sale to residential gardeners. This means that it will not be sold to the public on the shelves of local nurseries or general gardening stores.

Occupational exposure assessment:
Two occupational designations are assessed:

- Occupational pesticide handlers, exposed by the dermal and inhalation routes of exposure (Table 1).
- Post-application (re-entry) workers, exposed by the dermal route only, since glufosinate ammonium and its residues are not volatile (inhalation exposure to residues on plants is excluded).

The product supplier has indicated that the herbicide is not intended for aerial application (e.g., by low-flying aircraft) and this method of application is excluded from the assessment.

Table 1: Occupational pesticide handlers' activities and crops assessment summary.

Pesticide handler activity: Mixing/loading/application				
Application method	**Vineyards**	**Citrus, pome, stone and subtropical fruits**	**Tree nuts**	**Unplanted/industrial land: weeds and the common reed**
Groundboom, broadcast spray	X	X	X	X
Backpack, Ground/soil-directed	X	X	X	X
Liquid, mechanically-pressurized handgun, broadcast (foliar)	X	X	X	X
Liquid, mechanically-pressurized handgun, ground-directed	X	X	X	X

Completely mechanised post-application re-entry activities are highly unlikely to be associated with any significant exposure to workers and are not assessed.

SILENT is a herbicide, and clear instructions on the label caution that it must be ensured that the applied spray does not make contact with the foliage or stems of young plants. Furthermore, herbicide sprays are not directed at the buds, flowers or fruit. Most post-application re-entry activities involves contact only or mainly with fruit, leaves, and the twigs and branches of fruit trees and vines, which are not sprayed.

Thus, most re-entry activities will involve negligible contact with herbicide residues, such as:

- Harvesting, pruning, leaf pulling or thinning fruit by hand.
- Scouting or inspecting crops.
- Propping fruiting branches and other orchard or vineyard maintenance activities.
- Propagating or transplanting vines.
- Hand-setting of irrigation pipes, which should be done, in any case, with gloves protecting hands against superficial injury.

Dietary exposure to treated crops

Being a non-selective herbicide that will damage the crop on contact, it is understandable that contact with crops is avoided, and this caution appears on the product label. The herbicide is never applied directly to the commodity to be harvested, and insignificant translocation of glufosinate ammonium within the various parts of the plant has been noted. Therefore, it is concluded that the herbicide residue content of the harvested fruits or nuts, would be negligible and practically zero. This concurs with assessments by other international regulatory agencies, concluding that there would not be dietary risks to consumers of food originating from crops grown in farmlands where glufosinate ammonium herbicides had been applied.

Health risk assessment results and conclusion

The results of the health risk assessment indicated that there are not reasons for concern, including of reproductive/developmental toxicity effects, in agricultural operators handling the product, mixing or applying the product, or in contact with treated crops after 12 to 24 hours post-application.

Ecological risks

The emergence of herbicide resistant weeds is an increasing problem that has become a significant economic issue to growers. This has made glufosinate, as a broad spectrum postemergence herbicide with little weed-resistance, which is suitable for use on· a wide variety of crops, a valuable tool for weed management. Although risks to mammals and birds foraging in treated weeds cannot be totally excluded, it has been concluded that reducing either the single application rate or the number of applications on glufosinate labels could have an impact on growers (and food production) that outweighs the potential chronic risk to mammals.

Restricted use application

The restricted use applied for is according to the intended product use:

- Herbicide not for sale to and used by residential gardeners.
- Mixing of the treatment solution in accordance with the instructions on the product label.
- Personal protection instructions on the SDS must be followed; that is, washing hands, forearms and face thoroughly after handling chemical products.
- At least baseline PPE must be worn when applying the product; that is, clothing covering the arms and legs, closed shoes and chemical-resistant gloves as well as eye protection (safety goggles). The product SDS additionally recommends face protection.
- The recommended 1-day post-application restricted-entry interval (“REI”) must lapse before crop re-entry.

1 Background

In a document circulated to “All Regulatory Holders” on 14 April 2022, the Registrar: Act 36 Of 1947, of the Department of Agriculture, Land Reform and Rural Development (“Registrar” and “The Department”) refers to an assessment that was carried out at the international level to determine risks to human health due to exposure to active ingredients and their formulations that meet the criteria of carcinogenicity, mutagenicity, and reproductive toxicity (“CMR”) categories 1A or 1B according to the Globally Harmonized System of Classification and Labelling of Chemicals (“GHS”). The Department then stated that “*the assessment identified the need to reduce risks to human health associated with such products*”.

Category 1A covers substances that are known to be CMR, mainly according to human evidence. Category 1B covers substances presumed to be CMR based on data from animal studies.

The Registrar stated his intention to “*prohibit the use of ingredients and their formulations that meets* (sic) *the criteria of CMR categories 1A or 1B of the GHS as from 01 June 2024*”.

However, in exceptional circumstances, the Registrar may grant registration of an implicated agricultural remedy when it can be demonstrated that:

“a) The risk to humans, animals or the environment from exposure to the active substance in an agricultural remedy, under realistic worst-case conditions of use, is negligible”
(and other conditions not relevant to this INFOTOX report).

In February 2024, the Registrar issued a Guideline for the Application for a Derogation for an Agricultural Remedy Identified as a Substance of Concern.

This INFOTOX report deals with the assessment of risk to humans, animals and the environment associated with the use of glufosinate ammonium.

2 Deployment of this INFOTOX document

This INFOTOX report covers various aspects of the study in logical sections, as outlined below:

Section 1 states the intention of the Department to prohibit the use of ingredients and their formulations that meet the criteria for CMR categories in a notice dated 14 April 2022 (“Notice”). The Notice defines the point of departure for this INFOTOX study.

Section 2 outlines the deployment of this report, providing context of a particular section in the overall presentation.

Section 3 provides hazard information for glufosinate ammonium according the Globally Harmonized System of Classification and Labelling of Chemicals (“GHS”).

Section 4 describes essential, concise steps of the health risk assessment paradigm.

Section 5 explains the herbicide action and benefits assessment of glufosinate ammonium.

Section 6 explains more detail of the human health risk assessment methodology followed in this assessment report.

Section 7 provides an environmental fate assessment for glufosinate ammonium.

Section 8 summarises toxicological reviews and presents toxicological parameters for application in health risk assessment.

Section 9 presents an overview of ecological risk assessment.

Section 10 summarises human incident reports.

Section 11 deals with ecological incidents.

Section 12 provides information on endocrine screening assessments.

Section 13 describes occupational exposure calculations and results.

Section 14 describes dietary exposure and risk assessment.

Section 15 presents a summary of conclusions.

Section 16 presents recommendations for granting of derogation.

Section 17 lists the scientific literature references that were consulted in compiling this document.

Annexure 1 presents post-application agricultural workers glufosinate ammonium residue transfer coefficients.

3 Hazard identification

3.1 The need for GHS classification

Internationally, there is a demand for safer chemicals and technologies, and it is appropriate to utilise information in the GHS as a starting point. This INFOTOX report relates specifically to active ingredients and their formulations that meet the criteria of CMR categories 1A or 1B in the GHS. Information in the GHS represents hazard data, not information on risk.

3.2 Glufosinate ammonium CMR hazard classification

The GHS hazard classification identifying the product as a CMR hazardous substance of concern, is: Reproductive toxicity category 1B (H360FD); “F” indicating an effect on fertility, and a suspected detrimental effect on foetal development (Table 3.2.1).

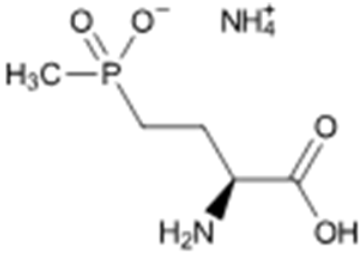
	**Glufosinate ammonium** **CAS # 77182-82-2**

Table 3.2.1: CMR GHS classification of glufosinate ammonium.

Hazard class and category code	Hazard Statement Code	Hazard statement	Signal word	Pictogram
Carcinogenic	Not classified	Not applicable	Not applicable	Not applicable
Mutagenic	Not classified	Not applicable	Not applicable	Not applicable
Reproductive Toxicity Cat. 1B	H360Fd	May damage fertility Suspected of damaging the unborn child	Danger	
Classification according to the European Chemicals Agency (ECHA online); harmonised EU classification.				

GHS Category 1B criteria for substance classification:

- **Presumed human reproductive toxicants - largely based on animal studies**
- Clear evidence of adverse effects on sexual function and fertility or on development in absence of other toxic effects has been identified; or
- If occurring with other toxic effects, the reproductive toxicity is not considered to be a second non-specific consequence of the other toxic effects.

4 The health risk assessment paradigm

A significant factor in the Organisation for Economic Co-operation and Development (OECD 2021) guidance document on key considerations for the identification and selection of safer chemical alternatives assessment, deals with the likelihood of exposure (human and ecological). OECD recommended that routes of exposure to a hazardous chemical that are unlikely, based on measured exposure data or physical-chemical properties of the substance of concern, should be excluded from the assessment. More correctly, the statement should refer to pathways of exposure (air, soil, water, and sediment), and routes of exposure (inhalation, ingestion, and dermal contact).

This recommendation of the OECD (2021) takes the assessment a step further from the hazard data of chemicals represented in the GHS, to the level where the potential for exposure of humans and ecological receptors is assessed, and through accounting for the toxicology of a substance or formulation, the level of risk is determined. This is aligned with the observations and recommendations of Karamertzanis et al. (2019).

Karamertzanis et al. (2019) evaluated the impact on classifications of carcinogenicity, mutagenicity, reproductive and specific target organ toxicity after repeated exposure in the first ten years of implementation of the REACH[1] regulation. The authors highlighted that classification for carcinogenicity, mutagenicity, reproductive toxicity, and specific target organ toxicity (repeated exposure) ("STOT RE") triggers several obligations for manufacturers, importers, and professional users.

Karamertzanis et al. (2019) then stated:
"*In addition to such consequences under other legislations* (sic)*, registrants are required to carry out exposure assessment and risk characterisation for substances that are classified and, hence, classification under REACH is a trigger for risk assessment for human health."*

[1] Registration, evaluation and authorization of chemicals.

OECD (2021) refers to the European Centre for Ecotoxicology and Toxicology of Chemical's ("ECETOC")[2] Targeted Risk Assessment ("TRA") tool for calculating the risk of exposure from chemicals to workers, consumers, and the environment. This illustrates the logic of basing the final decision about the safety of a chemical or formulation on health risk assessment, rather than only on hazard identification, as represented in the GHS.

The original paradigm for regulatory human health risk assessment ("HHRA") in the USA was developed by the US National Research Council (NRC 1983). This model has been adopted and refined by the US Environmental Protection Agency ("USEPA") and other international agencies as published under the International Programme on Chemical Safety (IPCS 1999; IPCS 2010), and is widely used for quantitative human health risk assessments.

Figure 4.1 illustrates the health risk assessment paradigm in a simple diagram.

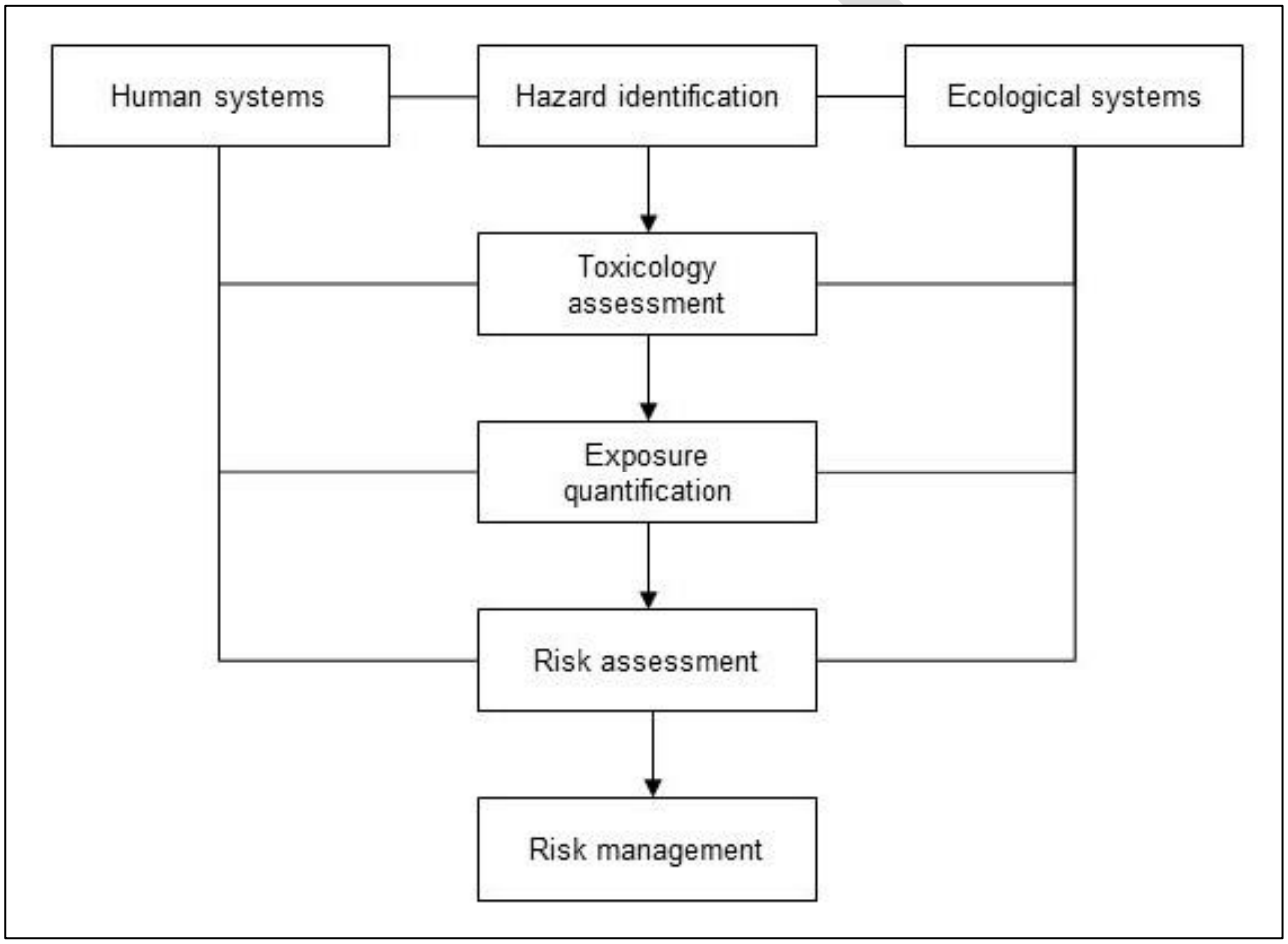


Figure 4.1: The holistic health risk assessment paradigm.

It is shown in this INFOTOX report that exposure assessment and health risk quantification are essential steps in managing health risks associated with hazardous chemicals.

[2] http://www.ecetoc.org/tools/targeted-risk-assessment-tra/.

5 Herbicide action and benefits assessment

Glufosinate ammonium is a non-selective, foliar herbicide that acts by inhibiting glutamine synthetase needed for the ammonification of glutamate to the amino acid glutamine. The disruption in the production of this key amino acid leads to disruption of the cell membrane, build-up of excess ammonium, and death of the cell. It dissociates to produce ammonium and glufosinate acid, a racemic mixture of ionic isomers. Of these, only the L-isomer (or (S)-enantiomer) mimics the enzyme glutamine synthetase and, therefore, is herbicidally active.

Glufosinate ammonium is registered in the USA and elsewhere in the world as a broad spectrum, non-selective foliar-applied herbicide for control of broad leaf, grass, and sedge weeds in numerous agronomic crops, orchards, vegetables, and non-crop sites (USEPA 2016). In the USA, glufosinate ammonium has been used on more than thirty crops and other use sites between 1998 and 2014. Quantities applied and areas treated with glufosinate have more than tripled over this period, primarily due to increases in weed species that are resistant to other herbicides, and the introduction and increased production of glufosinate-tolerant crops. The emanation of herbicide-resistant weeds is an increasing problem that has become a significant economic issue to growers.

USEPA (2016) acknowledged the benefits of glufosinate ammonium in its registration decision (USEPA 2016).

6 Human health risk assessment methodology

The human health risk assessment ("HHRA") paradigm divides human health risk assessment into a number of logical steps. All of these are not fully applicable to the generic toxicological risk assessment for the purpose of derogation:

- **Hazard assessment** is the identification of the chemical constituent of concern and the hazard it poses, in this case Glufosinate ammonium and the reproductive/developmental toxicity hazard.

- **Dose-response assessment** (toxicological assessment) addresses the relationship between levels of uptake and the manifestation of adverse effects (reproductive/developmental toxicity). For this purpose, the following INFOTOX actions are needed:
  - Collection of human reproductive toxicity data on glufosinate ammonium from scientific publications.

  - Retrieval of toxicological information from available reproductive/ developmental studies, and will apply standard risk assessment methodologies to derive a point of departure ("POD") and level of concern ("LOC") or acceptable exposure level ("AEL") for the HHRA purposes, by applying appropriate uncertainty factors and safety factors for infants and children, referring to dose through the routes of exposure. The derived toxicological values will be protective specifically against potential reproductive effects of the product. This will ensure compliance with the Guideline for the Application for a Derogation for an Agricultural Remedy Identified as a Substance of Concern, issued by the registrar: Act 36 of 1947, in February 2024. Health risks will be assessed following the margin of exposure ("MOE") approach. The MOE approach is basically a comparison of the calculated exposure dose and the toxicity limit value for a specific health effect, referred to as the health effect endpoint.

- The calculated MOE is compared to the level of concern ("LOC"), also referred to as a benchmark MOE. The LOC is the margin of exposure between the calculated exposure and the POD that indicates a risk of health effects associated with the calculated exposure. Each POD is associated with a specific numerical LOC value. Therefore, if a calculated MOE is higher in value than the LOC associated with the POD used for the MOE calculation, a risk to health under the assessed exposure conditions is highly unlikely and excluded for all practical purposes. However, if the calculated MOE is lower than the associated LOC, a risk to health cannot be excluded.

- **Exposure assessment considers** the identification of environmental pathways, potentially exposed groups, routes of direct and indirect exposure, and estimates of concentrations and duration of exposure. A conceptual model/matrix of application practices and exposure pathways and routes applicable to the identified receptors will be constructed to guide the exposure assessment for the health risk assessment.

  The HHRA focuses on the following occupational exposure scenarios:
  - The dermal and inhalation routes of exposure of herbicide mixers and applicators.
  - The dermal post-application exposure of workers re-entering treated fields.

  Residential exposure scenarios are not assessed, because the herbicide assessed with the methodology explained in this report is not for sale in retail outlets catering to the general public. Therefore, potential spray drift in non-occupational settings, which may result in exposures to adults and children to glufosinate ammonium, need not be considered.

  Dietary exposure, by the ingestion of herbicide residues in fruit and vegetable crops, is considered for consumers, including children.

  INFOTOX covers the occupational and dietary exposure scenarios in the health risk assessment, referring to published risk assessment studies.

- **Risk characterisation** involves the integration of the components described above. The risk characterisation also provides a review of documented human exposure incidents, if available.

- **Uncertainty review** identifies the nature and, when possible, the magnitude of the uncertainty and variability inherent in the characterisation of risks.

7 Environmental fate assessment

7.1 Summary of physical and chemical properties of glufosinate ammonium

All studies on the fate and behaviour in the environment were performed with the ammonium salt of glufosinate (glufosinate-ammonium). Due to the fact the ammonium ion is ubiquitous in the environment; the fate of the ammonium resulting from the application of glufosinate-ammonium was not followed (EFSA 2005). Physical/chemical properties and aspects of environmental fate are summarised in Table 7.1.1.

Table 7.1.1: Physical/chemical properties of glufosinate ammonium that determine its environmental fate.

Property	Value	Reference	Comments
Molecular weight (g/mol)	198.2		
Solubility in water (mg/litre, 20°C)	1.37E+06	USEPA 2013	Very soluble
Vapour pressure (mPa)	3.10E-02	*Lewis et al. 2016	
Henry's law constant (Pa m^3 mol^{-1})	4.48E-09		
Octanol-water partition coefficient (K_{OW}), pH7, 20 ºC	9.77E-05		
Octanol-water partition coefficient (Log K_{OW})	-4.01		
Soil-water distribution coefficient (K_d)	1.5		
Organic carbon adsorption coefficient (K_{OC})	173		
Hydrolysis half-life, 25 ºC (days)		USEPA 2013	No significant degradation at pH 5, 7 and 9
Aqueous photolysis half-life, pH 7 (days)			No significant degradation
Soil photolysis half-life (days)	17		
Aerobic soil metabolism half-life (days)	8.5 (sandy loam) 8.7 (silty loam) 8.8 (loamy sand)		1.62 ppm applied
	8.5 (sandy loam) 8.7 (silty loam) 8.8 (loamy sand)		7.23 ppm applied
Anaerobic soil metabolism half-life (days)	37 (silty loam)		
Aerobic aquatic metabolism half-life (days)	38 (sand)		1 ppm applied
	57 (silty loam)		
Anaerobic aquatic metabolism half-life (days)	415		
Organic carbon normalised soil partition coefficient (litre/kg) (K_{FOC})	16.5 (sand)		
	268 (silty loam)		
	605 (silty loam		
Fish bioconcentration factor (28 days)	0.19x (whole fish)		
	0.13x(edible)		
Terrestrial field dissipation half-lives (days)	8 (cropped plot) 16.5 (cropped plot) 5.1 (bare ground) 10.3 (cropped plot) 10.6 (bare ground) 14 (grapes)		
Aquatic field dissipation half-lives (days)	< 7 (soil, 1st application)		
	12 (soil, 2nd application)		
	3 (water, 1st and 2nd applications)		

* Lewis et al. 2016 is the reference to glufosinate ammonium properties listed in the Pesticide Properties DataBase ("PPDB") of the University of Hertfordshire.

7.2 Transport and mobility

As shown in Table 7.1.1, glufosinate ammonium has high water solubility, and will not volatilise significantly due to its low vapor pressure and Henry's law constant. Glufosinate is an ammonium salt, with a low octanol-water partition coefficient, and does not bioconcentrate in fish.

Glufosinate ammonium is mobile to highly mobile, with a Freundlich organic carbon partition coefficient 16.5 to 605 litre/kg_{oc} in soils from sand to silty loam. The normalised organic-carbon-to-water partition coefficient (K_{OC}) is described as the ratio between the distribution coefficient K_d, and the organic carbon content of the sorbent, in units of mass of organic carbon ("OC") per mass of soil (g OC/g soil).

$$K_{OC} = {}^{K_d}/_{OC} \qquad \text{Equation 7.2.1}$$

Where:

K_{OC}	Normalised organic-carbon-to-water partition coefficient
K_d	Soil-water distribution coefficient
OC	Mass of organic carbon per mass of soil

The mobility of glufosinate in soil can be expected to be lower for soils with higher organic carbon content.

7.3 Degradation

Data presented in Table 9.1 show that glufosinate ammonium does not significantly degrade via the abiotic mechanisms of hydrolysis or photolysis.

It is biodegraded moderately rapidly in aerobic soils, with some indication of sensitivity to concentration. At higher application rates (7.23 ppm applied, aerobic soil metabolism half-lives for glufosinate ranged between 20.6 and 23.0 days, while at a lower application rate (1.62 ppm applied) shorter half-lives of 8.5-to-8.8 days were observed. Biodegradation occurs less rapidly in anaerobic soils and in aerobic water, half-lives ranging between 38 and 87 days in the soils, whereas biodegradation is insignificant in anaerobic water.

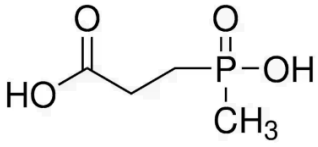
7.4 Field studies

USEPA (2013) reported on the results of several terrestrial field dissipation studies of glufosinate ammonium. It was found to dissipate from the upper 15 cm of soil with half-lives of 8-to-17 days. Despite the fact that glufosinate ammonium is expected to be mobile, it did not leach deeper than about 15 cm into loam or clay soils, or deeper than about 60 cm into a sandy soil.

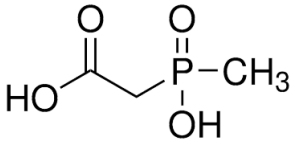
7.5 Transformation products

Primary aerobic metabolism degradation products of glufosinate include MPP (3-methylphosphinicopropionic acid), MPA (2-methylphosphinico-acetic acid), NAG (2-acetamido-4-methylphosphinico-butanoic acid), and carbon dioxide (USEPA 2013; EFSA 2005).

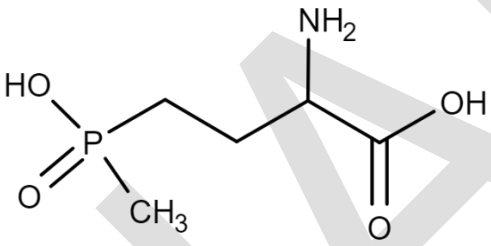
3-Methylphosphinicopropionic acid (MPP) CAS # 15090-23-0



2-Methylphosphinico-acetic acid (MPA) CAS # 72651-25-3



2-Acetamido-4-methylphosphinico-butanoic acid (NAG) CAS # 51276-47-2



The degradation products of glufosinate ammonium have lower mammalian toxicity than the parent compound (USEPA 2013). The degradation products are of interest only in considering the potential for groundwater contamination following agricultural applications of glufosinate ammonium. In the groundwater pathway, if glufosinate ammonium is not of concern, the degradation products will also not be of concern. These compounds are thus not of determining significance in this INFOTOX health risk assessment.

8 Toxicological reviews

8.1 Background to toxicological information systems

The USEPA uses Master Record Identifiers (“MRIDs”) to track and manage information submitted to the pesticide program[3]. An MRID is unique eight-digit number assigned to each study submitted to USEPA. The first six digits are referred to as the 'root' MRID. Some of the studies have not been published in the open scientific literature, but USEPA evaluates the integrity of all studies, and information is used only from studies that are classified as acceptable. USEPA also refers to accession numbers (“Acc No”) to access data from the non-confidential Toxic Substances Control Act (“TSCA”) Inventory.

The USEPA often references MRID numbers in assessment reports of the pesticide program, but do not always provide the complete study reference. However, it is accepted that the USEPA has evaluated the integrity of these studies before integration of study information into the pesticide assessments.

[3] https://www.epa.gov/pesticide-registration/study-formatting-and-supplemental-information#establish%20MRID.

8.2 Acute dietary endpoint - general population

A toxicological endpoint or POD for the assessment of health risks associated with a single acute dietary exposure for the general population, including infants and children, was not available in the glufosinate toxicity database.

8.3 Acute dietary endpoint - females 13-to-49 years of age

The USEPA derives a population-adjusted dose ("PAD") for the purposes of dietary risk assessments. The PAD is the maximum acceptable dose that is not expected to result in unreasonable adverse health effects, including of reproductive effects, as determined by the USEPA.

The USEPA (2022a) derived an acute PAD, referred to as the "aPAD", based on an acute dietary endpoint from a rabbit development toxicity study. The NOAEL was 6.3 mg/kg-day, based on increased foetal deaths at the LOAEL of 20 mg/kg-day (MRIDs 40345611 and 41144703, cited, but not referenced in USEPA 2022a). This acute PAD is thus suitable for the assessment of the potential reproductive effects of glufosinate ammonium.

8.4 Chronic dietary endpoint

The USEPA (2022a) derived a chronic PAD, referred to as the "cPAD", based on a weight-of-evidence ("WOE") assessment of four rat and dog studies:

- Rat studies based on altered brain glutamine synthetase in females:
  - Subchronic rat study with a LOAEL = 64 to 90 mg/kg-day (MRID 45179103), and
  - A chronic/carcinogenicity rat study with a LOAEL = 24.4 mg/kg-day (MRIDs 40345607 and 41144701).
- A chronic dog study with a LOAEL = 8.5 mg/kg-day, based on altered EKG and mortality (MRID 40345608).
- A rat developmental neurotoxicity ("DNT") study with a LOAEL = 14 mg/kg-day) based on altered brain morphometrics in the postnatal day 72 ("PND72") adult offspring (MRID 46455701).

Based on the WOE approach, USEPA (2022a) chose the chronic NOAEL of 6 mg/kg-day, based on glutamine synthetase inhibition in the brains of male rats in the 13-week oral feeding study. Effects observed in the DNT study were at a dose only about two times higher than the NOAEL.

The reproductive toxicity study in rats indicated postnatal developmental toxicity at the highest dose tested as evidenced by a decrease in viable pups, but no parental toxicity was observed. This was taken as evidence of quantitative increased susceptibility in offspring. It is notable that the reproductive effect was only observed at the highest dose tested, which is 3.3 times higher than the NOAEL of 6 mg/kg-day used as a POD for the chronic risk assessment. Therefore, the POD based on glutamine synthetase inhibition in the brains of male rats is also protective of reproductive effects observed at higher doses.

8.5 Short- and intermediate-term incidental oral and dermal endpoints

USEPA (2022a) selected the short-term incidental oral and short- and intermediate-term dermal endpoints from the rat DNT study where the LOAEL = 14 mg/kg-day, based on alterations in brain morphometrics seen in adults on postnatal day 72 following in utero and/or early postnatal exposure.

As explained in Section 8.4, this endpoint is also protective of reproductive effects observed at higher doses.

Since an oral endpoint was used for a dermal exposure scenario, a dermal absorption factor ("DAF") of 1 per cent was used in the calculating human equivalent dose. This is also the absorption factor used by the USEPA (2022) to calculate health risks associated with dermal exposure.

8.6 Short- and intermediate-term inhalation endpoint

USEPA (2022(b)) selected the short- and intermediate-term inhalation endpoint from a 28-day rat inhalation study with LOAEL = 0.056 mg/litre-day, based on lung/bronchial congestion and increased lung/bronchi weight in female rats. A NOAEC was not observed. HECs/HEDs for residential and occupational scenarios were calculated based on the health endpoint of lung bronchial congestion (MRID 47058101, cited but not referenced in USEPA 2022(b)).

The USEPA (2022(b)) inhalation absorption factor is 1 (100%).

- Residential handler HEC (lung/bronchi endpoint) = 0.035 mg/litre-day, derived using Equation 8.6.1:

$$Residential\ handler\ HEC = Rat\ POD \times Thoracic\ RDDR \quad \text{Equation 8.6.1}$$

Where:

Residential handler HEC	Human equivalent concentration for the residential handler (mg/litre-day)
Rat POD	Point of departure from a rat study = 0.056 mg/litre-day
Thoracic RDDR	Thoracic regional deposited dose ratio = 0.618

- Residential handler HED (lung/bronchi endpoint) = 0.82 mg/kg-day, derived using Equation 8.6.2:

$$Residential\ handler\ HED = \text{Residential handler HEC} \times CF \times ED \quad \text{Equation 8.6.2}$$

Where:

Residential handler HED	Human equivalent dose for the residential handler (mg/kg-day)
Residential handler HEC	Residential handler human equivalent concentration = 0.035 mg/litre-day
CF	Human-specific conversion factor = 11.8 litre/hr-kg
ED	Exposure duration = 2 hours

- Occupational handler HEC (lung/bronchi endpoint) = 0.026 mg/litre-day, derived using Equation 8.6.3:

$$Occupational\ handler\ HEC = Rat\ POD \times EF \times ED \times Thoracic\ RDDR \quad \text{Equation 8.6.3}$$

Where:

Occupational handler r HEC	Human equivalent concentration for the occupational handler (mg/litre)
Rat POD	Point of departure from a rat study = 0.056 mg/litre-day
EF	Daily duration adjustment = 6 hours/8 hours)
ED	Weekly duration adjustment = 5 days/5 days
Thoracic RDDR	Thoracic regional deposited dose ratio = 0.618

- Occupational handler HED (lung/bronchi endpoint) = 2.46 mg/kg-day, derived using Equation 8.6.4:

$$Occupational\ handler\ HED = Occupational\ handler\ HEQ \times CF \times ED \qquad \text{Equation 8.6.4}$$

Where:

Occupational handler HED	Human equivalent dose for the occupational handler (mg/kg-day)
Occupational handler HEC	Occupational handler human equivalent concentration = 0.026 mg/litre-day
CF	Human-specific conversion factor = 11.8 litre/hr-kg
ED	Exposure duration = 8 hours

8.7 Cancer (oral, dermal, inhalation)

Glufosinate ammonium was classified by the Hazard Identification Assessment Review Committee ("HIARC") as "*not likely to be a human carcinogen"*. There was no evidence of a treatment-related increase in tumours in either rats or mice (HIARC, TXR 0051833, B. Tarplee, 17-APR-2003, cited but not referenced in USEPA 2022(b)).

Glufosinate ammonium is also not classified as carcinogenic in the Pesticide Properties Data Base of the University of Hertfordshire (Lewis et al. 2016).

Table 8.7.1: Summary of glufosinate toxicological doses and endpoints for use in HHRA.

Point of Departure (POD)	Uncertainty/FQPA Safety Factors	RfD, PAD, Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute dietary (general population, including infants and children)			
An endpoint attributable to a single exposure was not available from the toxicity studies, including the developmental toxicity and developmental neurotoxicity studies.			
Acute dietary (females 13-49 years of age)			
NOAEL = 6.3 mg/kg-day	UFA = 10× UFH = 10× FQPA SF = 1× Total UF = 100×	Acute RfD = 0.063 mg/kg-day aPAD = 0.063 mg/kg-day	Developmental toxicity study in rabbits LOAEL = 20 mg/kg-day based on increased foetal deaths
Chronic dietary (all populations)			
NOAEL= 6 mg/kg-day	UFA = 10× UFH = 10× FQPA SF = UFL = 10× Total UF = 1000×	Chronic RfD = 0.006 mg/kg-day cPAD = 0.006 mg/kg-day	"Weight of evidence" approach from four studies. 1. Rat subchronic LOAEL = 64-90 mg/kg-day and chronic studies with the LOAEL = 29 mg/kg-day based on inhibition of brain glutamate synthetase 2. Dog chronic study with the LOAEL = 8.5 mg/kg-day based on altered electrocardiogram and mortality 3. Rat developmental neurotoxicity study with a LOAEL = 14 mg/kg-day (without a NOAEL, basis for UFL) based on altered morphometrics in the offspring as adults
Incidental oral short-term (1-30 days) and Intermediate term (1-6 months)			
LOAEL= 14 mg/kg-day (LDT)	UFA = 10× UFH = 10× FQPA SF= UFL=10× Total UF = 1000×	Residential LOC for MOE = 1000	Developmental neurotoxicity study in rats LOAEL = 14 mg/kg-day based on brain morphometric changes at PND 72. No NOAEL identified.
Dermal short-term (1-30 days), and intermediate-term (1-6 months)			
LOAEL= 14 mg/kg-day (LDT) DAF = 1 %	UFA = 10× UFH = 10× FQPA SF = UFL = 10× Total UF = 1000×	Residential and occupational LOC for MOE = 1000 for short and intermediate term exposures	Developmental neurotoxicity study in rats LOAEL = 14 mg/kg-day based on brain morphometric changes at PND 72. Lowest dose tested ("LDT"), no NOAEL identified.
Inhalation acute, short-term (1-30 days), intermediate (1-6 months)			
LOAEL=12.5 mg/kg-day (56 mg/m^3)	UFA = 3× UFH = 10× FQPA SF = UFL = 10×	Residential and occupational LOC for MOE = 300 for short and intermediate term	28-day inhalation study (LOAEL = 12.5 mg/kg-day based on lung/bronchial congestion and increased lung/bronchi weight in female rats and increased kidney and liver weights.

Point of Departure (POD)	Uncertainty/FQPA Safety Factors	RfD, PAD, Level of Concern for Risk Assessment	Study and Toxicological Effects
	Total UF = 300× Residential handler HEC = 0.035 mg/litre-day HED = 0.82 mg/kg-day Occupational handler HEC = 0.026 mg/litre-day HED = 2.45 mg/kg-day		
Cancer (oral, dermal, inhalation)			
Not likely to be a human carcinogen			

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures
NOAEL = no observed adverse effect level
LOAEL = lowest observed adverse effect level
UF =uncertainty factor
UFA = extrapolation from animal to human (interspecies)
UFH = potential variation in sensitivity among members of the human population (intraspecies)
UFL = use of a LOAEL to extrapolate a NOAEL.
FQPA SF = FQPA Safety Factor
PAD = population adjusted dose (a = acute, c = chronic)
RfD = reference dose
MOE = margin of exposure
LOC = level of concern
N/A = not applicable

9 Ecological risk assessment

9.1 Introduction

USEPA (2013) applied a surrogate-species approach in its risk assessment of glufosinate ammonium. Toxicity data generated from surrogate test species, intended to be representative of broad taxonomic groups, were used to extrapolate potential effects on a variety of species (receptors) included under these taxonomic groupings.

USEPA (2013) presented comprehensive data on ecological risk assessment. Acute and chronic toxicity data from studies submitted by pesticide registrants, together with available open literature data, were used to evaluate potential direct effects of glufosinate to terrestrial and aquatic receptors. The approach was based primarily on screening-level assessments, applying the risk quotient ("RQ") method. The RQ method involves dividing estimated environmental concentrations ("EECs") by point estimates of the most sensitive acute and chronic toxicity values. The resulting RQs are then compared to LOC values for the surrogate species.

The risk assessment results in USEPA (2013) must be evaluated together with the context presented in USEPA (2016), as discussed in this INFOTOX document.

9.2 Terrestrial risks

9.2.1 Introduction

USEPA (2013) calculated terrestrial wildlife exposure estimates for birds and mammals by focusing on the dietary exposure route of uptake of pesticide active ingredients. These exposures served as surrogates for exposures of terrestrial-phase amphibians and reptiles. For exposures to terrestrial organisms, such as birds and mammals, pesticide residues on food items were estimated on the assumption that organisms were exposed to pesticide residues as a function of the pesticide use pattern.

9.2.2 Risk to mammals

In the preliminary risk assessment for glufosinate, USEPA (2013) identified chronic risks of concern for mammals, with dose-based RQs ranging from 48 for use on blueberries, to an RQ of 7 for potato vine desiccation, where the LOC for chronic risks to non-listed mammals[4] is 1.0. The calculated RQs were based on reductions in growth and in offspring fitness and viability, which effects were seen across generations and in multiple species. When assessed as chronic dose-based RQ values, risks to mammals of all sizes (except those that feed exclusively on seeds and grains) were of concern for most use sites.

When refinements in the assessment were introduced, namely, including the use of a foliar dissipation rate on measured glufosinate residues rather than the default value, median values rather than maximums, average rather than maximum application rates, and/or alternative application dates, risk quotients were reduced. For example, the highest dose-based chronic mammalian RQ for glufosinate ammonium use on blueberries was reduced from 48 to 9.

[4] Endangered and threatened species are referred to as "listed".

9.2.3 Risk to birds, reptiles and terrestrial-phase amphibians

Screening level risks assessed as chronic dietary-based RQs were the highest for the use on blueberry (RQ of 1.67) and lowest for stone fruit (RQ of 1.12). The LOC for chronic risks to birds is 1.0, and observed effects were lethargy, diarrhoea, and in bobwhite quail, decreases in the ratio of live-to-viable embryos after parental exposure.

The refinements referred to above reduced all the RQs to below the LOC (RQs of 0.14 for blueberries and 0.22 for stone fruit).

9.2.4 Invertebrates (pollinators)

Glufosinate ammonium is practically nontoxic to honey bees, both on an acute contact and oral exposure basis (adults only), but USEPA (2013 and 2016) raised uncertainty regarding the toxicity of glufosinate ammonium to bee larvae, since no data on this age group of honey bees were available at the time of the review.

9.2.5 Terrestrial plants

As can be expected from its herbicidal mode of action, glufosinate ammonium adversely affected the most sensitive monocotyledonous (monocot) and dicotyledonous (dicot) species at all treatment levels in vegetative vigour studies (USEPA 2013 and 2016). Screening-level RQs for listed monocot species were as high as 10.9 and 6.2 for ground and aerial applications, respectively, in agricultural settings, and as high as 11.8 in non-agricultural settings. The LOC for terrestrial plants is 1.0.

Refinements to the assessment included, among others, application timing, precipitation, and percolation of water into the soil. These refinements reduced risk estimates, although not to below the LOC. The refined risk assessment for glufosinate ammonium identified potential risks of concern for non-target terrestrial plants[5] for nearly all the modelled exposure scenarios. The non-listed terrestrial plant RQs ranged from 1.25 and 1.35 for monocots, and to 1.91 and 2.06 for dicot species, for ground and aerial applications, respectively, at maximum label application rates.

9.2.6 Risks to non-target aquatic organisms

Non-target organisms include aquatic plants, fish and aquatic invertebrates. The USEPA (2013) preliminary risk assessment did not identify risks of concern for aquatic plants, fish, or aquatic invertebrates, except for the use of glufosinate ammonium on rice. Considering the use of glufosinate ammonium on rice is not relevant in South Africa, it can be concluded that the use of glufosinate ammonium poses no ecological risks of concern for aquatic organisms.

9.3 USEPA critical review of ecological risk assessment

The screening ecological risk assessment recorded by USEPA (2016) indicated that chronic RQs exceeded LOC for mammals and birds at the maximum label single application rate for most crops, with the greatest exceedances in mammals. USEPA subsequently undertook a refined assessment that calculated RQs using average application rates and average EECs. These refinements reduced chronic avian and mammalian RQs, but not to below the LOC.

[5] Plants adjacent to the treated site.

In the final consideration, USEPA (2016) did not recommend risk mitigation measures for birds, reptiles, and terrestrial-phase amphibians. This decision took into account the low chronic dietary-based avian RQs in the screening-level assessment, and reductions of these RQs in the refined assessment, also considering the benefits of glufosinate ammonium uses.

USEPA (2016) also concluded that chronic risks to mammals from glufosinate ammonium use could be less than what had been estimated at the screening level. Firstly, the average number of glufosinate ammonium applications per year among growers in the USA was less than two for all agricultural use sites, except for table grapes. Based on these data, on a national basis, the amount of time during the growing season that mammalian exposure to glufosinate ammonium would lead to risks above the LOC would be less than what had been modelled. Secondly, the applied assessment methodology assumed that mammals (and birds) obtain their entire diet within the treated field. Even in situations where this might have been the case, the availability of treated foliage to mammals as a food item would be limited due to the fast-acting nature of glufosinate ammonium on target weeds. Signs of phytotoxicity would be observed within the first few days after application, and would increase over time, rendering the foliage unattractive as food. Furthermore, available qualitative information indicates that rabbits may prefer untreated forage to forage treated with glufosinate ammonium, and that voles may prefer untreated habitat over glufosinate-treated habitat.

Given the increasing threat of herbicide-resistance, glufosinate, as a broad spectrum postemergence herbicide used on a wide variety of crops, with little weed-resistance of its own, is a valuable tool for weed management.

Based on these considerations, the USEPA (2016) concluded that reducing either the single application rate or the number of applications on glufosinate labels could have an impact on growers that outweighs the potential chronic risk to mammals. Consequently, neither option has been pursued as mitigation measures in the USEPA Interim Decision.

9.4 Implications for use and ecological risks in South Africa

The points of reasoning by the USEPA are also valid for South Africa. In particular, the average number of glufosinate ammonium applications per year of the product SILENT is generally not more than two. Secondly, the dietary intake by mammals and birds is likely to be aligned with the lower intakes proposed by the USEPA, as explained in Section 9.3, rather than with the modelled high intake levels. Thirdly, the emergence of herbicide resistant weeds is also an increasing problem in South Africa, and a significant economic issue to herbicide-dependant farmers. Therefore, as assessed by the USEPA, limiting glufosinate ammonium application rates could have a negative impact on crop producers that outweighs the potential chronic risk to mammals. Consequently, limiting of application rates should also not be pursued as a mitigation measure in South Africa.

10 Human incident reports

USEPA (2016) consulted the USEPA Office of Pesticide Programs (“OPP”) Incident Data System (“IDS”), and the Centers for Disease Control and Prevention (“CDC”)/National Institute for Occupational Safety (“NIOSH”) and Health Sentinel Event Notification System for Occupational Risk-Pesticides (“SENSOR”) databases for poisoning incident data on glufosinate.

The main IDS, from 2007 to 2012, reported six incidents for glufosinate only, and three incidents involving glufosinate and at least one more pesticides. All of these incidents were classified as of

moderate severity and occurred with residential applicators. Reported health effects included gastrointestinal, dermal, neurological, and cardiovascular outcomes. In aggregate IDS, from 2007 to 2012, there were 31 reported incidents classified as of minor severity.

SENSOR pesticides data from 1998 to 2008 identified five cases, resulting from three events involving glufosinate. Four of the five cases involved glufosinate only, and one case involving multiple active ingredients, all regarded as of low severity. Four of these cases reported dermal symptoms, and one case reported respiratory symptoms. Three of the cases were bystanders, one was a residential handler, and the circumstances of the fifth case were unknown, but described as work-related.

USEPA (2016) concluded on the basis of the low frequency and minor-to-moderate severity of the reported incidents for glufosinate, that there was not concern that would warrant further investigation at that time.

11 Ecological incidents

USEPA (2016) searched the 2012 Ecological Incident Information System ("EIIS"), and found 51 incidents associated with the use of glufosinate, reported between 1999 and 2011. Of these incidents, 49 were associated with phytotoxic effects on agricultural crops, and 39 were associated with glufosinate alone.

Eighteen of the crop plant incidents were classified as having a "probable" association with glufosinate exposure, whereas the other 31 crop plant incidents were classified as having a "possible" association with glufosinate use. Most of the incidents of crop damage resulted from direct spray application on corn or canola.

Two freshwater fish-kill incidents were reported with nearby terrestrial applications of glufosinate. It was not known whether these fish incidents were associated with a particular glufosinate formulation, or whether these resulted from oxygen depletion from direct effects of glufosinate exposure on the aquatic plant community.

The reported ecological incidents were not unambiguously associated with glufosinate contact, and could have been prevented with more careful application procedures.

12 Endocrine disruptor screening programme

As required by the Federal Food, Drug, and Cosmetic Act ("FFDCA"), glufosinate is subject to the endocrine screening part of the Endocrine Disruptor Screening Program ("EDSP") of the USA.

The EDSP applies a two-tiered approach in assessing potential endocrine disrupting effects. Tier 1 consists of a set of 11 screening assays to identify the potential of a chemical substance to interact with the oestrogen, androgen, or thyroid ("E, A, or T") hormonal systems. Chemicals that show in Tier 1 screening to have the potential to interact with E, A, or T hormonal systems, proceed to the next stage of the EDSP where USEPA determines which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance, and to establish a dose-response relationship for the E, A, or T effect.

Results of testing for endocrine disrupting effects of glufosinate ammonium are not available in USEPA documentation at this time. The Pesticide Action Network (PAN online) North America states that endocrine disrupting effects of glufosinate ammonium have been insufficiently studied. The Pesticide Properties Database ("PPDB") of the University of Hertfordshire (Lewis et al. 2016) listed glufosinate ammonium as not an endocrine disrupter.

There is thus insufficient data to classify glufosinate ammonium as an endocrine disruptor.

13 Occupational exposure calculations

13.1 Proposed use pattern and exposure profile

Personal Protective Equipment ("PPE") requirements

The product label should include the following PPE requirements for applicators:

- Baseline attire: single layer clothes defined as long-sleeved shirt, long pants, shoes, and socks.
- Chemical resistant gloves.

Restricted-entry interval ("REI")

Generally, labels recommend an REI of 1 day for all activities, with the exception of:

- 2 days to move irrigation pipes in irrigated crops.

The occupational exposure profile generally considered for pesticides is summarised in Table 13.1.1.

Table 13.1.1: Occupational exposure profile.

Type of worker	Exposure duration	Inhalation exposure	Dermal exposure	Oral exposure
Occupational pesticide handlers	Short-term (1 to 30 days)	✔	✔	N.a.
	Intermediate-term (1 to 6 months)	✔	✔	N.a.
Post-application workers	Short-term (1 to 30 days)	N.a.	✔	N.a.
	Intermediate-term (1 to 6 months)	N.a.	✔	N.a.

N.a: Not applicable

Handler exposures

The term "handlers" describes those involved in the pesticide application process. Distinct job functions or tasks related to applications and exposures were identified by the USEPA, depending on the specifics of each task, such as:

- Job requirements (amount of chemical used in each application).
- Kinds of equipment used.
- Treated target.
- Level of protection used by a handler.

The expected exposure scenarios and the quantitative exposure/risk assessment matrix developed for occupational handlers are summarized in Table 13.3.1.

Post-application exposures

The term post-application to describe exposures that occur when individuals are present in an environment that has been previously treated with a pesticide (also referred to as re-entry exposure).

Such exposures may occur when workers enter previously treated areas to perform job functions, including activities related to crop production, such as scouting for pests, moving irrigation pipes, or harvesting (USEPA 2022(b)).

The expected exposure scenarios and the quantitative exposure/risk assessment matrix developed for occupational post-application workers are summarized in Table 13.4.5.

13.2 Exposure and risk equations

Risk assessment example calculations for occupational handler and post-application workers are presented in this section. USEPA examples results for occupational handlers are presented in Section 13.3. Example results for post-application worker exposure and risk calculations in crops targeted in South Africa are not provided by the USEPA (2022(b)).

Occupational handler equations

Potential daily exposures for handlers are calculated using the following formulas:

$$E = UE * AR * A * 0.001\ mg/ug$$

Equation 13.2.1

where:

E	exposure (mg a.i./day)
EU	unit exposure (µg a.i./kg a.i.)
AR	maximum application rate according to proposed label (kg a.i./ha or kg a.i./litre)
A	area treated or amount handled (e.g., ha/day, litre/day)

The daily doses are calculated using the following formula:

$$ADD = \frac{E * AF}{BW}$$

Equation 13.2.2

where:

ADD	*average daily dose absorbed in a given scenario (mg ai/kg-day)*
E	*exposure (mg ai/day)*
AF	*absorption factor (dermal and/or inhalation)*
BW	*body weight (kg)*

Non-cancer risk estimates for each scenario are calculated using the Margin of Exposure (MOE) approach, which is a ratio of the POD to the daily dose of concern.

All MOE values are calculated using the following formula:

$$MOE = \frac{POD}{ADD}$$

Equation 13.2.3

where:

MOE	*margin of exposure: value used by the USEPA to represent risk estimates (unitless)*
POD	*point of departure (mg/kg-day)*
ADD	*average daily dose absorbed in a given scenario (mg ai/kg-day)*

Occupational post-application equations

Potential daily exposures for occupational post-application workers are calculated using the following formulas:

$$DFR_t = AR * F * (1-D)^t * \left(4.54E8 \frac{ug}{lb}\right) * \left(2.47E\text{-}8 \frac{A}{cm^2}\right)$$

Equation 13.2.4

where:

DFR_t	dislodgeable foliage residue on day "t" (µg/cm^2)
AR	application rate (kg a.i./ha)
F	fraction of a.i. retained on foliage, or default of 25% (unitless)
D	fraction of residue that dissipates daily, or default of 10% (unitless)
T	number of days after application day (days)

$$E = TC * DFR_t * ET * 0.001 \frac{mg}{ug}$$

Equation 13.2.5

where:

E	exposure (mg ai/day)
TC	transfer coefficient (cm^2/hr)
DFR_t	dislodgeable foliar residue on day “t” (µg/cm^2)
ET	exposure time (hours/day)

The transfer coefficients (TCs) used for these calculations, and presented in Annexure 1, are based on standard clothing worn by agricultural field workers: shoes, socks, long-legged pants, and long-sleeved shirts. Gloves, face/head and respiratory protection and, in the case of slashing and clearing of treated common reeds, respiratory dust protection, are not included.

Regarding the DFR_t, the USEPA (2022(b)) noted that residue dissipation follows first-order kinetics; generally declining to below detection after 2 to 7 days, with an estimated half-life of 1.2 days.

The daily doses are calculated using the following formula:

$$ADD = \frac{E * AF}{BW}$$

Equation 13.2.6

where:

ADD	average daily dose absorbed in a given scenario (mg a.i./kg-day)
E	exposure (mg a.i./day)
AF	absorption factor (dermal and/or inhalation)
BW	body weight (kg)

The MOE is calculated with Equation 13.2.3.

Summary of terms and values for calculations

A summary of terms and values for the above calculations is presented in Table 13.2.1.

Table 13.2.1: Summary of terms and values for calculations.

Term	Term symbol	Units	Value
Unit exposure	UE	µg a.i./kg a.i.	Table 13.3.1, for different exposure scenarios
(Maximum) application rate	AR	kg a.i./ha or kg a.i./litre	According to product label
Area treated or amount handled	A	ha/day or litre/day	Default values in Table 13.3.1
Absorption factor	AF	unitless	Dermal: 1% Inhalation: 100%
Adult body weight	BW	kg	80 (USEPA 2011)
Point of departure	POD	mg/kg-day	Table 8.7.1, for different routes of exposure
Fraction of a.i. retained on foliage	F	unitless	0.25 (25%, default)
Fraction of residue that dissipates daily	D	unitless	0.10 (10%, default)
Number of days after application day	T	days	Restricted-entry interval (REI) recommended on label, or general value of 12 hours (0.5 days) Moving irrigation pipes: 2 days
Transfer coefficient	***TC	cm^2/hr	See Annexure 1
Dislodgeable foliar residue on day "t"	DFRt	$\mu g/cm^2$	*1.59 **Half-life = 1.2 days
Exposure time	ET	hours/day	Assumed 8 hours (workday), but only one exposure event before complete dissipation of deposited pesticide.

* Residue level on corn leaves, day 0 (USEPA 2022(b))

** Biological half-life: time required for the dissipation, by natural processes, of half of the amount of pesticide deposited on day 0.

***TC: based on standard clothing worn by agricultural field workers: shoes, socks, long-legged pants, and long-sleeved shirts. Gloves, face/head and respiratory protection, in the case of slashing and clearing of treated common reeds, respiratory dust protection, are not included

13.3 USEPA exposure and risk example results

Occupational handler exposure and risk assessment data and results, using the example calculations presented in Section 13.2, are summarised in Table 13.3.1. The USEPA did not prepare an example of post-application worker exposure and risk calculations.

It should be noted that dermal and inhalation PODs are based on different effects, and doses determined for these routes cannot be combined.

Handler exposure resulting from application of pesticides outdoors is likely to result in higher exposure than post-application exposure. Therefore, it is expected that handler inhalation exposure estimates would be protective of most occupational post-application inhalation exposure scenarios, and a quantitative occupational post-application inhalation exposure assessment is not performed (USEPA 2022(b)).

Table 13.3.1: USEPA example of glufosinate ammonium occupational handlers' exposure doses and MOEs.

Exposure scenario	Crop or Target[1]	Unit exposure[2] (µg/kg a.i.) [PPE types]		Maximum App. Rate[3]	Area treated daily or amount handled daily[4]	Dermal[5]		Inhalation[6]	
		Dermal	Inhalation			Dose (mg/kg-day)	MOE LOC=1 000	Dose (mg/kg-day)	MOE LOC=300
Mixer / loader									
Liquid, groundboom, broadcast	Orchard/ Vineyard	82.9 [SL/G]	0.483 [No-R]	3.31 kg a.i./ha	16.2. ha	0.00033	43 000	0.00016	15 000
	Field crop, typical hectares				32.4 ha	0.00065	21 000	0.00033	7 500
	Field crop, high hectares			1.74 kg a.i./ha	80.9 ha	0.00086	16 000	0.00043	5 700
Applicator									
Spray groundboom, broadcast	Orchard/ Vineyard	35.5 [SL/G]	0.75 [No-R]	3.31 kg a.i./ha	16.2. ha	0.00014	100 000	0.00026	9 600
	Field crop, typical hectares				32.4 ha	0.00028	50 000	0.00050	4 800
	Field crop, high hectare			1.74 kg a.i./ha	80.9 ha	0.00037	38 000	0.00067	3 700
Mixer/loader/ applicator									
Liquid, Backpack, Ground/soil-directed	Orchard/ Vineyard	18 210.18 [SL/G]	5.69 [No-R]	0.004 kg a.i. / litre solution	151.4 litres solution	0.0015	9 500	0.00004	62 000
Liquid, mechanically-pressurized handgun. Broadcast (foliar)	Orchard/ Vineyard	4 520 [SL/G]	19.14 [No-R]		3 785 litres solution	0.0092	1 500	0.0034	730
	Field crop, typical hectares								
Liquid, mechanically-pressurized handgun. Drench/soil-/ground-directed	Orchard/ Vineyard								
	Field crop, typical hectares								

Notes to table:

1. Orchard/Vineyard crops include fig. avocado, hops, tropical and subtropical, small fruit, edible peel, and fruit, small, vine climbing, except fuzzy kiwifruit.
   Typical field crops include bushberries and cucurbits.
   High hectares field crops include expanded use on tuberous vegetables and corn.
2. Based on the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (USEPA 2021).
   Type of PPE: SL/G: Single layer clothes (baseline attire) with gloves.
   No-R: No respirator (baseline inhalation PPE)
3. Based on end-use label proposed to USEPA
4. Exposure Science Advisory Council Policy #9.1.
5. Algorithms for dermal and inhalation dose and MOE calculations presented in Section 13.2.

13.4 SILENT calculations and results

The calculation of the input values needed for the SILENT occupational exposure and risk calculations are presented in Table 13.4.1. Data are as obtained from the product label, and calculated based on the label directions for spray solution preparation.

Exposure calculations according to the USEPA equations described in Section 13.2, performed for occupational herbicide handlers, these are mixers, loaders and applicators, are presented in Tables 13.4.2 and 13.4.3. The product supplier has indicated that the herbicide is not intended for aerial application (e.g., by low-flying aircraft) and this method of application is excluded from the assessment.

The comparison between the MOEs and the LOCs indicate the absence of a risk of a health effect in operators involved in mixing, loading and spraying SILENT on any of the assessed crops, and to control weeds on industrial sites, by any of the methods assessed in Tables 13.4.2 and 13.4.3.

Post-application (re-entry) agricultural workers are exposed by the dermal route only, since glufosinate ammonium and its residues are not volatile (inhalation exposure is excluded).

Completely mechanised application or post-application re-entry activities are highly unlikely to be associated with any significant exposure to workers and are not assessed.

Re-entry exposure is assessed according to the crop types indicated on the SILENT label. Specific examples of nut- and fruit types are assessed, in order to present a range of possible exposures and risks, according to Table 13.4.4. Re-entry exposure and risk results are presented in Table 13.4.5. The assumed re-entry period is 1 day, as noted on the product label. It appears that re-entry of sprayed reeds generally takes place after approximately 7 days, but this possibility was not assessed, since a 7-day re-entry period is not recommended on the product label. Nonetheless, re-entry of sprayed reeds after 1 day is also not associated with risks to health (Table 13.4.5).

SILENT is a herbicide, and clear instructions on the labels caution that foliar parts of plants, and the stems of young plants, must be protected to ensure that the applied spray does not make contact with the foliage. Furthermore, herbicide sprays are not directed at the buds, flowers or fruit. Most post-application re-entry activities involves contact only or mainly with fruit, leaves, and the twigs and branches of fruit trees and vines, which are not sprayed.

Thus, most re-entry activities will involve negligible contact with herbicide residues, such as:

- Harvesting, pruning, leaf pulling or thinning fruit by hand.
- Scouting or inspecting crops.
- Propping fruiting branches and other orchard or vineyard maintenance activities.
- Propagating or transplanting vines.
- Hand-setting of irrigation pipes, which should be done, in any case, with gloves protecting hands against superficial injury.

The only activities that might involve more-than-negligible contact with residues on weeds is weeding by hand and slashing and clearing of treated reeds in commercial or non-crop areas.

Table 13.4.1: Input values for SILENT exposure and risk calculations.

Crop	Groundboom broadcast spray			Spot spray (Backpack and mechanically-pressurized handgun)		Broadcast spray (foliar) (Mechanically-pressurized handgun)	
	Label: kg glufosinate / litre product	Label: Litre product / ha, maximum	Calculated kg glufosinate / ha, maximum	Label: Maximum product (ml) / litre spray solution	Calculated spot spray solution concentration (kg glufosinate / litre)	Label: litre solution / ha	Calculated kg glufosinate / litre solution
Citrus	0.2	7.5	1.5	25	0.005	300	0.005
Pome fruit and stone fruit	0.2	7.5	1.5	25	0.005	300	0.005
Vineyard	0.2	7.5	1.5	25	0.005	300	0.005
Subtropical fruit	0.2	7.5	1.5	25	0.005	300	0.005
Nuts	0.2	7.5	1.5	25	0.005	300	0.005
Industrial: low-to-medium height weeds	0.2	7.5	1.5	25	0.005	300	0.005
Industrial: common reeds	0.2	15.0	3.0	25	0.003	1 000	0.003

Notes to table:
Calculated kg glufosinate / ha = (kg glufosinate / litre product) * (litre product / ha, maximum)
Calculated spot spray solution concentration (kg glufosinate /litre) = 25 ml * (kg glufosinate / litre product) / 1000 ml
Calculated broadcast spray solution concentration (kg glufosinate /litre) = (Calculated kg glufosinate / ha, maximum) / (maximum total litre solution / ha)
Label: litre solution / ha is the volume solution associated with the highest concentration of glufosinate per litre solution

Table 13.4.2: Groundboom application: occupational handler exposure and MOEs.

Crop	AR: Maximum Application Rate (kg/ha)	Dermal exposure			Inhalation exposure		
		Dose (mg/kg-day)	LOC = 1000		Dose (mg/kg-day)	LOC = 300	
			MOE	MOE > LOC?		MOE	MOE > LOC?
Mixer / loader: Liquid, groundboom, broadcast							
Orchard: Citrus	1.5	0.0003	55 598	Yes	0.00015	16 699	Yes
Orchard: Pome fruit	1.5	0.0003	55 598	Yes	0.00015	16 699	Yes
Orchard: Stone fruit	1.5	0.0003	55 598	Yes	0.00015	16 699	Yes
Orchard: Subtropical fruit	1.5	0.0003	55 598	Yes	0.00015	16 699	Yes
Orchard: Nuts	1.5	0.0003	55 598	Yes	0.00015	16 699	Yes
Vineyard	1.5	0.0003	55 598	Yes	0.00015	16 699	Yes
*Industrial sites, non-crop weeds	1.5	0.0003	55 598	Yes	0.00015	16 699	Yes
*Industrial sites, non-crop, common reed	3.0	0.0005	27 799	Yes	0.00029	8 350	Yes
Applicator: Groundboom broadcast spray							
Orchard: Citrus	1.5	0.0001	129 832	Yes	0.00023	10 754	Yes
Orchard: Pome fruit	1.5	0.0001	129 832	Yes	0.00023	10 754	Yes
Orchard: Stone fruit	1.5	0.0001	129 832	Yes	0.00023	10 754	Yes
Orchard: Subtropical fruit	1.5	0.0001	129 832	Yes	0.00023	10 754	Yes
Orchard: Nuts	1.5	0.0001	129 832	Yes	0.00023	10 754	Yes
Vineyard	1.5	0.0001	129 832	Yes	0.00023	10 754	Yes
*Industrial sites, non-crop, weeds	1.5	0.0001	129 832	Yes	0.00023	10 754	Yes
*Industrial sites, non-crop, common reed	3.0	0.0002	64 916	Yes	0.00461	5 377	Yes

Notes to table:
***Industrial sites:** The area (ha) to be treated is assumed to be small to medium, as for orchards and vineyards

Table 13.4.3: Backpack and handgun application: occupational handler exposure and MOEs.

Crop	AR (kg/litre solution)	Dermal exposure			Inhalation exposure		
		Dose (mg/kg-day)	LOC = 1000		Dose (mg/kg-day)	LOC = 300	
			MOE	MOE > LOC?		MOE	MOE > LOC?
Mixer / loader / applicator: Liquid, backpack, ground/soil-directed. "Spot spraying" on product label.							
Orchard: Citrus	0.005	0.0017	8 125	Yes	0.00005	45 504	Yes
Orchard: Pome fruit	0.005	0.0017	8 125	Yes	0.00005	45 504	Yes
Orchard: Stone fruit	0.005	0.0017	8 125	Yes	0.00005	45 504	Yes
Orchard: Subtropical fruit	0.005	0.0017	8 125	Yes	0.00005	45 504	Yes

Crop	AR (kg/litre solution)	Dermal exposure			Inhalation exposure		
		Dose (mg/kg-day)	LOC = 1000		Dose (mg/kg-day)	LOC = 300	
			MOE	MOE > LOC?		MOE	MOE > LOC?
Orchard: Nuts	0.005	0.0017	8 125	Yes	0.00005	45 504	Yes
Vineyard	0.005	0.0017	8 125	Yes	0.00005	45 504	Yes
*Industrial sites, non-crop weeds	0.005	0.0017	8 125	Yes	0.00005	45 504	Yes
*Industrial sites, non-crop, common reed	0.003	0.0010	13 541	Yes	0.00003	75 840	Yes
Mixer / loader / applicator: Liquid, mechanically-pressurized handgun. Broadcast (foliar) or drench / soil- / ground-directed							
Orchard: Citrus	0.005	0.0107	1 309	Yes	0.0045	541	Yes
Orchard: Pome fruit	0.005	0.0107	1 309	Yes	0.0045	541	Yes
Orchard: Stone fruit	0.005	0.0107	1 309	Yes	0.0045	541	Yes
Orchard: Subtropical fruit	0.005	0.0107	1 309	Yes	0.0045	541	Yes
Orchard: Nuts	0.005	0.0107	1 309	Yes	0.0045	541	Yes
Vineyard	0.005	0.0107	1 309	Yes	0.0045	541	Yes
*Industrial sites, non-crop, weeds	0.005	0.0107	1 309	Yes	0.0045	541	Yes
*Industrial sites, non-crop, common reed	0.003	0.0064	2 182	Yes	0.0027	902	Yes
Notes to table: **AR:** Maximum Application Rate ***Industrial sites:** The area (ha) to be treated is assumed to be small to medium, as for orchards and vineyards							

Table 13.4.4: Assessed crops and examples of fruits.

Crop	Examples
Vineyard	Grapes: table / raisin / juice / wine
Orchard: Pome fruit	Apples, pears
Orchard: Stone fruit	Apricot, cherries, peaches, nectarine
Orchard: Citrus	Oranges, etc.
Orchard: Subtropical fruit	Bananas, papayas, avocado, mango, lychees, pineapples
Orchard: Nuts	Almond, pecan, hazelnut, walnut, macadamia, pistachio
Industrial sites, non-crop, weeds	Only mechanised post-application re-entry activities (or no re-entry activities) are assumed, e.g., mechanised clearing of dead weeds, if done at all
Industrial sites, non-crop, common reed	Slashing and clearing of reeds, whether by hand or using tractor-driven machinery

Table 13.4.5: Post-application exposure and risks.

Activity	AR: Maximum App. Rate	Dermal			
		Dislodgeable foliar residue at time of entry	Dose	LOC=	1000
	kg/ha	DFR_t (µg/cm^2)	(mg/kg-day)	MOE	MOE > LOC?
Weeding by hand					
Vineyard	1.5	3.4	0.0022	6 481	Yes
Citrus fruit orchards	1.5	3.4	0.0003	41 481	Yes
Pome and stone fruit orchards	1.5	3.4	0.0003	41 481	Yes
Subtropical fruits: Bananas	1.5	3.4	0.0003	41 481	Yes
Subtropical fruits: Avocado	1.5	3.4	0.0003	41 481	Yes
Subtropical fruits: Lychees	1.5	3.4	0.0003	41 481	Yes
Subtropical fruits: Pineapples	1.5	3.4	0.0002	59 259	Yes
Tree nuts (any listed in Table 13.4.4)	1.5	3.4	0.0003	41 481	Yes
Slashing and clearing of common reeds					
Entry after 1 day	3.0	6.75	0.0074	1 886	Yes
Entry after 3 days	3.0	5.47	0.0060	2 328	Yes

14 Dietary exposure and risk assessment

14.1 Background

Dietary risk assessment of glufosinate ammonium residues in food is based on its toxicity, on consumer crop intake rates, and on the pesticide residue concentrations in fruits and vegetables at the time of consumption. As discussed in Section 8, the assessment is based on the population-adjusted dose ("PAD"). The acute PAD is referred to as the "aPAD", and the chronic PAD is referred to as the "cPAD". The PAD is equivalent to the POD, the NOAEL, or the LOAEL, divided by applicable uncertainty factors, including the FQPA Safety Factor. For acute and non-cancer chronic exposures, concern is raised when estimated dietary risk exceeds 100 per cent of the aPAD (USEPA 2022(a)).

14.2 Residue intake from food and water

Although there were no dietary risks of concern for glufosinate ammonium from exposure to residues in either food or drinking water, drinking water exposure resulting from use of glufosinate ammonium on rice was a significant contributor to previous estimates of dietary risk (USEPA 2013). However, the use of glufosinate ammonium on rice is currently not applicable to South Africa.

The USEPA (2016) concluded that there would be no dietary, residential, or aggregate risks of concern for glufosinate ammonium from exposure to residues in food and drinking water. The 2016 assessment had included the following crops: apples, berries, canola, citrus, corn, cotton, currants, grapes, potatoes, soybeans, sugar beets, and tree nuts.

15 Summary of conclusions

- SILENT is not intended for sale to residential gardeners; therefore, risks to health, associated with the herbicidal application of SILENT, are assessed only for occupational pesticide handlers and post-application (re-entry) workers.

- The results of the health risk assessment indicated no reasons for concern, including of reproductive/developmental toxicity effects, in agricultural operators handling the product, mixing or applying the product, or in contact with treated crops 12 to 24 hours after application.

- Dietary exposure of consumers or treated produce is highly unlikely and not an issue of concern, firstly because the herbicide is never applied directly to the commodity to be harvested. Secondly, translocation of glufosinate ammonium within the various parts of the pant, e.g., root-to-fruit, is insignificant.

- Although ecological risks to mammals and birds foraging in treated weeds cannot be totally excluded, reducing either the single application rate or the number of applications on glufosinate labels is not contemplated. Such reductions could have an impact on growers (and food production) that outweighs the potential decrease in chronic risk to mammals.

16 Recommendations

An application for the restricted use of the glufosinate ammonium-containing commercial herbicide SILENT should be granted according to the intended product use:

- Herbicide not for sale to and used by residential gardeners.
- Preparation of the treatment solution in accordance with the instructions on the product label.
- Personal protection instructions on the SDS must be followed; that is, washing hands, forearms and face thoroughly after handling chemical products.
- At least baseline PPE must be worn when applying the product; that is, clothing covering the arms and legs, closed shoes and chemical-resistant gloves. The product SDS additionally recommends face protection.
- The recommended 1-day post-application restricted-entry interval (“REI”) must lapse before crop re-entry.

17 References

EFSA. 2005. Conclusion regarding the peer review of the pesticide risk assessment of the active substance glufosinate. Official Journal of the European Food Safety Authority, 27:1-81. Finalised: 14 March 2005.

ECHA. Online. Classification and Labelling Inventory of the European Chemical Agency. Accessed August 2024 at http://echa.europa.eu/information-on-chemicals/cl-inventory-database.

IPCS. 2010. WHO Human Health Risk Assessment Toolkit: Chemical Hazards. Harmonization Project Document No. 8. Published under the joint sponsorship of the World Health Organization, the International Labour Organization and the United Nations Environment Programme, and produced within the framework of the Inter-Organization Programme for the Sound Management of Chemicals.

IPCS. 1999. Principles for the Assessment of Risks to Human Health from Exposure to Chemicals. Environmental Health Criteria 210. International Programme on Chemical Safety. A cooperative agreement between UNEP, ILO, FAO, WHO, UNIDO, Unitar and OECD.

Karamertzanis PG, Atlason P, Nathanail AV, Provoost J, Karhu E and Rasenberg M. 2019. The impact on classifications for carcinogenicity, mutagenicity, reproductive and specific target organ toxicity after repeated exposure in the first ten years of the REACH regulation. Regulatory Toxicology and Pharmacology, 106: 303-315.

Lewis KA, Tzilivakis J, Warner D and Green A. 2016. An international database for pesticide risk assessments and management. Human and Ecological Risk Assessment: An International Journal, 22(4), 1050-1064. DOI: 10.1080/10807039.2015.1133242.

NRC. 1983. Risk Assessment in the Federal Government: Managing the Process. National Research Council. Committee on the Institutional Means for the Assessment of Risks to Public Health. Washington, DC: National Academy Press.

OECD. 2021. Guidance on Key Considerations for the Identification and Selection of Safer Chemical Alternative, OECD Series on Risk Management, No. 60, Environment, Health and Safety, Environment Directorate, OECD.

PAN. Online. Glufosinate-Ammonium. PesticideInfo, Pesticide Action Network (PAN) North America. https://www.pesticideinfo.org/chemical/PRI3436.

USEPA. 2022a. Glufosinate. Acute and Chronic Aggregate Dietary (Food and Drinking Water) Exposure and Risk Assessment for the Proposed Section 3 Registration of Glufosinate for Use on (*a variety of commodities*[6]). PC Code: 128850; Decision No: 564822, 565288; Petition No: 0E8859; DP Barcode: D461847, D461848; Registration No: 7969-448. Office of Chemical Safety and Pollution Prevention, US Environmental Protection Agency, Washington, DC.

[6] INFOTOX insert.

USEPA. 2022b. Glufosinate. Occupational and Residential Exposure Assessment for the Proposed Use of Glufosinate on (*a variety of commodities*[7]). PC Code: 128850; Decision No: 564822, 565288; Petition No: 0E8859; DP Barcode: D464499, D464500; Registration No: 7969-448. Office of Chemical Safety and Pollution Prevention, US Environmental Protection Agency, Washington, DC.

USEPA. 2021. Occupational Pesticide Handler Unit Exposure Surrogate Reference Table. May 2021. Office of Pesticide Programs, US Environmental Protection Agency, Washington, DC. https://www.epa.gov/sites/default/files/2021-05/documents/occupational-pesticide-handler-unit-exposure-surrogate-reference-table-may-2021.pdf

USEPA. 2016. Glufosinate Ammonium Interim Registration Review Decision. Case Number 7224, Docket Number EPA-HQ-OPP-2008-0190. US Environmental Protection Agency.

USEPA. 2013. Environmental Fate and Ecological Risk Assessment for the Registration Review of Glufosinate. Office of Pesticide Programs, Environmental Fate and Effects Division (EFED), Environmental Risk Branch, US Environmental Protection Agency, Washington, DC.

USEPA. 2011. Exposure Factors Handbook 2011 Edition (Final Report). EPA/600/R-09/052F, 2011. US Environmental Protection Agency, Washington, DC.

[7] INFOTOX insert.

Annexure 1

Table A1: Post-application agricultural workers glufosinate ammonium residue transfer coefficients.

Crop group USEPA TC Table	Crop or Target	Crop USEPA TC Table	Activity with highest-to-lowest TC values	Transfer coefficient (TC)
				cm^2/hr
Vine / trellis	Vineyard	Grape, table	Girdling / Turning	19 300
Vine / trellis	Vineyard	Grape, juice / wine	Harvesting hand, Tying / training, Leaf pulling	10 100
Vine / trellis	Vineyard	Grape, raisin / table	Harvesting hand, Tying / training, Leaf pulling	5 500
Vine / trellis	Vineyard	Grape, table / raisin / juice / wine	Pruning / weeding by hand, Scouting, propagating	640
Vine / trellis	Vineyard	Grape, table / raisin / juice / wine	Irrigation hand set	1 900
Vine / trellis	Vineyard	Grape, table / raisin / juice / wine	Transplanting	230
Vine / trellis	Vineyard	Grape, table / raisin / juice / wine	Irrigation (non-hand set) & All mechanised activities	0
Tree, "fruit", deciduous	Pome fruit	Apples, Pears	Thinning fruit	3 600
Tree, "fruit", deciduous	Pome fruit	Apples, Pears	Harvesting hand	1 400
Tree, "fruit", deciduous	Pome fruit	Apples, Pears	Pruning hand	580
Tree, "fruit", deciduous	Pome fruit	Apples, Pears	Weeding by hand, Propping, Orchard maintenance	100
Tree, "fruit", deciduous	Pome fruit	Apples, Pears	Irrigation (non-hand set) & All mechanised activities	0
Tree, "fruit", deciduous	Stone fruit	Apricot, Cherries, Peaches, Nectarine	As for Pome fruit	As for Pome fruit
Bunch / bundle	Subtropical fruit	Banana	Harvesting hand	1400
Bunch / bundle	Subtropical fruit	Banana	Weeding hand	100
Bunch / bundle	Subtropical fruit	Banana	Irrigation (non-hand set) & All mechanised activities	0
Tree, "fruit", evergreen	Subtropical fruit	Papaya	Harvesting hand	1400
Tree, "fruit", evergreen	Subtropical fruit	Papaya	Pruning hand, Scouting	580
Tree, "fruit", evergreen	Subtropical fruit	Papaya	Orchard maintenance	100

Crop group USEPA TC Table	Crop or Target	Crop USEPA TC Table	Activity with highest-to-lowest TC values	Transfer coefficient (TC)
				cm^2/hr
Tree, "fruit", evergreen	Subtropical fruit	Papaya	Irrigation (non-hand set) & All mechanised activities	0
Tree, "fruit", evergreen	Subtropical fruit	Avocado	Harvesting hand	1400
Tree, "fruit", evergreen	Subtropical fruit	Avocado	Pruning hand, Scouting	580
Tree, "fruit", evergreen	Subtropical fruit	Avocado	Weeding by hand / Orchard maintenance	100
Tree, "fruit", evergreen	Subtropical fruit	Avocado	Irrigation (non-hand set) & All mechanised activities	0
Tree, "fruit", evergreen	Subtropical fruit	Mango	Thinning fruit	3 600
Tree, "fruit", evergreen	Subtropical fruit	Mango	Harvesting hand	1400
Tree, "fruit", evergreen	Subtropical fruit	Mango	Pruning hand, Scouting	580
Tree, "fruit", evergreen	Subtropical fruit	Mango	Irrigation (non-hand set) & All mechanised activities	0
Tree, "fruit", evergreen	Subtropical fruit	Lychees	Harvesting hand	1400
Tree, "fruit", evergreen	Subtropical fruit	Lychees	Pruning hand, Scouting	580
Tree, "fruit", evergreen	Subtropical fruit	Lychees	Weeding by hand / Orchard maintenance	100
Tree, "fruit", evergreen	Subtropical fruit	Lychees	Irrigation (non-hand set) & All mechanised activities	0
Vegetable, stem / stalk	Subtropical fruit	Pineapple	Harvesting hand	1 100
Vegetable, stem / stalk	Subtropical fruit	Pineapple	Scouting	210
Vegetable, stem / stalk	Subtropical fruit	Pineapple	Weeding by hand	70
Vegetable, stem / stalk	Subtropical fruit	Pineapple	Irrigation (non-hand set) & All mechanised activities	0
Tree, "fruit", evergreen	Citrus	Orange, Grapefruit, Lemon	Harvesting hand	1 400
Tree, "fruit", evergreen	Citrus	Orange, Grapefruit, Lemon	Pruning hand, Scouting	580
Tree, "fruit", evergreen	Citrus	Orange, Grapefruit, Lemon	Transplanting	230
Tree, "fruit", evergreen	Citrus	Orange, Grapefruit, Lemon	Weeding by hand / Orchard maintenance	100
Tree, "fruit", evergreen	Citrus	Orange, Grapefruit, Lemon	Irrigation (non-hand set) & All mechanised activities	0
Tree, "nut"	Nuts	Almond, Pecan, hazelnut, Walnut, Macadamia	Pruning by hand, Scouting	580

Crop group USEPA TC Table	Crop or Target	Crop USEPA TC Table	Activity with highest-to-lowest TC values	Transfer coefficient (TC)
				cm^2/hr
Tree, "nut"	Nuts	Almond, Pecan, hazelnut, Walnut, Macadamia	Transplanting	230
Tree, "nut"	Nuts	Almond, Pecan, hazelnut, Walnut, Macadamia	Harvesting, mechanical shaking	190
Tree, "nut"	Nuts	Almond, Pecan, hazelnut, Walnut, Macadamia	Poling, orchard maintenance, weeding by hand	100
Tree, "nut"	Nuts	Almond, Pecan, hazelnut, Walnut, Macadamia	Irrigation (non-hand set) & All mechanised activities	0
Tree, "nut"	Nuts	Pistachio	Harvesting hand (net)	1 400
Tree, "nut"	Nuts	Pistachio	Scouting	580
Tree, "nut"	Nuts	Pistachio	Transplanting	230
Tree, "nut"	Nuts	Pistachio	Harvesting, mechanical shaking	190
Tree, "nut"	Nuts	Pistachio	Weeding by hand	100
Tree, "nut"	Nuts	Pistachio	Irrigation (non-hand set) & All mechanised activities	0
Industrial sites and unplanted areas	Weeds	Weeds	Post-treatment activities all assumed to the mechanical, no dermal contact, no TC needed	0
Industrial sites and unplanted areas	Common reeds	Common reeds	Slash and gather: as for scouting sugarcane	1 100