Australian Government

Australian Pesticides and Veterinary Medicines Authority

Public Release Summary

on the evaluation of the new active mesotrione

in the product Callisto Herbicide

APVMA product number 87588

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This publication is available from the APVMA website.

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PREFACE

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is the Australian Government regulator responsible for assessing and approving agricultural and veterinary chemical products prior to their sale and use in Australia. Before approving an active constituent and/or registering a product, the APVMA must be satisfied that the statutory criteria, including the safety, efficacy, trade and labelling criteria, have been met. The information and technical data required by the APVMA to assess the statutory criteria of new chemical products, and the methods of assessment, must be consistent with accepted scientific principles and processes. Details are outlined on the APVMA website.

The APVMA has a policy of encouraging transparency in its activities and seeking community involvement in decision making. Part of that process is the publication of public release summaries for products containing new active constituents. This Public Release Summary is intended as a brief overview of the assessment that has been conducted by the APVMA and of the specialist advice received from advisory agencies, including other Australian Government agencies and State departments of primary industries. It has been deliberately presented in a manner that is likely to be informative to the widest possible audience to encourage public comment.

About this document

This Public Release Summary indicates that the APVMA is considering an application for registration of an agricultural or veterinary chemical. It provides a summary of the APVMA's assessment, which may include details of:

- the toxicology of both the active constituent and product
- the residues and trade assessment
- occupational exposure aspects
- environmental fate, toxicity, potential exposure and hazard
- efficacy and target crop or animal safety.

Comment is sought from interested stakeholders on the information contained within this document.

Making a submission

In accordance with sections 12 and 13 of the Agvet Code, the APVMA invites any person to submit a relevant written submission as to whether the application for approval of the new active constituent, mesotrione and registration of the product Callisto Herbicide should be granted. Submissions should relate only to matters that the APVMA is required, by legislation, to take into account in deciding whether to grant the application. These matters include aspects of public health, occupational health and safety, chemistry and manufacture, residues in food, environmental safety, trade, and efficacy and target crop or animal safety. Submissions should state the grounds on which they are based. Comments received that address issues outside the relevant matters cannot be considered by the APVMA.

Submissions must be received by the APVMA by close of business on **17 December 2019** and be directed to the contact listed below. All submissions to the APVMA will be acknowledged in writing via email or by post.

Relevant comments will be taken into account by the APVMA in deciding whether the product should be registered and in determining appropriate conditions of registration and product labelling.

When making a submission please include:

- contact name
- company or group name (if relevant)
- email or postal address (if available)
- the date you made the submission.

All personal information, and confidential information judged by the APVMA to be confidential commercial information (CCI)[1] contained in submissions will be treated confidentially. Unless requested by the submitter, the APVMA may release a submission, with any CCI redacted, to the applicant for comment.

Written submissions on the APVMA's proposal to grant the application for registration that relate to the grounds for registration should be addressed in writing to:

Case Management and Administration Unit

Australian Pesticides and Veterinary Medicines Authority

GPO Box 3262

SYDNEY NSW 2001 Australia

Phone: +61 2 6770 2300

Email: enquiries@apvma.gov.au

Further information

Further information can be obtained via the contact details provided above.

Copies of technical evaluation reports covering chemistry, efficacy and safety, toxicology, occupational health and safety aspects, residues in food and environmental aspects are available from the APVMA on request.

Further information on public release summaries can be found on the APVMA website.

[1] A full definition of "confidential commercial information" is contained in the Agvet Code.

1 INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of the product Callisto Herbicide, and approval of the new active constituent, mesotrione.

1.1 Applicant

SYNGENTA AUSTRALIA PTY LTD

1.2 Purpose of application

SYNGENTA AUSTRALIA PTY LTD has applied to the APVMA for registration of the new product Callisto Herbicide, containing 480 g/L, as a suspension concentrate formulation of the new active constituent mesotrione.

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of the product Callisto Herbicide, and approval of the new active constituent mesotrione.

1.3 Proposed claims and use pattern

The proposed product Callisto Herbicide is intended for pre-emergent control of a range of broadleaf weeds in wheat and barley.

1.4 Mode of action

Mesotrione is a member of triketone class of herbicides that inhibits the enzyme 4-hydroxyphenylpyruvate dioxygenase (HPPD), the second enzyme in the catabolic pathway of tyrosine. In susceptible plants, inhibitors of HPPD prevent carotenoid pigment formation, which in turn leads to chlorophyll degradation. The active is absorbed through the roots and affected plants will turn white or pale yellow before finally being controlled, because susceptible plants (which excludes barley and wheat) become chlorotic as they are unable to detoxify mesotrione. Mesotrione is slightly soluble in nature and may redistribute through the soil profile depending on soil texture, soil organic matter and rainfall patterns. For weed resistance management mesotrione is a Group H herbicide.

1.5 Overseas registrations

The product is currently registered as Callisto herbicide (480 g/L mesotrione, SC formulation) in: Argentina, Belarus, Bosnia and Herzegovina, Botswana, Brazil, Canada, Chile, China, Colombia, Croatia, Czech Republic, Ecuador, France, Hungary, Italy, Macedonia, Mexico, Mozambique, Serbia, Slovenia, South Africa, South Korea, Turkey and the United States of America.

2 CHEMISTRY AND MANUFACTURE

2.1 Active constituent

The active constituent mesotrione is manufactured overseas. Details of the chemical name, structure, and physicochemical properties of mesotrione are listed below (Tables 1–2).

Mesotrione is a pale yellow solid granular powder with a slightly sweet odour in the case of the technical active. It has a moderate solubility in water (180 mg/L) and soluble in most organic solvents (< 104 g/L). It is hydrophilic. Both the purified active ingredient and the technical grade active ingredient are not surface-active. There are no flammability, explosive, and/or oxidizing properties of concern with mesotrione.

Table 1: Nomenclature and structural formula of the active constituent mesotrione

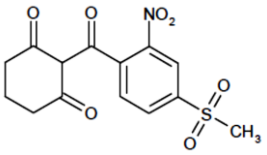
Common name (ISO):	Mesotrione
IUPAC name:	2-(4-mesyl-2-nitrobenzoyl)cyclohexane-1,3-dione
CAS registry number:	2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione
Molecular formula:	$C_{14}H_{13}NO_7S$
Molecular weight:	339.3 g/mol
Structural formula:	

Table 2: Key physicochemical properties of the active constituent mesotrione

Physical form:	Technical grade (81.6% purity)—solid, purified active (99.7% purity)—solid
Colour:	Technical grade—pale amber, purified active—pale yellow
Odour:	Technical grade—slightly sweet odour, purified active—odourless
Melting point:	Technical grade—165.3°C, purified active—148.7 to 152.5°C
Boiling point:	The test substance decomposes without boiling
Relative density	Technical grade—1.46 g/mL at 20 °C
Stability:	Data provided shows that in an ambient temperature mesotrione is stable over the period of one year without decomposition. In an accelerated temperature 1% decomposition of the active was observed after two weeks storage at 54 ºC. No adverse reaction to metal or metal ions including metallic zinc was observed following storage for 2 weeks at 54 ºC.
Safety properties:	Not considered flammable. Not explosive. Auto-flammability is 144 °C. Except photo-degradation in water, the mesotrione technical does not show any chemical incompatibility with oxidising, reducing and fire extinguishing agents and is essentially non-hazardous.
Solubility in water:	At 25 ºC 180 mg/L (pure water) 3.1 g/L (pH 4.9) 4.4 g/L (pH 6.7) 18 g/L (pH 8.0)
Organic solvent solubility:	Methanol 3.7 g/L Ethyl acetate 17 g/L Toluene 2.7 g/L Dichloroethane 89 g/L Acetonitrile 104 g/L Xylenes 1.4 g/L Heptane < 0.3 g/L Acetone 81 g/L
pH:	pH 3.4 at a 1% dilution in pure water at 24 – 25 ºC
Octanol/water partition coefficient (Log K_{ow}/K_{OW}):	log P_{ow} = 1.15, pH 5 log P_{ow} = -2.4, pH 6.8 log P_{ow} = -2.6, pH 9.0 at 25 °C

Vapour pressure:	<3.3 x10^{-6} Pa at 50 ºC and 25 ºC for technical active <5.7 x10^{-6} Pa at 20 ºC for purified active
Henry's law constant:	< 5.1 x 10^{-7} Pa m^3/mol
UV/VIS absorption spectra:	λ_{max} 256 nm

2.2 Formulated product

The product Callisto Herbicide will be manufactured overseas. Tables 3 and 4 outline some key aspects and physicochemical properties of the product.

Callisto Herbicide will be available in 5 L to 110 L PET (polyethylene terephthalate) containers and high density polyethylene (HDPE) containers.

Table 3: Key aspects of the formulation of the product Callisto Herbicide

Distinguishing name:	Callisto Herbicide
Formulation type:	Suspension concentrate (SC)
Active constituent concentration/s:	480 g/L mesotrione

Table 4: Physicochemical properties of the product Callisto Herbicide

Physical form:	Light brown coloured liquid
pH:	3.4 (1% aqueous dilution)
Density:	1.203 g/cm^3 at 20 ºC
Kinematic viscosity:	642 mPa^{-s} at 20 ºC and 439 mPa^{-s} at 40 ºC
Pourability:	Pour residue = 4.37%; rinsed residue = 0.18%
Persistent foaming:	20–22 mL foam
Suspensibility:	93%–95%
Corrosion of metal:	No corrosion on stainless steel
Safety properties:	No flash point below 100 °C. Auto-ignition temperature is 405 °C. Heat decomposition is 704 J/g. Not classified as a flammable liquid or an explosive and/or as an oxidising substance.
Storage stability:	There was sufficient data to conclude that the product is expected to remain within specifications for at least two (2) years when stored under normal conditions

2.3 Recommendations

The APVMA has evaluated the chemistry of the active constituent mesotrione and the associated product Callisto Herbicide, including the manufacturing process, quality control procedures, stability, batch analysis results and analytical methods, and found them to be acceptable. The available storage stability data indicate that the formulated product is expected to remain stable for at least two years when stored under normal conditions.

On the basis of the data provided it is proposed that the following minimum compositional standard be established for mesotrione:

Table 5: Proposed minimum compositional standard for mesotrione

Constituent	Specification	Level
Mesotrione	Pale yellow to light tan as wet paste	Minimum purity 740 g/kg Water maximum 230 g/kg

Other compounds or impurities of toxicological significance are not expected to occur in mesotrione as a result of the raw materials and the synthetic route used. Based on a review of the chemistry and manufacturing details, the registration of Callisto Herbicide, and approval of the active constituent mesotrione, are supported from a chemistry perspective.

3 TOXICOLOGICAL ASSESSMENT

Based on a review of the submitted toxicological data, the approval of mesotrione and registration of Callisto Herbicide is supported from a human health perspective.

3.1 Evaluation of toxicology

Chemical class

Mesotrione is a member of the class of herbicides that competitively inhibits the enzyme 4-hydroxyphenylpyruvate dioxygenase (HPPD), the second enzyme in the catabolic pathway of tyrosine. In susceptible plants, inhibitors of HPPD prevent carotenoid pigment formation, which in turn leads to chlorophyll degradation. Susceptible plants, which excludes barley and wheat, become chlorotic because they are unable to detoxify mesotrione. In mammals, inhibition of HPPD typically leads to increased serum levels of tyrosine.

Pharmacokinetics

The kinetics of mesotrione have been assessed in studies investigating its absorption, distribution, metabolism and excretion in rats and mice following single and multiple oral gavage and single intravenous dosing. Clearance was rapid and followed first-order kinetics. Excretion of radioactivity was primarily in the urine (44 to 67 per cent and 41 to 70 per cent in rat and mouse respectively), although significant amounts were also detected in faeces (11 to 31 per cent and 21 38 per cent in rat and mouse respectively). Biliary excretion was more extensive in male rats (10 to 14 per cent) than in females (two to four per cent). In the rat and mouse, the majority of absorbed mesotrione is excreted unchanged (~ 90 per cent) in the urine. Small amounts of 4-hydroxy mesotrione, 5-hydroxy mesotrione, MNBA and AMBA were excreted in rat and mouse urine. Tissue residues, 72 h after administration, were low with the exception of the liver and kidney. In a human volunteer study, the kinetics of oral mesotrione in humans were similar to those observed in mice and rats. Mesotrione was rapidly absorbed (peak plasma concentrations within two hours of dosing) and rapidly excreted unchanged in the urine within 12 hours of dosing

Acute toxicity (active constituent)

Mesotrione has low acute oral (LD50 >5000 mg/kg), dermal (LD50 >2000 mg/kg) and inhalational toxicity in rats (4-h LC50 >4750 mg/m3). Mesotrione was non-irritating to the skin and mildly irritating to the eyes. It was not a skin sensitiser in the Guinea pig maximisation test.

Acute toxicity (product)

Callisto Herbicide has low acute oral, dermal and inhalational toxicity in rats (LD_{50} >5000 mg/kg bw, LD_{50} >5000 mg/kg bw and 4-h LC_{50} >5190 mg/m^3 respectively). It was a slight skin and eye irritant but not a skin sensitiser (maximisation test).

Repeat-dose toxicity

In a 90-day oral toxicity study in mice, animals were given diets containing mesotrione at a concentration of 0, 10, 50, 350 or 7000 ppm (equal to 0, 1.7, 8, 62 and 1212 mg/kg bw/d for males and 0, 2.4, 12, 80 and 1537 mg/kg bw/d for females, respectively). The NOAEL was 7000 ppm (equal to 1212 mg/kg bw/d), the highest dose tested.

In a 13-week oral capsule toxicity study in dogs, animals were exposed to 0, 100, 600 or 1000 mg/kg bw/d. At 1000 mg/kg bw/d, bodyweight was decreased in males relative to controls and there was an increase in minimal/slight focal mesothelial proliferation of the atrium of the heart in two males. In a one year oral capsule toxicity study in dogs, animals were exposed to 0, 10, 100 or 600 mg/kg bw/d. At the high dose, body weights were decreased in females, and lenticular opacity was observed in one male and one female. In the male, the lenticular opacity was associated with unilateral keratitis and periorbital haemorrhage; in the female, it was associated with unilateral corneal erosion. The overall NOAEL for both dog studies was 100 mg/kg bw/d.

Chronic toxicity and carcinogenicity

In a one year oral toxicity study in mice, animals were given diets containing mesotrione at a concentration of 0, 10, 50, 350 or 7000 ppm (equal to 0, 1.5, 8, 56 and 1114 mg/kg bw/d for males and 0, 2.1, 10, 72 and 1495 mg/kg bw/d for females, respectively). At the highest dose tested, males had a decreased bodyweight and bodyweight gain. There were no effects in females at the highest dose tested. The NOAEL was 350 ppm (equal to 56 mg/kg bw/d). In an 18-month oral toxicity and carcinogenicity study in mice, animals were given diets containing mesotrione at a concentration of 0, 10, 350 or 3500/7000 ppm (equal to 0, 1.4, 50 and 898 mg/kg bw/d for males and 0, 1.8, 64 and 1103 mg/kg bw/d for females, respectively). As seen in the one year study, body weight, body weight gains and feed efficiency were decreased in males at the highest dose tested, and there were no effects in females at the highest dose tested. The NOAEL was 350 ppm (equal to 50 mg/kg bw/d). There was no evidence of carcinogenicity.

Reproductive and developmental toxicity

In a two-generation reproductive toxicity study in mice, animals were given diets containing mesotrione at a concentration of 0, 10, 50, 350, 1500 or 7000 ppm (equal to 0, 2, 10, 71, 312 and 1472 mg/kg bw/d for males and 0, 2, 10, 71, 302 and 1439 mg/kg bw/d for females, respectively). At the highest dose tested, F1 adults and pups showed evidence of cataractous changes at clinical, gross and histopathological examination. Pups at the next lower dose also exhibited decreased body weight and body weight gain, clinical, gross and histopathological changes to the eyes (opaque/cloudy eyes, cataractous change) and increased plasma tyrosine levels. The NOAEL for parental toxicity was 1500 ppm (equal to 302 kg bw/d). The NOAEL for reproductive toxicity was 7000 ppm (equal to 1439 kg bw/d), the highest dose tested. The NOAEL for offspring toxicity was 350 ppm (equal to 71 kg bw/d).

In a three-generation reproductive toxicity study in rats, animals were given diets containing mesotrione at a concentration of 0, 2.5, 10, 100 or 2500 ppm (equal to 0, 0.3, 1, 12 and 278 mg/kg bw/d for males and 0, 0.3, 1, 12 and 297 mg/kg bw/d for females, respectively), with an F2 recovery group in which the dams were not treated through gestation. Effects in the parental generations consisted of ocular changes in clinical, ophthalmological, gross and histopathological examinations at dietary concentrations of 10 ppm and above,

along with increased plasma tyrosine levels. In pups, cloudy/opaque eyes, keratitis and/or corneal vascularization were observed in all treated groups in males and at 100 and 2500 ppm in females in litters exposed to mesotrione in utero. Plasma tyrosine levels were measured in pups in the F3 groups and were increased in all treatment groups in the continuous treatment animals; levels were comparable with those of controls in all the recovery groups. Decreased litter size, decreased survival, decreased percentage of pups born live and increased whole litter loss were observed at the highest dose tested.

A MoA study in rats was performed to determine the link between tyrosinaemia and the changes noted in the rat reproductive toxicity study. In a modified one-generation reproductive toxicity study, animals were exposed to 0 ppm mesotrione with 0 per cent, 0.5 per cent, one per cent or two per cent tyrosine or to 2500 ppm mesotrione with 0 per cent, 0.5 per cent, one per cent or two per cent tyrosine from day one of gestation until termination on day 29 postpartum. Tyrosine and mesotrione increased plasma tyrosine levels and caused increases in whole litter losses, although the effect of mesotrione was greater than that of dietary tyrosine. It was concluded that the reproductive effects observed in rats were likely a consequence of the elevated levels of tyrosine.

In a developmental toxicity study in mice, pregnant females were dosed at 0, 10, 60, 150 or 600 kg bw/d. There were no signs of maternal or embryo/foetal toxicity up to 600 kg bw/d, the highest dose tested. In a developmental toxicity study in rats, pregnant females were dosed at 0, 100, 300 or 1000 kg bw/d. Maternal body weight and feed consumption were decreased at all doses. In foetuses, delays in ossification were increased at all doses.

In a developmental toxicity study in rabbits, pregnant females were dosed at 0, 100, 250 or 500 mg/kg bw/d. At 250 and 500 mg/kg bw/d, there were abortions and decreased defecation. The NOAEL for maternal toxicity was 100 mg/kg bw/d, based on increased abortions and decreased defecation at 250 mg/kg bw/d. The NOAEL for embryo and foetal toxicity was 500 mg/kg bw/d, the highest dose tested. An investigative study was performed with pregnant female rabbits treated as follows: control (no tyrosine or mesotrione), tyrosine (one per cent dietary), mesotrione (500 mg/kg bw/d by gavage) and tyrosine and mesotrione (one per cent dietary tyrosine and 500 mg mesotrione/kg bw/d by gavage). Plasma tyrosine levels were increased in all groups treated with mesotrione, tyrosine or a combination of the two. In groups treated with both mesotrione and tyrosine, the plasma tyrosine levels were highest, followed by mesotrione-only treated dams and, lastly, tyrosine-only treated dams. Likewise, delays in ossification were most prevalent in the foetuses of dams treated with both mesotrione and tyrosine, followed by mesotrione-only and tyrosine-only treated dams; however, delays were prevalent in all treated groups at rates higher than those in the concurrent controls. There was only one abortion, which occurred in the group treated with both mesotrione and tyrosine. As a consequence, it was concluded that delays in ossification were related to the increase in plasma tyrosine levels.

Genotoxicity

Mesotrione was tested for genotoxicity in an adequate range of assays, both in vitro and in vivo. There was no evidence of genotoxicity.

Neurotoxicity/immunotoxicity

In the absence of any effects in an immunotoxicity study in mice, the NOAEL for the Antibody-Forming Cell (AFC) (humoral immune response) was at the highest tested dose of 1168 mg/kg bw/d. There was no evidence of any neurotoxic effects in an acute toxicity study or a three month repeat-dose toxicity study in rats.

Mode of action (toxicology)

From toxicity studies in laboratory animals, the main adverse toxicological finding following steady-state exposure to dietary mesotrione was elevated plasma tyrosine levels resulting in ocular lesions, with rats being especially sensitive. Several mode of action (MoA) studies have shown that the primary activity of mesotrione in mammals (and plants) is the inhibition of HPPD, the second enzyme in the tyrosine catabolic pathway. When HPPD activity is completely inhibited, the clearance of excess tyrosine is dependent upon catabolism by the first and rate-limiting enzyme in the catabolic pathway, tyrosine aminotransferase (TAT) and elimination of the products of this catabolism (mainly 4-hydroxyphenylpyruvate) in urine. In rats, the inherent activity of TAT is low and hence they catabolize tyrosine slowly and accumulate it to very high concentrations in plasma which then results in a spectrum of toxicity (ie ocular, kidney, liver and thyroid effects). The steady-state levels of plasma tyrosine after mesotrione administration are much higher in rats (males > females) than in mice, where they do not reach the threshold for toxic effects (~1000 nmoles/mL), even at the highest tested oral dose. The difference in sensitivity between male and female rats as well as between rats and mice can be attributed to differences in TAT activity in these species. In humans, genetically deficient or highly reduced HPPD activity is associated with levels of tyrosinaemia comparable to those observed in mice but it does not result in any ocular toxicity. It is concluded that due to similarities in tyrosine metabolism between mice and humans, the mouse can be considered a better animal model than the rat for human risk assessment purposes. A complete toxicological database for mesotrione was available in the mouse covering kinetics, repeat dose, chronic, carcinogenicity and reproductive toxicity endpoints.

Toxicity of metabolites and/or impurities

For MNBA, a plant and livestock metabolite, studies of metabolism, acute toxicity, short-term toxicity, genotoxicity and HPPD inhibition were performed. When administered to rats as a single oral dose of 75 mg/kg bw, MNBA was minimally absorbed and excreted in the urine. The majority was converted to AMBA in the gut, which was excreted unabsorbed. MNBA is of low acute oral toxicity, with an LD50 of greater than 5000 mg/kg bw. In a 28-day gavage study in rats, MNBA was administered at a dose of 0, 15, 150 or 1000 mg/kg bw/d. The NOAEL was 1000 mg/kg bw/d, the highest dose tested. In a 90-day study in rats, animals were given MNBA in the diet at a concentration of 0, 100, 650 or 3000 ppm (equal to 0, 8, 51 and 231 mg/kg bw/d for males and 0, 9, 57 and 264 mg/kg bw/d for females, respectively). At 3000 ppm, triglyceride levels were increased (by 36 per cent) in females. The NOAEL was 650 ppm (equal to 51 mg/kg bw/d), based on increased triglyceride levels.

MNBA was tested in an adequate range of genotoxicity assays. No evidence of genotoxicity was observed.

In a two-generation reproductive toxicity study or a developmental study, MNBA showed no parental, reproductive, offspring or embryo-foetal toxicity at the limit dose of 1000 mg/kg bw/d when administered to rats by oral gavage.

Relative to mesotrione, MNBA and AMBA were very weak inhibitors of HPPD. AMBA is of low acute oral toxicity, with an LD50 of greater than 5000 mg/kg bw. AMBA showed no evidence of genotoxicity in a reverse mutation assay or in a mammalian cell cytogenetic assay in the presence of metabolic activation but gave positive results in a mammalian cell cytogenetic assay in the absence of metabolic activation. However, it was negative for clastogenicity in a mouse in vivo micronucleus assay. The weight of evidence suggests that AMBA is unlikely to be genotoxic.

Reports related to human toxicity

In a study in which human volunteers were exposed to a single oral dose of mesotrione of 0.1, 0.5 or 4 mg/kg bw in capsules, there were no symptoms, clinical signs or changes on ophthalmological examination. In volunteers given 4 mg/kg bw, plasma tyrosine levels were increased up to 48 hours following dosing, with a peak tyrosine concentration of up to 420 nmol/mL plasma; unchanged mesotrione was found in the urine. Sub-headings below are suggested for microbial-based actives.

3.2 Health-based guidance values and poisons scheduling

Poisons standard

The Delegate of the Secretary of Health has published a final Scheduling decision to include mesotrione in Schedule 5 of the Poisons Standard with no exemptions or concentration cut-offs. The reasons for the Delegate's decision was based on the toxicity profile of mesotrione that was consistent with criteria for listing in Schedule 5. An implementation date in the Poisons Standard was given as 1 January 2012.

Health-based guidance values

Acceptable Daily Intake (ADI)

The ADI for humans is the level of intake of a chemical that can be ingested daily over an entire lifetime without appreciable risk to health. It is calculated by dividing the overall NOAEL for the most sensitive toxicological endpoint from a suitable study (typically an animal study) by an appropriate uncertainty factor. The magnitude of the uncertainty factor is selected to account for uncertainties in extrapolation of animal data to humans, intraspecies variation, and the completeness of the toxicological database and the nature of the potential toxicologically significant effects.

An ADI for mesotrione has been established at 0.5 mg/kg bw/d on the basis of a NOAEL of 50 mg/kg bw/d for reduced bodyweight gain among male mice in an 18 month dietary mouse study. An uncertainty factor of 100 was applied to the NOAEL to account for intra- and inter-species variability and extrapolation.

Acute Reference Dose (ARfD)

An ARfD is the estimate of the amount of a substance in food or drinking water, expressed on a milligram per kilogram body weight basis, that can be ingested over a short period of time, usually in one meal or during one day, without appreciable health risk to the consumer on the basis of all known facts at the time of the evaluation.

Establishing an ARfD for mesotrione was considered unnecessary due to its low acute oral toxicity and the absence of any developmental toxicity after a single oral dose in experimental laboratory animals.

3.3 Recommendations

After consideration of the toxicological profile and probable exposure associated with the use of the product Callisto Herbicide, the APVMA has concluded that the human health risk posed by the product is acceptable according to the criteria stipulated in Section 5A of the *Agricultural and Veterinary Chemicals Code Act (1994)*.

4 RESIDUES ASSESSMENT

Metabolism, analytical methodology, residue trial data, fate in storage, and trade aspects have been considered for mesotrione.

4.1 Metabolism

The applicant has provided details of mesotrione metabolism studies conducted plants (cranberries, maize, rice, peanut and tolerant soya beans) and target animals (lactating cows, laying hens and pigs). Confined rotational crop studies were conducted on endive, radish, soya bean and wheat.

In plants, the metabolic metabolism of mesotrione was extensive in all crops and proceeded by the same route. The metabolic pathway for mesotrione is largely based on:

- hydroxylation of the cyclohexanedione ring or by oxidative cleavage to MNBA
- reduction in the nitro group to give AMBA
- de-amination of AMBA to form MBA.

Residues of mesotrione and its metabolites were low in grains, <5 per cent of the TRR, with the exception of soya bean grain where mesotrione represented 10 per cent of the TRR.

The major compounds found in cranberry fruits were mostly mesotrione and AMBA, >60 and >20 per cent TRR respectively. The major compounds found in the maize, rice, peanut and soya feed commodities were MNBA (up to 25 per cent TRR in soy forage, 20 per cent TRR in soy hay and maize forage, 11 per cent in peanut foliage and <5 per cent TRR in rice whole tops, stalks and straw) and AMBA (up to 28 per cent TRR in maize fodder, 13 per cent TRR in maize forage and <5 per cent TRR in soy feeds, rice feeds and peanut foliage). Mesotrione and 4/5-hydroxy-mesotrione also contributed significantly towards the TRR in rice whole tops (up to 28 per cent TRR mesotrione, and 11 per cent TRR 5-hydroxyl-mesotrione) and soy feeds (up to 19 per cent TRR in soy forage and up to 25 per cent TRR in soy hay) and less significantly in maize forage (up to 7.6 per cent TRR).

In livestock, the metabolic pathway for mesotrione is largely based on:

- oxidative cleavage of the parent compound to MNBA
- reduction in the nitro group to give AMBA.

For all animals the majority of the TRR was excreted (at least 91 per cent in cows, 90 per cent in hens, and 89 per cent in pigs). The major compounds found in animal food items were parent mesotrione (up to 18 per cent TRR in cow liver and kidney, at least 70 per cent TRR in tissues of swine and poultry, and up to 80 per cent TRR in egg yolk) and AMBA (up to 15 per cent in cow kidney only) and at low levels in pig liver and kidney. Levels in milk were low for both compounds.

4.2 Analytical methods and storage stability

Analytical methods for commodities of plant origin

In the barley, wheat and oats trials, mesotrione and its metabolite MNBA were extracted with acetonitrile: water after addition of sodium chloride. Aliquots were diluted with ultra- pure water and concentrated using a polymeric solid phase extraction (SPE) cartridge and eluted using a solution of methanol containing formic acid. Samples were evaporated under a stream of dry nitrogen and dissolved in ultra- pure water: methanol prior to analysis by HPLC-MS/MS. The LOQ was 0.01 mg/kg, and the LOD was 0.003 mg/kg, for mesotrione and MNBA residues, as individual analytes, in all matrices. Average recoveries of mesotrione and MNBA from fortified control samples were within acceptable limits.

Analytical methods for commodities of animal origin

In foodstuff of animal origin (cow tissues [liver, kidney, muscle, fat], milk and egg), mesotrione was extracted with acetone or acetone and water. The mixture was centrifuged and an aliquot taken and added to water acidified with phosphoric acid. After partitioning with methylene chloride, the methylene chloride partitions were evaporated. The residuum was heated with hydrogen peroxide to oxidise mesotrione to MNBA. The MNBA was further reduced by heating with stannous chloride and hydrochloric acid. After cooling, AMBA was extracted from the reaction mixture and determined using a reversed-phase HPLC with Fluorescence detection. The LOQ was 0.01 mg/kg. Average recoveries from fortified control samples were within acceptable limits.

Storage stability

The freezer storage stability of mesotrione and its metabolite MNBA in plant matrices (corn grain, forage and fodder and soybean seed and radish root) was investigated. It was shown that residues of mesotrione were stable in corn grain, corn forage, corn fodder, soybean seed, and radish root for 40 months when maintained under freezer conditions.

For the wheat and barley trials, all samples were maintained under freezer conditions, (ie -18ºC) prior to analysis and tested within 10 months of collection.

4.3 Residue definition

Commodities of plant origin

The major compounds found in cranberry fruit were parent mesotrione (over 60 per cent TRR) and AMBA (over 20 per cent TRR). For tolerant soya bean, maize, rice and peanut the predominant components were mesotrione (up to 28 per cent TRR in rice tops), MNBA (up to 25 per cent TRR in soya bean forage) and AMBA (up to 29 per cent TRR in maize fodder). Total residues in edible commodities were low (≤ 0.03 mg eq. /kg) and when characterized, showed mesotrione as the main residue. The APVMA and JMPR have concluded that MNBA and AMBA appear to be of low toxicological concern. It is also noted that, from the submitted residues trials MNBA was not detected in grain, straw and forage.

A residue definition of parent mesotrione only is recommended for commodities of plant origin. The definition is suitable for both enforcement and risk assessment.

Commodities of animal origin

The major compound found in animal commodities was parent mesotrione (up to 18 per cent TRR in cow liver and kidney, at least 70 per cent TRR in tissues of swine and poultry, and up to 80 per cent TRR in egg yolk) and AMBA (up to 15 per cent in cow kidney only) and at low levels in pig liver and kidney. Levels in milk were low for both compounds.

A residue definition of parent mesotrione only is recommended for commodities of animal origin. The definition is suitable for both enforcement and risk assessment.

4.4 Residues in food and animal feeds

Australian residues trials conducted on wheat (seven trials) and barley (six trials) are supported by seven trials conducted on wheat in Canada and 16 trials conducted on oats in the United States of America. All cereal trials involved a single pre-emergence application relevant to the proposed use.

Residues of mesotrione (parent), in wheat and barley grain from the Australian trials, at 130–184 days after an IBS application at 96–118 g ai/ha (approximately 1× proposed) were <0.01 (n = 13) mg/kg. After application at approximately 2× proposed residues in grain were also <0.01 mg/kg (n = 13).

Residues of mesotrione (parent), in spring wheat grain from the Canadian trials, at 84–119 days after a pre-emergence application 103–141 g ai/ha (approximately 1–1.5× proposed) conducted on spring wheat were also <0.01 mg/kg (n = 3).

The United States oats trials involved a higher application rate (approximately 2×), however residues of mesotrione (parent) in oat grain at 80–246 days after pre-emergence application at 209–216 g ai/ha were also <0.01 mg/kg (n = 16).

MRLs at the LOQ of *0.01 mg/kg are recommended for mesotrione on GC 0654 Wheat and GC 0640 Barley, in conjunction with a harvest withholding period of ‘Not required when used as directed’.

Residues of mesotrione (parent), in wheat and barley forage from the Australian trials, at 68–70 days (10 weeks) after IBS application at 101–118 g ai/ha (approximately 1× proposed) were <0.01 mg/kg (n=6).

Residues of mesotrione (parent), in wheat and barley straw from the Australian trials, at 130–184 days after IBS application at 96–118 g ai/ha (approximately 1× proposed) were <0.01 mg/kg (n=13).

No residues above the LOQ of <0.01 mg/kg were seen in the three Canadian spring wheat trials for all forage samplings between 29–50 days after application or straw samplings between 84–119 days after application.

As forage and straw showed similar residues for both wheat and barley, a mesotrione MRL of *0.01 mg/kg for cereal forage and fodder is considered appropriate for the proposed use. The proposed 10 week grazing withholding period is supported with respect to mesotrione.

4.5 Crop rotation

The confined rotational crop studies indicate that mesotrione should not occur in rotational crops as a result of the proposed use. It is considered unlikely that residues will occur in the following crops, which is consistent with the conclusion made by the JMPR (2014). Plant back intervals with respect to residues or MRLs for following crops are not considered to be necessary.

4.6 Residues in animal commodities

Animal transfer studies for lactating cattle or laying hens have not been provided however metabolism studies for cattle, pigs and poultry were available for consideration.

From the available data for barley and wheat, no residues of mesotrione above the LOQ (0.01 mg/kg, wet or dry weight) were found, therefore the maximum dietary burden for cattle and poultry will be less than 0.01 ppm. As detectable residues of mesotrione are not expected to occur in animal feeds it is appropriate to establish animal commodity MRLs at the LOQ of the analytical method.

The following animal commodity MRLs are recommended;

- *0.01 mg/kg for MO 0105 edible offal (mammalian)
- *0.01 mg/kg for PE 0112 eggs
- *0.01 mg/kg for MM 0095 meat (mammalian)
- *0.01 mg/kg for ML 0106 milks
- *0.01 mg/kg for PO 0111 poultry, edible offal of
- *0.01 mg/kg for PM 0110 for poultry meat.

4.7 Spray drift

The product will be applied by ground application only with a droplet size no smaller than medium.

In the cow metabolism study, dosing with parent mesotrione at 10 ppm gave a maximum parent residue in liver at 0.013 mg/kg and kidney at 0.015 mg/kg. Based on the highest parent residues of approximately 0.02 mg/kg in kidney the estimated feeding level resulting in parent residues in kidney below the LOQ of 0.01 mg/kg is 5 ppm.

If a Regulatory Acceptable Level of 5 ppm is used in the APVMA spray drift risk assessment tool, the following label statements are recommended for the protection of international trade.

DO NOT apply by a boom sprayer unless the following requirements are met:

- spray droplets not smaller than a MEDIUM spray droplet size category

Mandatory buffer zones are not required for livestock areas for the proposed use on wheat and barley.

4.8 Dietary risk assessment

The chronic dietary exposure to mesotrione is estimated by the National Estimated Daily Intake (NEDI) calculation encompassing all registered/temporary uses of the chemical and the mean daily dietary consumption data derived primarily from the 2011–12 National Nutritional and Physical Activity Survey. The NEDI calculation is made in accordance with WHO Guidelines and is a conservative estimate of dietary exposure to chemical residues in food. The NEDI for mesotrione is equivalent to <1 per cent of the ADI. It is concluded that the chronic dietary exposure of mesotrione is acceptable.

The APVMA and JMPR have concluded an ARfD is considered to be unnecessary for mesotrione therefore an estimation of acute dietary exposure is not required.

4.9 Recommendations

The following amendments are required to be made to the APVMA MRL Standard (Table 6).

Table 6: Amendments to the APVMA MRL Standard

Amendments to Table 1			
Compound		**Food**	**MRL (mg/kg)**
ADD:			
	Mesotrione		
GC	0640	Barley	*0.01
MO	0105	Edible offal (mammalian)	*0.01
PE	0112	Eggs	*0.01
MM	0095	Meat (mammalian)	*0.01
ML	0106	Milks	*0.01
PO	0111	Poultry, edible offal of	*0.01
PM	0110	Poultry meat	*0.01
GC	0654	Wheat	*0.01
Amendments to Table 3			
Compound		**Residue**	
ADD:			
	Mesotrione	Mesotrione	

Amendments to Table 4		
Compound	**Animal feed commodity**	**MRL (mg/kg)**
ADD:		
Mesotrione		
	Cereal forage and fodder	*0.01

5 ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

5.1 Commodities exported and main destinations

Cereal grains are considered to be a major export commodities, as are commodities of animal origin, such as meat, offal and dairy products, which may be derived from livestock fed feeds produced from treated cereal grains. Residues in these commodities resulting from the use of Callisto Herbicide may have the potential to unduly prejudice trade.

Total exports of wheat (including flour) were 15,492 kilotonnes valued at $4.7 billion and for barley, 404 kilotonnes valued at $138 million in 2017/18. Major export destinations are summarised below:

Table 7: Major export destinations for wheat and barley

Commodity	Major destinations
Wheat	Indonesia, India, Korea, China, Japan, Thailand, Malaysia, Philippines, Vietnam, Egypt, Nigeria, Yemen, Kuwait, New Zealand
Barley	China, Japan, Republic of Korea, Philippines, Taiwan, Thailand, Vietnam, Kuwait, Saudi Arabia, United Arab Emirates.

The significant export markets for Australian beef, sheep, pig meat, and offals are listed in the APVMA Regulatory Guidelines—Data Guidelines: Agricultural—Overseas trade (Part 5B).

5.2 Overseas registrations and approved label instructions

The applicant has indicated that Callisto Herbicide is registered in numerous European Union and South American countries and the United States of America for both pre and post emergence applications. The registered uses are mainly for weed control in maize and sugar cane. The other crops which have registered uses include asparagus, berries, citrus hybrids, corn (popcorn and sweet corn), grasses and turf, flaxseed, linseed, millet, oats, okra, pome fruits, rhubarb, sorghum, soybean, stone fruits and tree nuts.

5.3 Comparison of Australian MRLs with Codex and international MRLs

The Codex Alimentarius Commission (Codex) is responsible for establishing Codex Maximum Residue Limits (CXLs) for pesticides. CXLs are primarily intended to facilitate international trade, and accommodate differences in Good Agricultural Practice (GAP) employed by various countries. Some countries may accept Codex CXLs when importing foods. Mesotrione has been considered by Codex.

The following relevant international MRLs have been established for mesotrione (Table 8).

Table 8: Proposed Australian and current international MRLs for mesotrione

Country	Residue definition	Commodity	MRL (mg/kg)
Australia (proposed)	Mesotrione	Barley	*0.01
		Wheat	*0.01
		Edible offal (mammalian)	*0.01
		Meat (mammalian)	*0.01
		Milks	*0.01
		Poultry, edible offal of	*0.01
		Poultry meat	*0.01
		Eggs	*0.01
Codex	Mesotrione	Barley	Not established for wheat and barley however maize, millet, oats and sorghum are established at *0.01
		Wheat	
		Edible offal (mammalian)	*0.01
		Meat (mammalian)	*0.01 (mammals other than marine mammals)
		Milks	*0.01
		Poultry, edible offal of	*0.01
		Poultry meat	*0.01
		Eggs	*0.01
European Union	Mesotrione	Barley	*0.01
		Wheat	*0.01
		Edible offal (mammalian)	*0.01 (liver)
		Meat (mammalian)	*0.01 (kidney)
		Milks	*0.01 (other edible offals)
		Poultry, edible offal of	*0.01 (in muscle and fat)
		Poultry meat	*0.01
		Eggs	*0.01 (liver)
			*0.01 (kidney)
			*0.01 (other edible offals)
			*0.01 (in muscle and fat)
			*0.01
United States of America	Mesotrione	Barley	Not established for wheat and barley however maize, millet, oats and sorghum are established at *0.01
		Wheat	
Japan	Mesotrione	Barley	Not established specifically for wheat and barley however rice, corn and 'other cereal grains' are established at *0.01
		Wheat	

5.4 Potential risk to trade

Export of treated produce containing finite (measurable) residues of mesotrione may pose a risk to Australian trade in situations where (i) no residue tolerance (import tolerance) is established in the importing

country or (ii) where residues in Australian produce are likely to exceed a residue tolerance (import tolerance) established in the importing country.

Detectable residues of mesotrione are not expected to occur in wheat or barley or animal commodities from the proposed use. The risk to trade is considered to be low.

6 WORK HEALTH AND SAFETY ASSESSMENT

6.1 Health hazards

Callisto Herbicide is of low to very low acute oral, dermal and inhalation toxicity. It is a slight skin and eye irritant, but is not a skin sensitiser. Very low dermal toxicity was seen following repeat exposure, and it was considered that the main hazards posed related to the acute toxicity profile.

6.2 Occupational exposure

Exposure during use

Callisto Herbicide will be applied at a rate of 100 to 200 mL product/ha (48 to 96 g ai/ha) by ground boom application during crop sowing. It is anticipated that only one application (max. 10 weeks/season) will be required per cropping season. Based on the low hazard associated with repeat dose dermal exposure, no quantitative assessment of the exposure during use has been calculated. Risks related to exposure during use are related to the acute toxicity of Callisto Herbicide.

Exposure during re-entry or rehandling

As Callisto Herbicide is applied during crop sowing, there is anticipated to be very limited exposure due to re-entry to treated areas. The quantitative exposure to treated areas following re-entry was not assessed, due to the low toxicity following repeat dermal exposure.

6.3 Public exposure

Callisto Herbicide is not intended to be used by non-commercial applicators. The proposed use pattern would result in very limited bystander exposure, and, due to the low toxicity of mesotrione, a quantitative assessment of the risk to bystanders (including both workers and the public) has not been determined.

6.4 Recommendations

The following first aid instructions and safety directions are recommended for the product label.

First aid instructions

If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 131126; New Zealand 0800 764 766.

Safety directions

May irritate the eyes and skin. Avoid contact with eyes and skin. Wash hands after use.

7 ENVIRONMENTAL ASSESSMENT

7.1 Fate and behaviour in the environment

Soil

The route and rate of degradation of mesotrione (^{14}C labelled at the cyclohexane and or phenyl rings) in soil under dark aerobic conditions at 20ºC was investigated in 18 soils. Mesotrione exhibited low persistence in these experiments. A pH dependence was demonstrated from the available data which were fit to a lineal relationship[2] resulting in the following representative values for mesotrione: DT_{50} 28 days (pH 5.1), DT_{50} 14 days (pH 6.5), and DT_{50} 0.54 days (pH 7.9).

Mesotrione degraded to form metabolites MNBA[3] (max. 57 per cent AR) and AMBA[4] (max. 9.3 per cent AR). Both MNBA and AMBA also exhibited low persistence in soil (geomean DT_{50} values of 3.4 days and 14 days, respectively). Bound residues reached 38 per cent AR within 28 days and mineralisation reached 75 per cent AR within 63 days.

Mesotrione degradation in soil under anaerobic conditions was investigated in one study. Mesotrione exhibited low persistence under these conditions (mean DT_{50} 4.4 days). Metabolite AMBA reached a maximum of 41 per cent AR.

Photolysis of mesotrione in soil was investigated in microbially active soils under dry and wet conditions irradiated by simulated sunlight. Photolysis can enhance degradation of mesotrione (especially when dry conditions prevail and lower microbial competition occurs).

Field dissipation studies were carried out in European (six sites) and North America (five sites). Mesotrione also exhibited low persistence under field conditions (DT_{50} 3.0 to 14 days).

Batch soil adsorption/desorption studies were performed with mesotrione in over 50 soils. According to these studies, mesotrione may be considered to be mobile in soil. A pH dependence was demonstrated from the available data which were fit to an exponential curve[5] resulting in the following representative values: K_{Foc} 157 L/kg (pH 5.1), K_{Foc} 52 L/kg (pH 6.5) and K_{Foc} 17 L/kg (pH 7.9) with median 1/n 0.94.

MNBA is considered to be very mobile in soil (K_{oc}/ K_{Foc} 3.2 to 14 L/kg in three soils, default 1/n 0.90). AMBA is of comparable mobility to the parent mesotrione, also with pH dependence[6]: K_{Foc} 106 L/kg (pH 5.1), K_{Foc} 60 L/kg (pH 6.5) and K_{Foc} 22 L/kg (pH 7.9) with mean 1/n 0.85.

[2] DT_{50} = -9.8 * pH + 78

[3] 4-(methylsulfonyl)-2-nitrobenzoic acid

[4] 2-amino-4-(methylsulfonyl)benzoic acid

[5] $K_{Foc} = 8583e^{-0.785*pH}$

[6] $K_{Foc} = 1865e^{-0.563*pH}$

Water

Hydrolysis of mesotrione in water was investigated in buffered solutions (pH 4, 5, 7 and 9) at temperatures in the range of 25–50ºC. Mesotrione was stable in the whole range of pH investigated. Direct and indirect aqueous photolysis of mesotrione was investigated in two separated studies simulating sunlight radiation. The rates of photodegradation were relatively slow and aqueous photolysis is therefore not expected to be a major route of degradation under environmentally relevant conditions.

The fate and behaviour of mesotrione in dark water/sediment systems under aerobic conditions was investigated in four systems (two of them were investigated using mesotrione labelled in cyclohexane and phenyl rings). Mesotrione partitioned to the sediment at very low levels (max 4.3 per cent AR) and most of the product remained in the water phase. Degradation was relatively fast in all systems tested with geomean DT_{50} values of 5.5 days in water and 5.6 days in the whole system. Three metabolites were found in the water phase: MNBA (max. 7.4 per cent AR), AMBA (max. 16 per cent AR) and SYN546974[7] (max. 9.4 per cent AR after 29 d). Metabolites AMBA and SYN546974 were also found in the sediment at significant amounts (max. 8.8 per cent AR and 26 per cent AR, respectively). Mineralization was generally low (up to 28 per cent) and the bound residues in the sediment increased up to 74 per cent AR at end of the study.

A batch soil adsorption/desorption study was also performed with the aquatic metabolite SYN546974. SYN546974 may be considered to have low sorption to sediment (K_{Foc} 1702 to 27031 mL/g).

Air

It is considered that mesotrione concentrations in air after application would be negligible, given it has low volatility (<5.7 × 10^{-6} Pa at 20ºC) and was shown to have insignificant volatilisation from soil and plants and a low Henry's Law Constant (<5.1 × 10^{-7} Pa-m^3/ mol at 20ºC). Moreover, the rate of oxidative degradation of mesotrione by hydroxyl radicals was estimated to be DT_{50} 1.5 days. Therefore, mesotrione is unlikely to persist in the atmosphere.

7.2 Effects and associated risks to non-target species

Terrestrial vertebrates

Mesotrione is not considered to be acutely toxic to mammals (LD_{50} >5000 mg ac/kg bw, *Rattus norvegicus*) or birds (LD_{50} >2000 mg ac/kg bw, *Colinus virginianus*). Following long-term dietary administration in reproduction studies, a decreased litter size was observed in mammals at doses as low as 1.2 mg ac/kg bw/d (NOEL 0.30 mg ac/kg bw/d, *Rattus norvegicus*) and certain reproductive parameters related to eggs and chick development were significantly affected at dietary concentrations as low as 600 ppm in birds (NOEL 21 mg ac/kg bw/d, *Anas platyrhynchos*). The formulated product and major metabolites MNBA and AMBA were similarly not toxic to mammals.

The major potential routes of exposure to terrestrial vertebrates are considered to be feeding on food items (eg vegetation and invertebrates) directly contaminated from spray application of the product. The indicator

[7] 9-hydroxy-6-(methylsulfonyl)-3,4-dihydroacridin-1(2H)-one

species for applications to soil are a small granivorous mammal and a small granivorous bird. The screening level assessment assumed that the indicator species feed exclusively on oversprayed food items within the treatment area. Risks to birds were determined to be acceptable at the screening level. Risks to mammals were determined to be acceptable in a higher tier assessment that considered a mixed diet as opposed to a strict granivorous diet. Therefore, risks to terrestrial vertebrates are considered to be acceptable and no specific protection statements are required on the label.

Aquatic species

Mesotrione is not toxic to fish (LC_{50} >97 mg ac/L, four species tested), but is considered to be moderately toxic to aquatic invertebrates (lowest LC_{50} 3.2 mg ac/L, *Mysidopsis bahia*) and algae (lowest E_rC_{10} 0.93 mg ac/L, E_rC_{50} 13 mg ac/L, *Pseudokirchneriella subcapitata*). Mesotrione is very toxic to aquatic plants (lowest EC_{50} 0.0021 mg ac/L, *Lemna gibba*). Following long-term exposure to mesotrione, physical symptoms of toxicity in fish were observed at 25 mg ac/L (NOEC 12 mg ac/L, *Pimephales promelas*). No adverse effects were observed in the most sensitive species of aquatic invertebrate following long-term exposure at the highest test concentration (NOEC 0.049 mg ac/L, *Mysidopsis bahia*). Formulation toxicity data did not show any enhanced toxicity. The major metabolites MNBA, AMBA, and SYN546974 were considerably less toxic than the parent mesotrione.

The major potential routes of exposure of aquatic species are considered to be spray drift or runoff from the treatment area. Although the product is not applied to water, a screening level risk assessment assumes the worst-case scenario of a direct overspray of shallow aquatic habitat, in order to identify those substances and associated uses that do not pose a risk to aquatic species. Risks to fish and algae were acceptable at the screening level. Risks to aquatic invertebrates were only marginal, noting there were no adverse effects observed at the maximum concentration. Spray drift and runoff assessments were necessary to further examine risks to aquatic plants.

According to APVMA's updated approach to spray drift management[8], spray drift risks to aquatic plants were determined to be acceptable provided buffer zones of 40–110 metres at application rates up to 100 mL/ha and 70–200 metres at application rates up to 200 mL/ha are observed, depending on the boom height.

According to APVMA's method to refine estimates of pesticide runoff to waterways[9], runoff risks were determined to be acceptable at the Tier 3 level of assessment provided the product is incorporated within three days of application. The Tier 3 assessment was performed on both a spatial and temporal scale and considered appropriate rainfall values based on stream flow percentiles. The assessment also assumed that 20 per cent of the catchment is treated at the same time and all the treated area contributes to runoff.

Bees

Mesotrione is not considered to be acutely toxic to adult bees by contact exposure (LD_{50} >125 µg ac/bee, *Apis mellifera*) or oral exposure (LD_{50} >105 µg ac/bee, *Apis mellifera*) or to bee larvae (LD_{50} >118 µg ac/bee, *Apis mellifera*). Following long-term dietary exposure to mesotrione, mortality of adult bees was observed in a dose-response manner (LD_{10} 9.2 µg ac/bee, *Apis mellifera*) while no adverse effects were observed in

[8] apvma.gov.au/node/28071
[9] apvma.gov.au/node/15696; model subsequently updated to account for higher runoff expected from soils heavier than loamy soils

larvae at the highest test concentration (NOEL 46 µg ac/bee, *Apis mellifera*). Formulation toxicity data did not show any enhanced toxicity.

For soil application, it is generally assumed that exposure of bees from direct contact with the pesticide is minimal, given the nature of the application to bare soil. Furthermore, spray drift is not of concern considering the LD_{50} >125 µg ac/bee for contact exposure. A screening level risk assessment then assumes that soil-applied systemic pesticides such as mesotrione are transported to pollen and nectar, in order to identify those substances and associated uses that do not pose a risk. Risks to bee were determined to be acceptable at the screening level, and therefore no specific protection statements are required on the label.

Other non-target arthropods

Data on other beneficial (predatory and parasitic) arthropods were provided on contact toxicity of fresh dried residues of a representative SC formulation (480 g/L) to the indicator species—predatory mite (*Typhlodromus pyri*) and parasitic wasp (*Aphidius rhopalosiphi*). The respective Tier 1 (glass plate) studies resulted in LR50 values of >150 g ac/ha and 159 g ac/ha. Extended laboratory tests on natural substrates were also supplied that examined toxicity of another SC formulation (100 g/L) to the indicator species *Typhlodromus pyri* (LR_{50} >300 g ac/ha, ER_{50} >150 g ac/ha) and *Aphidius rhopalosiphi* (LR_{50} >225 g ac/ha, ER_{50} >225 g ac/ha). Additional ground-dwelling arthropod species were also tested with no adverse effects at the highest rates tested: carabid beetles on quartz sand (LR_{50} >200 g ac/ha, ER_{50} >200 g ac/ha, *Poecilus cupreus*), spiders on soil (LR_{50} >150 g ac/ha, ER_{50} >150 g ac/ha, *Pardosa* sp.), and rove beetles on soil (ER_{50} >200 g ac/ha, *Aleochara bilineata*).

Beneficial arthropods could be directly exposed to the active constituent within the crop during treatment or as a result of spray drift. A screening level risk assessment utilises Tier 1 toxicity data and assumes the non-target arthropods are exposed to fresh-dried residues within the treatment area immediately after application. Risks were determined to be acceptable at the first tier of assessment. Therefore, the use of the product is considered compatible with integrated pest management programs (IPM) utilising beneficial arthropods, and no specific protection statements are required on the label.

Soil organisms

Mesotrione is not toxic to soil macro-organisms such as earthworms (LC_{50} >2000 mg ac/kg dry soil, *Eisenia fetida*). Following long-term exposure in soil, mesotrione inhibited reproduction of three species of soil macro-organisms in a dose-dependent manner (lowest EC_{10} 37 mg ac/kg dry soil, *Hypoaspis aculeifer*). No adverse effects were observed on soil processes such as nitrogen and carbon mineralisation at exaggerated soil concentrations (NOEC 0.53 to 1.1 mg ac/kg dry soil). Formulation toxicity data did not show any enhanced toxicity. The major metabolites MNBA and AMBA were less toxic than the parent mesotrione.

A screening level risk assessment assumes the worst-case scenario of a direct overspray of soil without interception, in order to identify those substances and associated uses that do not pose a risk to soil organisms. Risks to soil organisms were determined to be acceptable at the screening level, and therefore no specific protection statements are required on the label.

Non-target terrestrial plants

Data were provided addressing the toxicity of a representative SC formulation (480 g/L) to non-target terrestrial plants following pre- and post-emergent exposure. These studies examined the effects on seedling emergence and vegetative vigour in ten crop species, with growth inhibition (dry weight) being the most significant response. The most sensitive species following pre-emergent exposure was lettuce (ER_{25} 1.0 g ac/ha, ER_{50} 2.2 g ac/ha, *Lactuca sativa*). The most sensitive species following post-emergent exposure was cucumber (ER_{25} 1.9 g ac/ha, ER_{50} 3.2 g ac/ha, *Hordeum vulgare*). The soil metabolites MNBA and AMBA did not show any herbicidal activity.

According to APVMA's updated approach to spray drift management, spray drift risks to non-target terrestrial plants were determined to be acceptable provided buffer zones of 50–140 metres at application rates up to 100 mL/ha and 95–325 metres at application rates up to 200 mL/ha are observed, depending on the boom height.

7.3 Recommendations

The following restraints and protection statements are advised from the viewpoint of environmental safety.

General restraints

DO NOT apply by aircraft.

DO NOT apply by a vertical sprayer.

DO NOT apply if heavy rains or storms are forecast within three days.

DO NOT irrigate to the point of runoff for at least three days after application.

DO NOT apply unless incorporation by sowing (IBS) can occur within three days.

DO NOT apply more than one application per season.

Spray drift restraints

DO NOT apply by a boom sprayer unless the following requirements are met:

- spray droplets not smaller than a MEDIUM spray droplet size category
- minimum distances between the application site and downwind sensitive areas (see 'Mandatory buffer zones' section of Table 9) are observed.

Table 9: Spray drift restraints

Application rate	Boom height above the target canopy	Mandatory buffer zones		
		Natural aquatic areas	Vegetation areas	Pollinators
Up to maximum label rate	0.5 m or lower	70 metres	95 metres	Not required
	1.0 m or lower	200 metres	325 metres	Not required
100 mL/ha or lower	0.5 m or lower	40 metres	50 metres	Not required
	1.0 m or lower	110 metres	140 metres	Not required

Protection statements

Very toxic to aquatic life. DO NOT contaminate wetlands or watercourses with this product or used containers.

8 EFFICACY AND SAFETY ASSESSMENT

8.1 Proposed product use pattern

Callisto Herbicide is proposed for pre-emergent control of common broad-leaved weeds when applied prior to sowing of wheat and barley.

8.2 Efficacy and target crop/animal safety

Data are supplied from multiple sites in cereal growing areas and a range of seasonal conditions for evaluation of Callisto Herbicide against a range of broadleaf weeds in wheat and barley. The data provided also covered claims of residual control, target crop safety and crop safety to following crops.

The selectivity of Callisto Herbicide, depends on good spatial separation of the herbicide and the developing seedlings and so anything that affects separation, impacts on efficacy and crop safety. The depth of cultivation and the re-distribution of soil during cultivation has been shown to affect efficacy and may impact crop safety by concentrating herbicide near the seedlings.

Efficacy

Callisto Herbicide was evaluated for residual control of broadleaf weeds in 80 small plot replicated field trials in cereal growing areas of Western Australia, South Australia, Victoria, NSW and Queensland, in a range of seasonal conditions from 2014 to 2018.

Callisto Herbicide was applied prior to sowing of winter cereals at rates ranging from 104 to 416 mL/ha (proposed label rate is for 100 to 200 ml/ha) mixed with an 800 g/L prosulfocarb herbicide (grass control) applied at 3 to 5 L/ha. Commercial standards including 500 g/L trifluralin, 750 g/kg metribuzin and 750 g/kg triasulfuron were compared alone and in mixtures in the trials.

Efficacy was assessed by percentage control, percentage biomass reduction and weed density (total plot, inter row and intra row) from 47 to 119 days after sowing on wild radish, *Raphanus raphanistrum*, Indian hedge mustard, *Sisymbrium orientale*, wild turnip, *Brassica rapa,* flaxleaf fleabane, *Conyza bonariensis*, *bifora, Bifora testiculata,* common fumitory*, Fumaria officinalis,* wireweed*, Polygonum erectum,* capeweed*, Arctotheca calendula,* fat hen, *Chenopodium album,* common vetch, *Vicia sativa,* sowthistle*, Sonchus oleraceus,* slender celery*, Cyclospermum sp.,* buckwheat*, Fallopia sp.,* deadnettle*, Lamium sp.,* doublegee (spiny emex*), Emex sp.,* prickly lettuce, *Lactuca serriola,* loosestrife, *Lythrum hyssopifolia,* Jersey cudweed*, Gnaphalium luteo-album.,* shepherd's purse*, Capsella bursa-pastoris,* crassula*, Crassula sp.,* Patterson's curse*, Echium plantagineum,* red flowered mallow*, Malva caroliniana.,* chickweed, *Stellaria media*, sub clover, *Trifolium sp.,* thistle, *Carthamus sp.,* ball medic*, Medicago sphaerocarpus,* rough poppy, *Papaver, Juncus,* common storksbill*, Erodium sp.,* Serradella, *Ornithopus sp*., and volunteer pulses, faba beans*, Vicia faba,* field pea*, Pisum sp,* chickpeas*, Cicer arietinum*, lentils, *Lens culinaris*, and lupins*, Lupinus sp.*

Crop safety

Crop safety was assessed in dedicated crop safety trials at label and double label rates, by crop phytotoxicity, crop biomass reduction, crop vigour, crop density and Normalised Differential Vegetation Index on six wheat, and four barley varieties (plus two durum wheat) in 2016 and 10 wheat and five barley varieties in 2017.

Plantback safety was assessed on following crops and pasture species including, Triazine Tolerant canola, *Brassica napus* cv. Crusher, lucerne, *Medicago sativa,* lentils, *Lens culinarus*, field peas, *Pisum sativum,* faba beans*, Vicia faba,* lupins, *Lupinus angustifolius,* chickpeas, *Cicer arietinum,* vetch, *Vicia villosa*, sub clover, *Trifolium subterraneum and* medic, *Medicago polymorpha*.

8.3 Recommendations

The trials used appropriate trial design, scientific methodology and assessment parameters, with four replicates, industry standards and untreated controls. Results were analysed using standard statistical procedures (ANOVA and LSD).

Trial data demonstrated that Callisto Herbicide applied prior to sowing winter cereals at the proposed label rates, provided consistent and significant residual control and suppression of a wide variety of broadleaf weeds, with most trials demonstrating greater than 80 per cent control at up to 119 days after sowing. Callisto Herbicide was as effective or superior to the industry standard treatment.

In dedicated crop safety trials, there was low level of damage when Callisto Herbicide was applied at the proposed label rate. The effect was insignificant, having no impact on crop yield and was equivalent to the effects observed with the industry standards.

In the plantback trials, there was no significant biomass reduction, crop phytotoxicity, plant stand reduction or adverse impact on yield in any of the crop or pasture species planted the following season after application of either the label or double label rate of Callisto Herbicide. Where phytotoxicity was recorded, it was usually minor and transient and not recorded at later assessments with no impact on yield or pasture production.

Overall, the trial data confirmed that Callisto Herbicide, applied prior to sowing of wheat and barley, provided significant residual control of a wide range of broadleaf weeds, when applied at the proposed label rates and according to label instructions. The data also confirmed crop safety of Callisto Herbicide for the target crops, wheat and barley and crops and pasture planted the following season.

9 LABELLING REQUIREMENTS

POISON

KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTIONS BEFORE OPENING OR USING

Callisto

Herbicide

syngenta®

ACTIVE CONSTITUENT: 480 g/L MESOTRIONE

GROUP	H	HERBICIDE

For the control of a range of broadleaf weeds in Wheat and Barley when applied prior to crop sowing

5 to 100 LITRES

Syngenta Australia Pty Ltd
Level 1, 2-4 Lyonpark Road, Macquarie Park NSW 2113

In a transport emergency dial 000, Police or Fire Brigade
For specialist advice in an emergency only, call 1800 033 111 (24 hours)

APVMA Approval No. 87588/118718

DIRECTIONS FOR USE

Restraints:

DO NOT apply by aircraft
DO NOT apply by a vertical sprayer.
DO NOT apply if heavy rains or storms are forecast within 3 days.
DO NOT irrigate to the point of runoff for at least 3 days after application.
DO NOT apply unless incorporation by sowing (IBS) can occur within 3 days.
DO NOT apply more than 1 application per season.

Spray Drift Restraints:

Specific definitions for terms used in this section of the label can be found at apvma.gov.au/spraydrift.

DO NOT allow bystanders to come into contact with the spray cloud.

DO NOT apply in a manner that may cause an unacceptable impact to native vegetation, agricultural crops, landscaped gardens and aquaculture production, or cause contamination of plant or livestock commodities, outside the application site from spray drift. The buffer zones in the relevant buffer zone table/s below provide guidance but may not be sufficient in all situations. Wherever possible, correctly use application equipment designed to reduce spray drift and apply when the wind direction is away from these sensitive areas.

DO NOT apply unless the wind speed is between three and 20 kilometres per hour at the application site during the time of application.

DO NOT apply if there are hazardous surface temperature inversion conditions present at the application site during the time of application. Surface temperature inversion conditions exist most evenings one to two hours before sunset and persist until one to two hours after sunrise.

DO NOT apply by a boom sprayer unless the following requirements are met:

- Spray droplets are not smaller than a MEDIUM spray droplet size category.
- Minimum distances between the application site and downwind sensitive areas are observed (see ‘Mandatory buffer zones’ section of the following table titled ‘Buffer zones for boom sprayers’).

Buffer zones for boom sprayers

Application rate	Boom height above the target canopy	Mandatory downwind buffer zones	
		Natural aquatic areas	Vegetation areas
Up to maximum label rate	0.5 m or lower	70 metres	95 metres
	1.0 m or lower	200 metres	325 metres
100 mL/ha or lower	0.5 m or lower	40 metres	50 metres
	1.0 m or lower	110 metres	140 metres

Crop	Weeds	Rate	Critical Comments
Wheat, Barley	Control of Indian Hedge Mustard, Wild Radish, Wild Turnip Volunteer Chickpeas, Faba Beans, Field Peas, Lentils and Vetch Capeweed, Fleabane, Lesser Loosestrife, Prickly Lettuce, Serradella, Shepherd's Purse, Sow Thistle and Sub Clover Suppression of Ball Medic, Red Flowered Mallow, Rough Poppy, Paterson's Curse, Wireweed and Volunteer Lupins	100 to 200 mL/ha	Apply prior to sowing and incorporate mechanically by sowing operation (IBS). Incorporation must occur within 3 days of application. Use the higher rate when higher weed pressure is expected or longer residual activity is required. Cultivation must not occur prior to the use of CALLISTO from the previous crop until the sowing of the current crop. Wide points and harrows of any type must not be used at or after the seeding operation that incorporates CALLISTO. On sandy soils and especially where furrow wall collapse occurs, higher use rates may result in transient bleaching of newly emerged leaves, lasting around 2 weeks. Affected leaves will typically have a normal green colour restored after this time.
	Suppression of Chickweed, Fumitory, Jersey Cudweed	200 mL/ha	
	Suppression of Double Gee	100 to 150 mL/ha	Use the higher rate where Double Gee densities are expected to be high or where multiple germinations of Double Gee are expected to occur during the course of the growing season.
	Control of Double Gee	200 mL/ha	

NOT TO BE USED FOR ANY PURPOSE, OR IN ANY MANNER, CONTRARY TO THIS LABEL UNLESS AUTHORISED UNDER APPROPRIATE LEGISLATION.

WITHHOLDING PERIODS
Grazing: DO NOT HARVEST, GRAZE OR CUT FOR STOCK FOOD FOR 10 WEEKS AFTER APPLICATION
Harvest: NOT REQUIRED WHEN USED AS DIRECTED

GENERAL INSTRUCTIONS
CALLISTO Herbicide is a soil applied, residual herbicide that controls a wide range of broad leaved weeds. It should be applied prior to the sowing of wheat or barley and incorporated by the sowing action only. Incorporation must occur within 3 days of application.

The herbicide is absorbed through the roots of the target weeds and affected plants will turn white or pale yellow before finally being controlled. The active ingredient is slightly soluble in nature and may, depending on soil texture, soil organic matter and rainfall patterns, redistribute through the soil profile. However, to maximise efficacy, attention should be paid to incorporation at the time of seeding to ensure that the herbicide treated soil is distributed evenly, with soil clods minimised.

Incorporation and tillage
CALLISTO can only be used in knife point and press wheel seeding systems. Wide, conventional or sweep points will also substantially reduce the efficacy achieved with CALLISTO due to dilution of the herbicide

through the surface soil layer. Likewise, the use of harrows of any type following the seeding operation will also dramatically reduce weed control.

Tillage at any point between the harvest of the prior crop and the planting of the cereal crop treated with CALLISTO is likely to result in reduced efficacy.

Mixing
The recommended rate of CALLISTO Herbicide should be added to the spray tank after granular tank-mix partners (if used) are fully dissolved and in suspension. Good agitation should take place to ensure adequate mixing.

Adjuvants
An adjuvant is not required for the use of CALLISTO Herbicide.

Water Rate
A water volume of 50 L/ha or higher is required for the use of CALLISTO Herbicide.

Compatibility
Physical compatibility has been assessed for the following products and, providing strong agitation of the spray solutions is achieved, compatibility will be acceptable:
CALLISTO Herbicide is compatible with any one of the following products:
Weedmaster* Argo* (glyphosate), SPRAY.SEED® (paraquat + diquat), GRAMOXONE® 360 PRO (360 g/L paraquat), GRAMOXONE® 250 (250 g/L paraquat), BOXER GOLD® (prosulfocarb + S-metolachlor), ARCADE® (prosulfocarb), Triflur X* (trifluralin), Avadex* Xtra (triallate), Sakura* (pyroxasulfone), LOGRAN® 750WG (triasulfuron), GESAPRIM® (atrazine), GESATOP® (simazine), DUAL GOLD® (S-metolachlor), metribuzin, diuron, 2,4-D Ester 680

The spray mix must not be left standing in the case of equipment failure, particularly for those containing DUAL GOLD.

CALLISTO Herbicide is compatible with the following combinations of products;
BOXER GOLD + Alpha Scud (alpha-cypermethrin), BOXER GOLD + 2,4-D Ester 680.

As formulations of other manufacturer's products are beyond the control of Syngenta, and the quality of water may vary with location, all mixtures should be tested prior to mixing commercial quantities.

Clean up
Thoroughly clean the sprayer using the following procedure when you have finished spraying.
1. Drain and flush tank, boom and all hoses for several minutes with clean water containing a household detergent.
2. Fill the sprayer tank with clean water and add one litre of household ammonia (containing 3% ammonia) per 100 litres of water. Allow the solution to agitate for 15 minutes prior to flushing the solution through the boom and nozzles. Drain the system.
3. Remove the nozzles and screens and wash separately in a bucket containing the ammonia solution.
4. Thoroughly rinse the tank, hoses, booms, nozzles and screens with clean water for a minimum of 5 minutes to remove all traces of ammonia.

Mix only as much spray solution as needed. Immediately after spraying, clean equipment thoroughly using this procedure. Wear appropriate protective clothing.

Re-cropping Intervals
The following crop and pasture species can be sown 9 months after the use of CALLISTO as long as 250 mm of rain has fallen between application and the proposed sowing date:
Canola, Chickpeas, Faba Beans, Field Peas, Medic, Lentils, Lucerne, Lupins, Sub Clover, Vetch

In some instances, reduced biomass or vigour may be noted in Sub Clover. However, the effect will be minor and is unlikely to cause significant reductions in pasture biomass.

Resistant Weeds Warning **GROUP H HERBICIDE**

CALLISTO HERBICIDE is a member of the triketone group of herbicides. CALLISTO has the inhibitors of 4-hydroxyphenyl-pyruvate dioxygenase (HPPD) mode of action. For weed resistance management CALLISTO is a Group H herbicide. Some naturally occurring weed biotypes resistant to CALLISTO and other Group H herbicides may exist through normal genetic variability in any weed population. The resistant individuals can eventually dominate the weed population if these herbicides are used repeatedly. These resistant weeds will not be controlled by CALLISTO or other Group H herbicides. Since the occurrence of resistant weeds is difficult to detect prior to use, Syngenta Australia Pty Ltd accepts no liability for any losses that may result from the failure of CALLISTO to control resistant weeds.

PROTECTION OF CROPS, NATIVE AND OTHER NON-TARGET PLANTS

DO NOT apply under weather conditions or from spraying equipment which may cause spray to drift onto nearby susceptible plants/crops, cropping lands or pastures.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT

Very toxic to aquatic life. DO NOT contaminate wetlands or watercourses with this product or used containers.

STORAGE AND DISPOSAL

Store in the closed, original container in a dry, cool, well ventilated locked room or place away from children, animals, food, feedstuffs, seed and fertilisers. DO NOT store for prolonged periods in direct sunlight.

For non-returnable containers:

Triple rinse containers before disposal. Add rinsings to spray tank. DO NOT dispose of undiluted chemicals on site. If recycling, replace cap and return clean containers to recycler or designated collection point. If not recycling, break, crush, or puncture and deliver empty packaging to an approved waste management facility. If an approved waste management facility is not available, bury the empty packaging 500 mm below the surface in a disposal pit specifically marked and set up for this purpose, clear of waterways, desirable vegetation and tree roots, in compliance with relevant Local, State or Territory government regulations. DO NOT burn empty containers or product.

For returnable containers:

Empty contents fully into application equipment. Close all valves and return to point of storage for refill or storage.

SAFETY DIRECTIONS

May irritate the eyes and skin. Avoid contact with eyes and skin.
Wash hands after use.

FIRST AID

If poisoning occurs, contact a doctor or Poisons Information Centre. Phone 131 126.

SAFETY DATA SHEET

If additional hazard information is required refer to the Safety Data Sheet. For a copy phone 1800 067 108 or visit our website at www.syngenta.com.au

DISCLAIMER

This product complies with the specifications in its statutory registration. Implied terms and warranties are excluded. Syngenta's liability for breach of the express or any non-excludable implied warranty is limited to product replacement or purchase price refund. The purchaser must determine suitability for intended

purpose and take all proper precautions in the handling, storage and use of the product including those on the label and/or safety data sheet failing which Syngenta shall have no liability.

ABBREVIATIONS

ac	active constituent
ADI	Acceptable Daily Intake (for humans)
ai	active ingredient
ARfD	Acute Reference Dose
bw	bodyweight
d	day
DAT	Days After Treatment
DT_{50}	Time taken for 50% of the concentration to dissipate
EA	Environment Australia
EC_{50}	concentration at which 50% of the test population are immobilised
E_rC_{50}	concentration at which the rate of growth of 50% of the test population is impacted
EI	Export Interval
EGI	Export Grazing Interval
ESI	Export Slaughter Interval
g	gram
GAP	Good Agricultural Practice
h	hour
ha	hectare
IPM	Integrated Pest Management
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
kg	kilogram
L	Litre
LC_{50}	concentration that kills 50% of the test population of organisms
LD_{50}	dosage of chemical that kills 50% of the test population of organisms
LOD	Limit of Detection—level at which residues can be detected

Log K_{OW}	Log to base 10 of octanol water partitioning co-efficient, synonym P_{OW}
LOQ	Limit of Quantitation—level at which residues can be quantified
mg	milligram
mL	millilitre
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
NEDI	National Estimated Daily Intake
NESTI	National Estimated Short Term Intake
ng	nanogram
NOEC/NOEL	No Observable Effect Concentration Level
NOAEL	No Observed Adverse Effect Level
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
Q-value	Quotient-value
REI	Re-Entry Interval
s	second
SC	Suspension Concentrate
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons
TGA	Therapeutic Goods Administration
TGAC	Technical grade active constituent
µg	microgram
WHP	Withholding Period

GLOSSARY

Active constituent	The substance that is primarily responsible for the effect produced by a chemical product
Acute	Having rapid onset and of short duration
Carcinogenicity	The ability to cause cancer
Chronic	Of long duration
Codex MRL	Internationally published standard maximum residue limit
Desorption	Removal of a material from or through a surface
Efficacy	Production of the desired effect
Formulation	A combination of both active and inactive constituents to form the end use product
Genotoxicity	The ability to damage genetic material
Hydrophobic	Repels water
Metabolism	The chemical processes that maintain living organisms
Photolysis	Breakdown of chemicals due to the action of light
Toxicology	The study of the nature and effects of poisons

REFERENCES

APVMA 2019, *Spray drift risk assessment tool*, Australian Pesticides and Veterinary Medicines Authority, Canberra, available at apvma.gov.au/node/39701.

APVMA 2015, *Data Guidelines,* Australian Pesticides and Veterinary Medicines Authority, Canberra, available at apvma.gov.au/registrations-and-permits/data-guidelines.

WHO 1997, *Guidelines for predicting dietary intake of pesticide residues*, World Health Organization, Geneva, available at: who.int/foodsafety/publications/pesticides/en/.