Australian Government

Australian Pesticides and Veterinary Medicines Authority

PUBLIC RELEASE SUMMARY

on the evaluation of the new active metazachlor in the product Butisan Herbicide

APVMA Product Number 80664

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This publication is available from the APVMA website: www.apvma.gov.au.

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PREFACE

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is the Australian Government regulator with responsibility for assessing and approving agricultural and veterinary chemical products prior to their sale and use in Australia.

In undertaking this task, the APVMA works in close cooperation with advisory agencies, including the Department of Health and Ageing, Department of Environment and Energy, Department of Agriculture and Water Resources, and State Departments of Primary Industries.

The APVMA has a policy of encouraging openness and transparency in its activities and of seeking community involvement in decision making. Part of that process is the publication of Public Release Summaries for products containing new active constituents.

The information and technical data required by the APVMA to assess the safety 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 at www.apvma.gov.au.

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 its advisory agencies. It has been deliberately presented in a manner that is likely to be informative to the widest possible audience thereby encouraging public comment.

About this document

This is a Public Release Summary.

It 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 registration of Butisan 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 **10 January 2017** 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.

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
PO Box 6182
Kingston ACT 2604
Phone: +61 2 6210 4701
Fax: +61 2 6210 4721
Email: enquiries@apvma.gov.au

Further information

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

Further information on public release summaries can be found on the APVMA website www.apvma.gov.au.

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

1 INTRODUCTION

1.1 Applicant

BASF Australia Ltd

1.2 Details of the product

It is proposed to register Butisan Herbicide, a suspension concentrate product containing the 500 g/L metazachlor. Butisan Herbicide is intended for pre-emergent control of annual ryegrass, wild oats and wireweed in canola.

It is proposed that one application of Butisan Herbicide be applied to soil and incorporated by sowing at a maximum application rate of 1.8 L product/ha.

Metazachlor belongs to the chemical class of chloroacetamides and acts by a complex mode of action involving disruption of fatty acid syntheses. Butisan Herbicide acts as a pre- and post-emergence herbicide. Butisan Herbicide enters target plants primarily through the roots, the hypocotyl, and the cotyledons of the germinating and emerging weeds. It has, therefore, its best herbicidal effectiveness during early development stages of the weeds.

Butisan Herbicide is active against a broad range of mono and dicotyledonous weeds. Since it acts via both the roots and the developing shoot, it can be used pre-emergence as well as (early) post emergence.

1.3 Overseas registration

Herbicides containing metazachlor are currently registered for use in various crops in United Kingdom and other European countries, Taiwan and Chile. Butisan Herbicide is registered in the United Kingdom and some other European countries for use in canola.

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

2 CHEMISTRY AND MANUFACTURE

2.1 Active constituent

The active constituent metazachlor will be manufactured overseas and imported into Australia as a fully formulated product. Metazachlor belongs to the chloroacetamide class of compounds. It is a solid at room temperature, slightly soluble in water at neutral pH giving mildly acidic solutions, and highly soluble in polar and aromatic organic solvents. Metazachlor has good safety properties, not being flammable, explosive or oxidising. The nomenclature and physicochemical properties of metazachlor are summarised in the following two tables. The identity of metazachlor was confirmed through infrared, nuclear magnetic resonance and mass spectrometry.

Table 1: Nomenclature of metazachlor

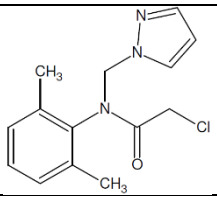
COMMON NAME (ISO):	Metazachlor
CHEMICAL NAME:	2-Chloro-*N*-(2,6-dimethylphenyl)-*N*-(1*H*-pyrazol-1-ylmethyl)acetamide
CAS REGISTRY NUMBER:	67129-08-2
EMPIRICAL FORMULA:	$C_{14}H_{16}ClN_3O$
MOLECULAR WEIGHT:	277.8
STRUCTURAL FORMULA:	

Table 2: Key physicochemical properties of metazachlor

APPEARANCE AND ODOUR:	Colourless solid (both pure and technical active constituent)
ODOUR:	No odour (pure active constituent) Faint aromatic odour (technical active constituent)
MELTING POINT:	82.5°C (technical active constituent)
DECOMPOSITION TEMPERATURE:	No boiling or other phase transition observed, decomposes at approximately 220°C
RELATIVE DENSITY (D_4^{20}):	1.30
WATER SOLUBILITY:	446 mg/L (pure active constituent, purified water, 20°C)
ORGANIC SOLVENT SOLUBILITY (G/100ML, 20 °C):	n-heptane: <1.0 Toluene: >25 Dichloromethane: >25 Methanol: >25 Acetone: >25 Ethyl acetate: >25
OCTANOL/WATER PARTITION COEFFICIENT (LOG KOW):	2.49
PH:	4.6 (0.5% dilution in pure water) 3.7 (2.0% dilution in pure water)
PKA:	No dissociation observed
HYDROLYSIS:	Hydrolytically stable at pH 4, 5, 7, and 9 (25°C)
VAPOUR PRESSURE AT 20°C:	0.095 mPa
HENRY'S LAW CONSTANT (20°C):	5.9×10^{-8} kPa·m^{3}mol^{-1}
SAFETY PROPERTIES:	Not flammable No auto-ignition up to 400°C No potential for explosivity No oxidising potential

2.2 Formulated product

The proposed formulation is a suspension concentrate, containing 500 g/L metazachlor as the only active constituent. Butisan Herbicide will be formulated overseas. The product will be packaged in high density polyethylene containers ranging in size from 1 L to 110 L. The stability data provided showed that the formulation would not be expected to have any adverse effect on the packaging, and vice versa. Key properties of the formulated product are summarised in the table below.

Table 3: Key physicochemical properties of Butisan Herbicide

APPEARANCE AND ODOUR:	White viscous liquid with a faint spicy odour
FORMULATION TYPE:	Suspension concentrate
PH:	6.5 (1% dilution)
RELATIVE DENSITY (D_4^{20}):	1.15
SURFACE TENSION	40.7 mN/m at 0.7% in water at 20°C
VISCOSITY	97 mPa.s at 100 s^{-1} (non-Newtonian liquid)
SAFETY PROPERTIES:	Not explosive Not flammable No oxidising potential

2.3 Summary

The APVMA chemistry and manufacture section has evaluated the chemistry aspects of metazachlor and Butisan Herbicide (spectroscopic identification, manufacturing and formulation processes, quality control procedures, stability data, specifications, batch analysis results, proposed packaging, and analytical methods) for both the technical active constituent and the formulated product and found them to be acceptable.

On the basis of the chemistry and toxicological assessments, it is proposed that the following APVMA active constituent standard be established for metazachlor:

Table 4: Proposed active constituent standard for metazachlor

CONSTITUENT	SPECIFICATION	LIMIT
Metazachlor	Metazachlor	Not less than 950 g/kg (on a dry weight basis)

3 TOXICOLOGICAL ASSESSMENT

3.1 Evaluation of toxicology

The toxicological database provided for metazachlor is extensive and comprises a full suite of acute and repeat dose toxicity studies in mice, rats and dogs as well as *in vitro* and *in vivo* genotoxicity studies, reproductive and developmental toxicity studies. Additionally, a series of acute, short-term, developmental and genotoxicity studies on a number of metabolites have also been provided.

In interpreting the data, it should be noted that toxicity tests generally use doses that are high compared with likely human exposures. The use of high doses increases the likelihood that potentially significant toxic effects will be identified. Findings of adverse effects in any one species do not necessarily indicate such effects might be generated in humans. However, from a conservative risk assessment perspective, adverse findings in animal species are assumed to represent potential effects in humans, unless convincing evidence of species specificity is available. Where possible, considerations of the species specific mechanisms of adverse reactions weigh heavily in the extrapolation of animal data to likely human hazard. Equally, consideration of the risks to human health must take into account the likely human exposure levels compared with those, usually many times higher, which produce effects in animal studies. Toxicity tests should also indicate dose levels at which the specific toxic effects are unlikely to occur.

Chemical class

Metazachlor belongs to the chloroacetamide chemical class of herbicides. It acts primarily by inhibition of the formation of very-long chain fatty acids in lipid biosynthesis, through interaction with the condensing elongase enzyme system. This leads to inhibited cell division and tissue differentiation, resulting in stunted and deformed seedlings. The uptake of metazachlor in germinating grass and dicotyledonous plants occurs predominantly *via* the roots and the developing shoot, and halts the germination process. Plants slowly die off as a result of abnormal growth.

Toxicokinetics and metabolism

Oral absorption, assessed in bile duct-cannulated rats as the sum of radioactivity excreted in urine and bile over 48 hours, was 92% (males) and 105% (females) after a 60 mg/kg bw gavage dose in tylose (cellulose), or 51% (males) and 79% (females) after a 600 mg/kg bw dose. Considerably higher concentrations of radioactivity were found in blood than plasma (blood:plasma ratios were approximately 25–71:1 at 60 mg/kg, and 200–350:1 at 600 mg/kg), indicating radioactivity probably binds more extensively to cellular blood constituents than to plasma proteins.

Terminal half-lives of radioactivity in plasma were comparable for both 600 mg/kg bw (29–39 hrs) and 60 mg/kg bw oral dose (28–31 hrs) and in both sexes). Time to reach plasma C_{max} was longer after the high dose (24 hrs) than the low dose (4–8 hrs). The rapid excretion (~80% in urine and faeces within 48 hours after single or repeat doses of 60 mg/kg bw; ~90% in urine and faeces 48 hours after single dose of 600 mg/kg bw) observed in the balance/excretion experiments is not consistent with a plasma half-life of approximately 30–40 hours, which may be due to binding of radioactivity not only to blood cells but also to plasma proteins, as well as enterohepatic circulation of radioactivity.

Metazachlor was well distributed after absorption, with mean tissue and organ concentrations generally peaking 4–8 hours after a single low oral dose. Concentrations of ^{14}C-metazachlor-derived radioactivity in blood, lung, heart, spleen, adrenals and brain remained relatively constant from 4–120 hours post-dosing. At 144 hours post-dosing, the mean proportion of the administered dose retained in tissues was highest in blood, liver, skin, and the gut. Considerably higher concentrations of radioactivity were found in blood than plasma, indicating radioactivity probably binds more extensively to cellular blood constituents than to plasma proteins. After 5 daily doses of 300 mg/kg bw/d in Sprague-Dawley rats, there was no evidence of accumulation of radioactivity in tissues, with only small amounts (<1% of total dose) measured in tissues 72 hours after the last (fifth) administration.

Metazachlor is rapidly and extensively metabolised. Phase 1 biotransformation comprised of hydroxylation and glucuronide conjugation. The main metabolic route was substitution of chlorine by glutathione, followed by successive degradation of the glutathione group by oxidation and hydrolytic cleavage reactions. Glutathione conjugates formed the majority of the non-extractable metabolites in tissues and blood cells in this study. Oxidation of the methyl groups of the phenyl ring and further conjugation by glucuronic acid was also observed.

Metazachlor and its metabolites are rapidly excreted via urine and bile. The excretion balance did not indicate significant differences in total excretion between single oral high dose, single oral low dose or multiple low dose administration. However, biliary excretion was clearly higher at the low dose (approximately 50–60%) than at the high dose (21–25 %). The bioavailability was 100% at the low dose level but absorption was saturated at the high dose level.

Percutaneous absorption

In vitro dermal absorption studies were conducted with ^{14}C-metazachlor applied to split-thickness dermatomed human skin as a formulation concentrate containing a nominal concentration of 500 g/L metazachlor (undiluted concentrate) and a representative aqueous spray dilution for field use (1/100 aqueous dilution containing about 5 mg/mL of the formulated concentrate). Actual applied nominal doses to 5 skin preparations per test material were 45.4 ± 0.6 µg/cm^2 (low dose) and 5,100 ± 76 µg/cm^2 (high dose).

The sum of the mean total absorbable and the mean amount absorbed was 0.31% for the high dose (undiluted concentrate), equating to 15.8 µg/cm^2 of absorbed/absorbable mass, and 3.54% for the low dose, equating to 1.6 µg/cm^2 absorbed/ absorbable mass.

Acute toxicity

In acute toxicity studies in rodents, metazachlor TGAC was of low acute oral toxicity in rats (LD_{50} = 2160/2140 mg/kg (M/F)) and mice (LD_{50} = 2010 mg/kg bw); low acute dermal toxicity in rats (LD_{50} > 6810 mg/kg bw; no deaths) and low acute inhalational toxicity in rats (LC_{50} >34500 mg/m^3, 4–hour exposure, no deaths). It was a slight skin irritant but not an eye irritant in rabbits. Different results were obtained in skin sensitisation studies. In an open cutaneous skin sensitisation study (i.e. non-adjuvant, topical open application), metazachlor was negative while a positive result was obtained in a guinea pig maximization test. Noting that the open cutaneous skin sensitisation test is no longer a validated skin

sensitisation assay, metazachlor is considered to have skin sensitisation potential based on the GPMT (Guinea Pig Maximization Test) results.

The applicant provided a number of acute toxicological studies from a reference formulation and two studies (acute oral toxicity and skin irritation) on the formulated product. Butisan Herbicide is of low acute oral toxicity ($500 < LD_{50} < 2000$ mg/kg bw), and is expected to be of low acute dermal toxicity and low acute inhalational toxicity. It is not irritating to the skin of rabbits and is expected to be a slight eye irritant, but not a skin sensitiser.

Systemic toxicity

The primary target organs for toxicity in short-term, subchronic and chronic toxicity studies with metazachlor were the liver, kidney and red blood cells. Effects observed in these studies also included non-specific toxicity (i.e. decreases in food consumption, body weight, or body weight gain), clinical signs (i.e. piloerection, ataxia, salivation, vomiting) and effects on the liver or kidney (i.e. serum liver enzyme changes, increased liver and/or kidney weights, or fatty degeneration of hepatocytes, renal parenchymal cell damage). The available data suggest that the rat is the most sensitive species.

No treatment related adverse effects were seen in a short-term dermal study in the rat at the limit dose.

Genotoxicity and carcinogenicity

Metazachlor was not genotoxic in a standard suite of *in vitro* and *in vivo* studies.

There were no treatment-related neoplastic findings in a 104–week dietary study in mice.

There was an increased incidence in thyroid para-follicular cell tumours (adenomas and carcinomas combined) in male rats at 2 000 and 6 000 ppm in the two-year carcinogenicity study in rats. The incidence of adenomas and carcinomas in the 2 000 and 6 000 ppm dose groups were comparable to a control group in a separately conducted satellite group. However, in isolation the incidence of adenomas appeared to be elevated in comparison to the concurrent control and the satellite group control. Examination of the data indicated that the treatment group incidences were within the historical control range for the laboratory strain of rat used in this study. Furthermore, in the absence of a clear dose response or pre-neoplastic markers such as hyperplasia or para-follicular cell dysplasia observed in interim kill or terminal kill animals, the evidence for potential carcinogenicity arising from metazachlor administration was considered to be weak. Therefore, the overall lack of treatment-related neoplastic findings in long term mouse and rat studies and the lack of genotoxicity in a battery of tests conducted with metazachlor and its metabolites supports the conclusion that metazachlor is unlikely to be a carcinogen.

Reproductive and developmental toxicity

There was no evidence of reproductive or developmental toxicity in the two-generation reproduction study in rats, or in the developmental studies in rats and rabbits.

Metabolite toxicity

A large number of metabolites were identified and subjected to further investigations in a variety of studies, including acute oral toxicity, 13–week (dietary) toxicity studies and developmental toxicity as well as a battery of genotoxicity studies.

Six metabolites were tested in genotoxicity assays and were found to be negative.

In acute oral studies, all metabolites were of low acute oral toxicity (oral LD_{50} > 500 mg/kg bw) and clinical signs observed in some of these studies were similar to those observed with the parent compound.

No toxicologically significant findings were noted in oral subchronic or developmental studies in rats on the metabolites.

3.2 Public health standards

Poisons scheduling

On 27 October 2016, the delegate of the Secretary of the Department of Health published a final scheduling decision to create a new Schedule 5 listing for metazachlor in the Standard for the Uniform Scheduling of Medicines and Poisons. An implementation date of 1 February 2017 was notified.

ADI (Acceptable daily intake)

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

The toxicological database for metazachlor included several long-term oral and carcinogenicity studies in the mouse and rat, as well as a 12–month study in beagle dogs, and was considered complete.

The critical health effect for metazachlor in long term repeat dose studies was the liver and red blood cell system in in dogs and rats, and the kidney in mice. The lowest systemic dose across the long-term studies was 500 ppm (equivalent to 17.6 and 21.3 mg/kg bw/d in males and females, respectively) in a 2–year rat chronic/carcinogenicity study. Findings at the next highest dose of 72.9/87.6 mg/kg bw/d included increased liver weights associated with histopathological changes, decreased food consumption and efficiency, reduced body weight gain and decreased red blood cell parameters.

The incidence of para-follicular cell adenomas at the mid- and high-dose in the carcinogenicity study in rats appeared to be elevated in comparison to controls. However, based on the weight of available evidence, the observed increased incidence of thyroid para-follicular cell tumours was not considered to be related to metazachlor treatment, and an additional safety factor for the derivation of the ADI was not required in this case.

The ADI for metazachlor is established at 0.2 mg/kg bw/day (rounded) based on the NOEL of 17.6 mg/kg bw/d from a 104 week dietary chronic/carcinogenicity study in male SD (Sprague Dawley) rats and applying a 100–fold safety factor (consisting of a 10–fold safety factor for both intra- and inter-species variation).

ARfD (Acute Reference Dose)

The Acute Reference Dose (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.

A review of the acute and short-term (including developmental toxicity) studies suggested that metazachlor has low oral toxicity. Although an increase in salivation among pregnant rats was observed at doses ≥150 mg/kg bw/d on gestation days 7–8 (i.e. second and third exposure) in a rat developmental toxicity study it was uncertain whether this was an acute and indeed even a reproducible response. In a dose range finding study in the same laboratory, an increased incidence of salivation among rats was only observed at 300 and 600 mg/kg bw/d and none at 150 mg/kg bw/d. At 600 mg/kg bw/d salivation was observed on the day of administration but at 300 mg/kg bw/d it only occurred after 4 consecutive daily doses. In a contemporary oral gavage study to establish a median lethal dose, no increase in salivation among rats was observed at doses up to 2000 mg/kg bw. In dogs, increased salivation and vomiting was observed following a single exposure to a gavage dose of 270 mg/kg bw. It is not usually considered appropriate to establish an acute reference dose for a compound which is known to cause vomiting in dogs as this is most likely to be the result of it being a gastric irritant.

In the absence of any reproducible adverse effects following a single oral exposure the establishment of an ARfD is considered to be unnecessary.

4 RESIDUES ASSESSMENT

4.1 Introduction

Butisan Herbicide contains the active constituent metazachlor for use on pre-emergent canola. It is proposed that one application of Butisan Herbicide (500 g/L metazachlor) be applied to soil and incorporated by sowing at a maximum application rate of 1.8 L product/ha (900 g metazachlor /ha).

A harvest withholding period of 'Not required when used as directed' and a grazing withholding period of 'DO NOT graze or cut for stockfeed for 12 weeks after application' is proposed.

As part of the residue assessment for registration of metazachlor, plant and animal metabolism studies, supervised residue trials, analytical methodology, fate in storage and processing data and residues in trade information were considered.

4.2 Metabolism

Studies examining the metabolism of ^{14}C-metazachlor labelled on the phenyl ring in canola, maize, white cabbage and confined rotational crops (lettuce, radish, wheat), and in goats and hens following oral ingestion, were considered. The fate of metabolite 479M16 (labelled on the phenyl ring) was also investigated following oral treatment to goats.

Plants

^{14}C-metazachlor was applied to canola (pre and post emergent), cabbage and rotational crops at a rate of 1.25 kg ai/ha and to maize (pre-emergent) at a rate of 1.0 kg ai/ha.

Parent metazachlor was not identified in any primary or rotational crop samples, except canola forage taken immediately after post-emergent application (64% Total Radioactive Residues—TRR, 0 DAT). Metazachlor was extensively metabolised and a significant number of metabolites were identified (at least 24 different metabolites).

For canola (seed, forage, straw, hulls) and cabbage, the major metabolite was the hydroxyl cysteine conjugate 479M16, representing up to 55% of the TRR (0.028–8.4 mg/kg). This metabolite was also found in significant quantities in maize (grain, plant, flags, straw), representing up to 25% of the TRR (0.003– 0.37 mg/kg).

For maize (grain, plant, flags, straw), the major metabolite was the oxalic acid metabolite 479M04, representing up to 35% of the TRR (0.002–0.45 mg/kg). This metabolite was also found in significant quantities in cabbage, representing 28% of the TRR (0.045 mg/kg).

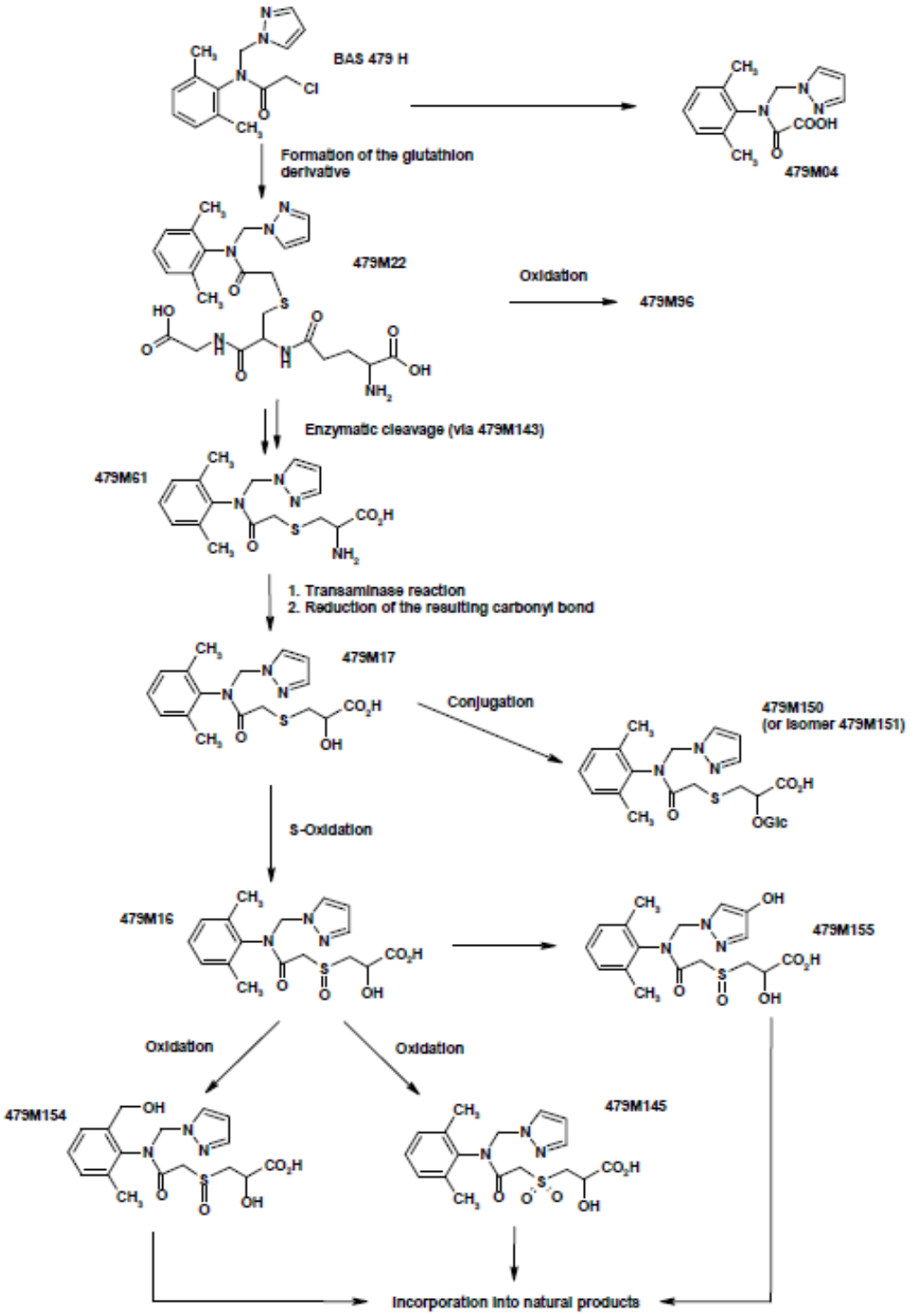
For confined rotational crops, the major metabolites were 479M08 / 479M04 (32.7–74.4% TRR, 0.009–4.8 mg/kg). Residues of metabolites 479M04/479M08 (determined together) in wheat forage, straw and chaff were at similar levels when planted 30–120 days after treatment, but then decreased significantly for a plant back interval 366 days after treatment.

The moiety common to the major plant metabolites mentioned is 2,6-dimethylaniline.

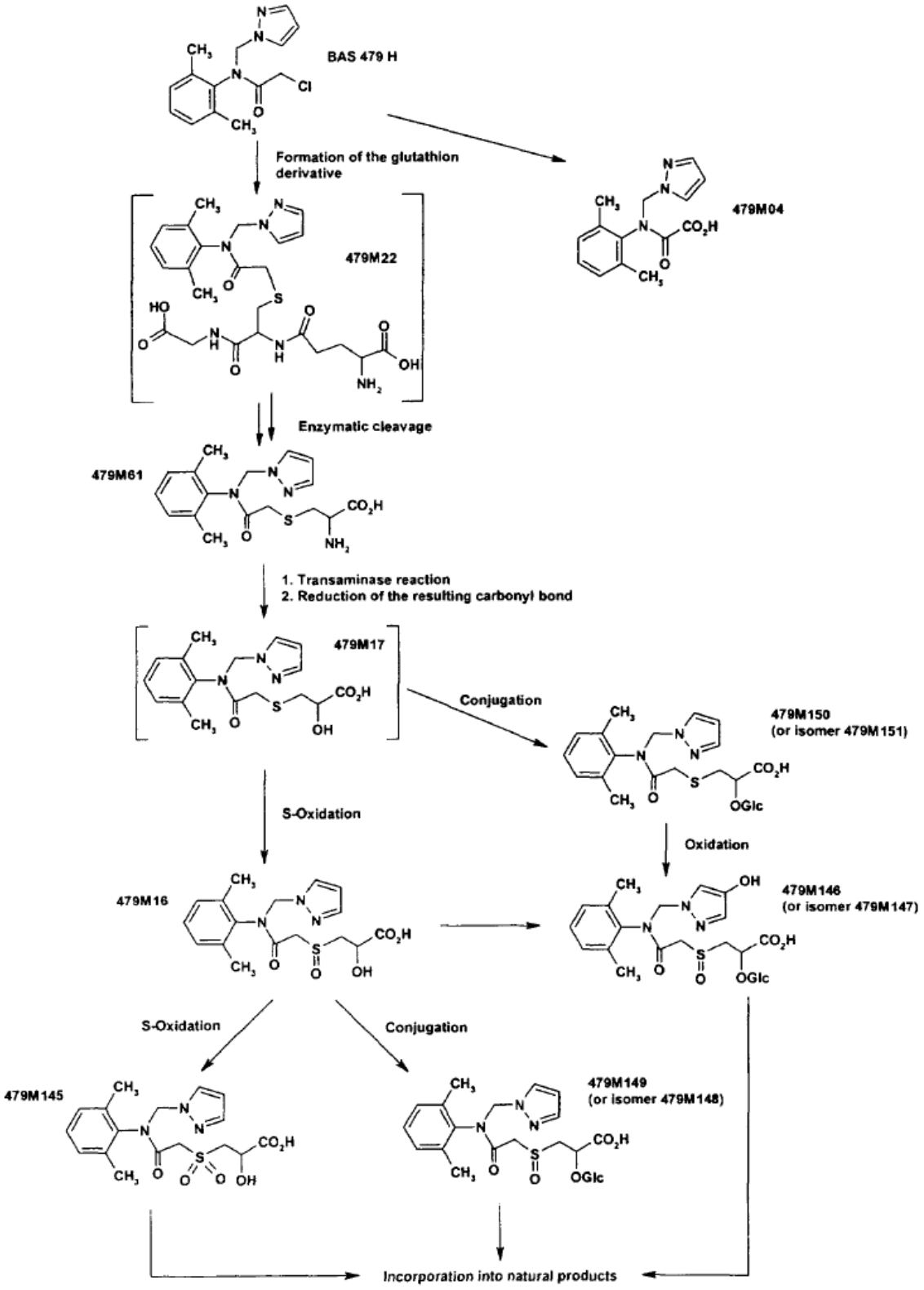
Metabolism varied depending on the plant and rotational crops, but the formation of the glutathion conjugate (479M22) and its subsequent cleavage was common to all pathways. The oxalic metabolite 479M04 was detected in maize, cabbage and rotational crops but not canola, and may be formed in primary crops by oxidation of the alcohol intermediate 479M01.

The proposed biotransformation pathways of metazachlor in primary and rotational crops are shown below:

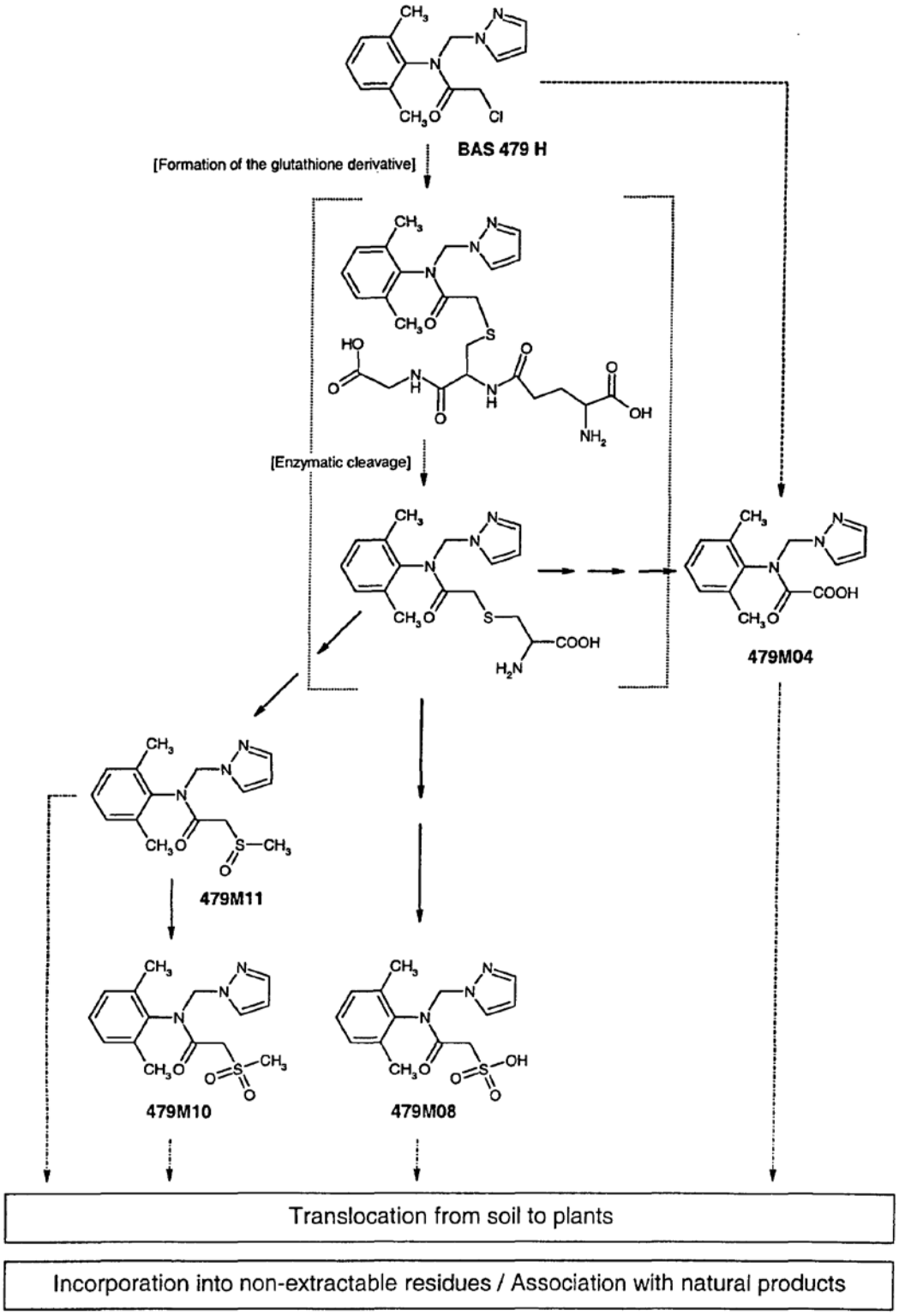
The proposed metabolic pathway for metazachlor in the primary crops maize and canola (noting the formation of metabolite 479M04 was not identified in the canola metabolism study):



The proposed metabolic pathway for metazachlor in the primary crop cabbage:



The proposed metabolic pathway for metazachlor in rotational crops:



Animals

Parent metazachlor was not identified in any animal samples. Metazachlor was extensively metabolised and a significant number of metabolites were identified (at least 124 different metabolites).

Goats were treated with ^{14}C-metazachlor for 5 days at either 3.3 ppm, 29 ppm or 36 ppm. A large number of metabolites in liver and kidney were characterised and identified. The major metabolite identified in liver was 479M61 (2.6–39% TRR, 0.09–1.2 mg/kg). For kidneys, no metabolites exceeded 10% TRR. Metabolite 479M04 (found in plant matrices) was not detected in either kidney or liver but was detected in trace amounts in urine.

Hens were treated with ^{14}C-metazachlor for 6 days at either 11 ppm or 137 ppm. Residues in liver were qualitatively identified as 479M61, 479M62, 479M67, 479M15, 479M48 and 479M116.

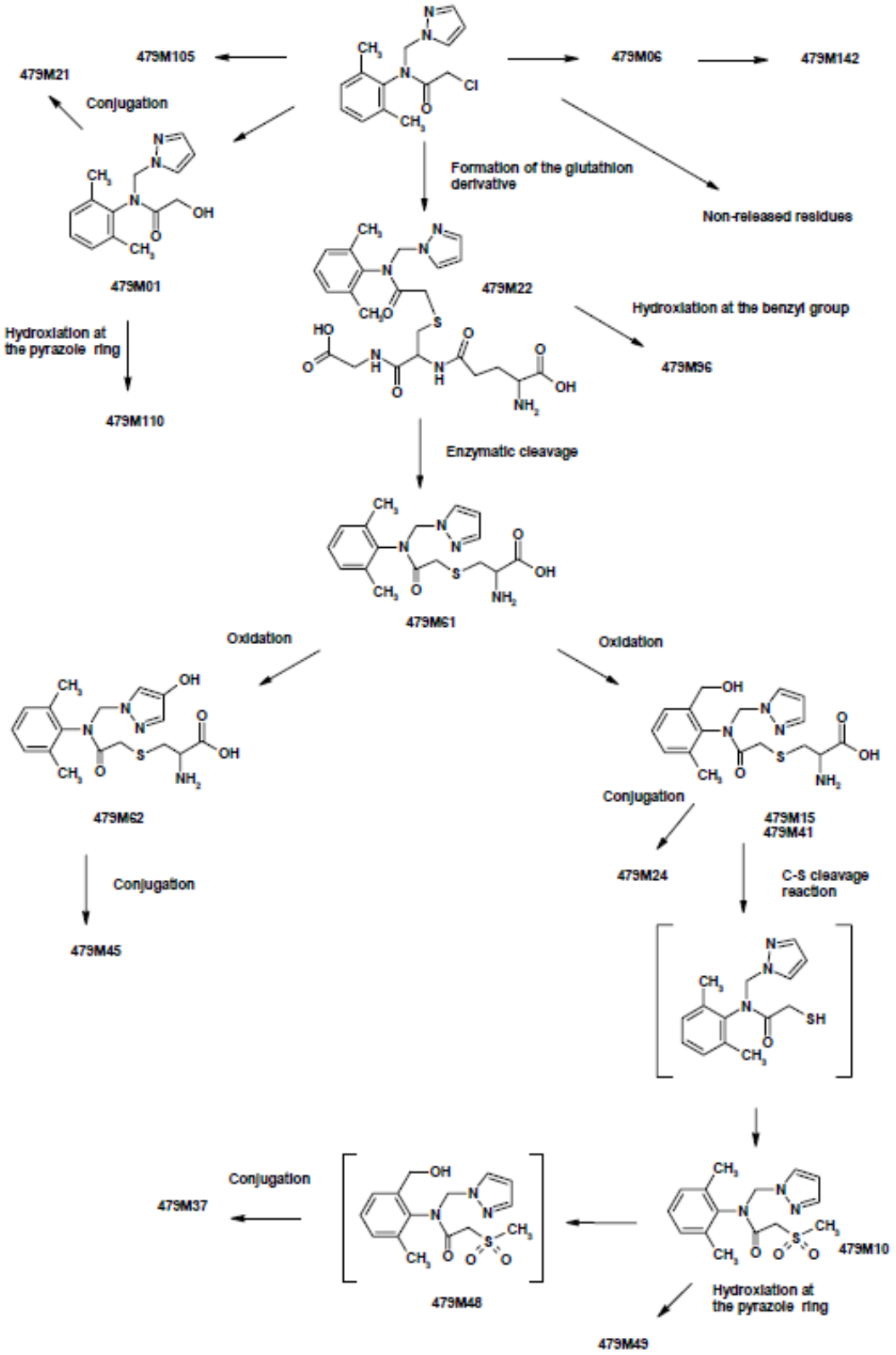
The fate of metabolite ^{14}C-479M16, a major metabolite in plants, was also investigated following oral treatment to a goat at 1.63 ppm for 9 days. Significant radioactive residues were not detected in fat, muscle, liver, kidney or milk and no further identification or characterisation was conducted on these matrices during the study. Residues in urine were characterised and included: 479M16, 479M17, 479M01, 479M49 and 479M48 (3% TRR, 0.01 mg/kg).

The majority of the animal metabolites contained either the 2,6-dimethylaniline or 2-hydroxy-6-methylaniline moieties.

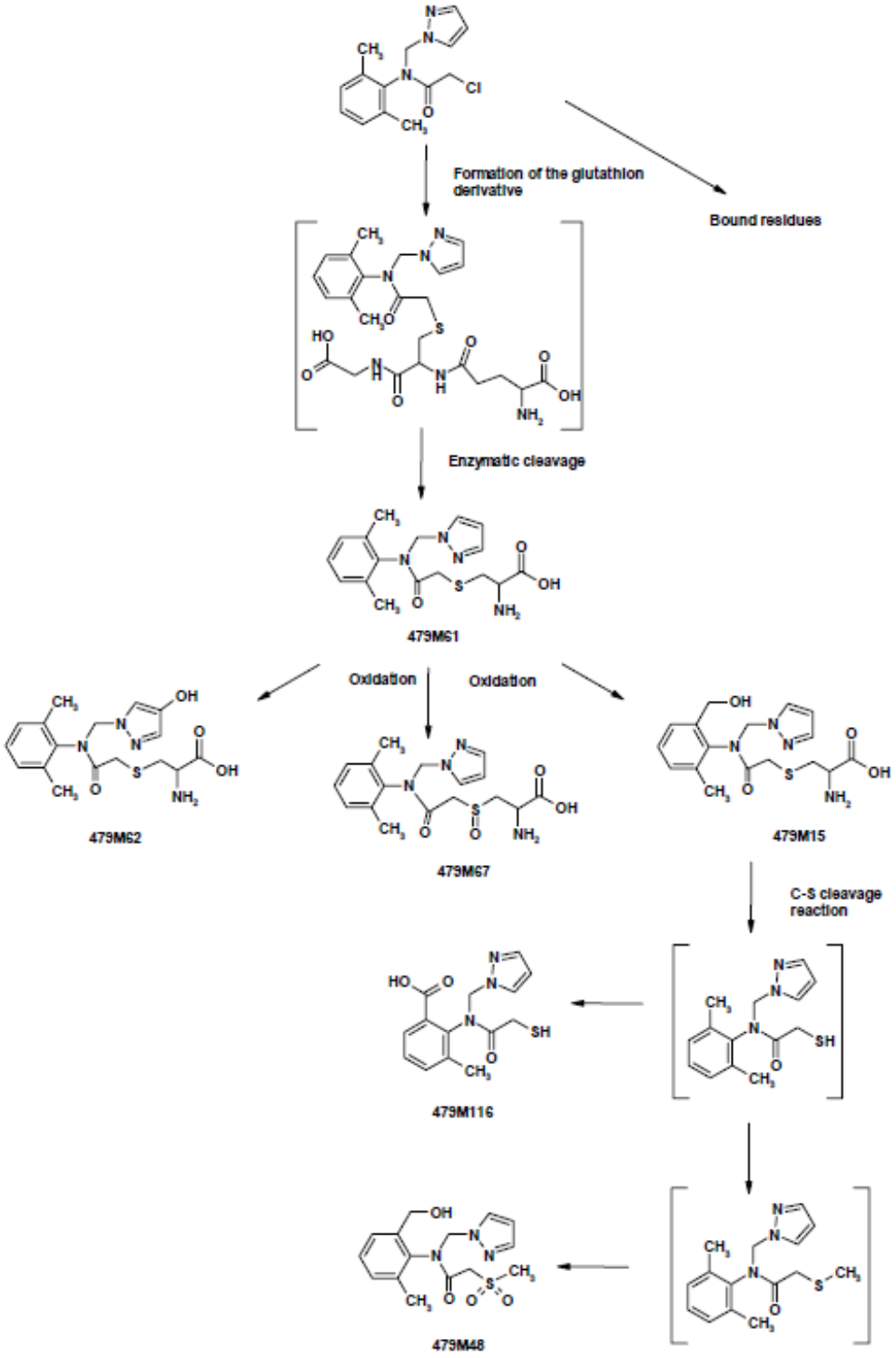
Metabolism varied depending on the animal species, but the formation of the glutathion conjugate (479M22) and its subsequent cleavage was common to goats and hens.

The proposed biotransformation pathways of metazachlor in goats and hens are shown below.

The proposed metabolic pathway for metazachlor in lactating goats:



The proposed metabolic pathway for metazachlor in laying hens:



4.3 Analytical methods

Two methods were available for the determination of metazachlor residues in canola. Residues were determined as the common moiety, 2,6-dimethylaniline using GC-MS (seed) or GC-N-FID (seed and plant) and expressed as metazachlor or residues were determined as a single metabolite (either 479M04, 479M08 or 479M16) using UPLC-MS/MS (seed, fodder and forage) and expressed as metazachlor. The limit of quantitation for metazachlor was 0.05 mg/kg when determined as the common moiety and was 0.01 mg/kg for each individual metabolite when determined as a single metabolite.

For animal commodities (muscle, liver, kidney, fat, milk, eggs), residues were determined as the common moiety, 2,6-dimethylaniline using LC-MS/MS and expressed as metazachlor. The limit of quantitation for metazachlor was 0.05 mg/kg for muscle, kidney, fat and eggs and 0.01 mg/kg for milk.

4.4 Stability of the pesticide in stored analytical samples

Stability studies were submitted which show that residues of metazachlor and metabolites 479M04, 479M08 and 479M16 in canola seed are stable for at least 2 years when stored at -20 °C. Residues of metazachlor in forage and fodder of maize are stable for at least 2 years when stored at -20 °C.

An animal transfer study was submitted which showed that residues of metazachlor were stable in milk, muscle, liver, kidney and fat for at least 170 days when stored at ≤ -18°C.

4.5 Residue definition

Parent metazachlor was not a component of radioactive residues observed in primary crops (canola, cabbage and maize) or in the confined rotational crop study.

Parent metazachlor was extensively metabolised by both primary and secondary crops to form a number of metabolites. Metabolite 479M16 was the major metabolite for both canola and cabbage and was also found in maize. The major metabolite for maize was 479M04 and was also found in cabbage. For confined rotational crops, the major metabolites were 479M04 and 479M08. The common moiety for these major metabolites is 2,6-dimethylaniline.

Analytical methods are available for plant commodities that determine residues of metazachlor as 2,6- dimethylaniline or as the single metabolites, 479M04, 479M08 and 479M16.

Given the available analytical methods and the extensive metabolism of metazachlor by plants, and considering that the 2,6-dimethylaniline moiety is found in other registered pesticides (i.e. benalaxyl and metalaxyl) the following residue definitions are recommended:

For enforcement—sum of metabolites 479M04, 479M08 and 479M16, expressed as metazachlor

For dietary exposure—sum of metazachlor and its metabolites containing the 2,6-dimethylaniline moiety, expressed as metazachlor.

In the animal metabolism studies, parent metazachlor was not a component of radioactive residues. Parent metazachlor was extensively metabolised by animals to form a number of metabolites. For goats, the major metabolite identified in liver was 479M61 and no metabolites exceeding 10% TRR were reported in kidneys. Multiple metabolites were qualitatively identified in poultry liver. Significant radioactive residues were not detected in goat fat, muscle, liver, kidney or milk when treated with metabolite 479M16.

The analytical method available for animal commodities determines residues of metazachlor as 2,6- dimethylaniline. It is noted that the 2,6-dimethylaniline moiety is common to the majority of metabolites reported for animal commodities and is not a moiety specific to metazachlor.

Benalaxyl and metalaxyl are registered in Australia and can also hydrolyse to 2,6-dimethylaniline. There are currently no animal feed or animal commodity MRLs established for benalaxyl. Animal commodity MRLs at the LOQ are established for metalaxyl. In the 2004 JMPR, feeding metalaxyl at 75 ppm gave a HR in liver of 0.12 mg/kg by the common moiety method. The highest animal feed commodity MRL for metalaxyl is 0.3 mg/kg for forage of cereal grains. It is therefore unlikely that the common moiety method will detect residues from other registered pesticides but this will be revisited if changes are made to the MRL standard, such as the establishment of animal commodity MRLs and animal feed commodity MRLs for actives that can be hydrolysed to 2,6-dimethylaniline.

The toxicology assessment of the active constituent metazachlor established an ADI at 0.2 mg/kg bw/day, with an ARfD not considered necessary. For acute oral studies, all metabolites were of low acute oral toxicity and no toxicologically significant findings were noted in oral subchronic or developmental studies in rats on the metabolites.

Based on the available animal metabolism data, the capability of the analytical method and toxicological advice, it is concluded that a suitable residue definition for commodities of animal origin, for both enforcement and dietary exposure is:

Sum of metazachlor and its metabolites containing the 2,6-dimethylaniline moiety, expressed as metazachlor.

4.6 Residue trials and rotational crops

One Australian study (4 trials) and 1 European study (3 trials) investigating residues of metazachlor in canola after one pre-emergent application were submitted. Both studies were conducted to GLP. In addition, 31 European studies that were not conducted to GLP were also submitted.

The combined dataset of Australian and European GLP canola trials for seed carried out at GAP and suitable for MRL estimation was in rank order (n = 7): <0.03 (4) and <0.05 (3) mg/kg.

For the supporting European trials, all residues of metazachlor in canola seed taken at harvest were <0.05 mg/kg (n = 25) following one application within 8 days of sowing at 1–2x the proposed rate.

For rotational crops, the applicant submitted the full details of three European rotational crop studies conducted to GLP on representative plant commodities (leafy vegetables, root vegetables and small grains) and summaries of 19 non-GLP supporting European trials.

Residues above the LOQ (0.05 mg/kg) were not observed in grains of rotational wheat (n = 10) and green beans (n = 2) treated at 1.1x or 1.4x the proposed rate (plant back intervals were 29–120 days). The highest residue observed in rotational crops was 0.85 mg/kg in lambs lettuce at a plant back interval of 94 days.

A minimum re-cropping interval of 12 months for all crops including wheat, durum, barley, oats, field peas, chickpeas and lupins was proposed.

Based on this information, MRLs of *0.03 mg/kg are recommended for metazachlor in oilseeds (which will cover the primary use on canola), cereal grains and pulses.

An all other foods MRL of 1 mg/kg is recommended based on the highest residue observed in rotational crops, to cover possible residues in follow crops other than cereals, oilseeds and pulses.

For canola fodder, the dataset on a dry weight basis from GLP Australian trials carried out at GAP and suitable for MRL estimation was in rank order (n = 4): <0.074, <0.087, <0.097 and <0.12 mg/kg.

For canola forage, the combined dataset on a dry weight basis from GLP Australian and European trials carried out at GAP and suitable for MRL estimation was in rank order (n = 7): <0.05 (3), <0.20, <0.29, <0.56 and <0.59 mg/kg.

Based on the available data, an MRL of 2 mg/kg is considered suitable for metazachlor on Canola forage and fodder (dry) (the OECD calculator estimated an MRL at 1.5 mg/kg).

For forage and fodder of rotational crops, the highest residue reported for rotational wheat forage and straw was 0.60 mg/kg (scaled to 1x the proposed rate). An MRL for Primary feed commodities of 2 mg/kg is recommended, which will cover residues in canola forage and fodder (dry).

Consideration was given to the potential peak concentration of rotational crop metabolites 479M04 and 479M08 in animal feeds over time. For the rotational crop study, the highest residues in animal feeds were reported at 0.4 and 0.093 mg/kg for metabolites 479M04 and 479M08 respectively in wheat forage, planted nominally 120 days after the application of metazachlor to soil at 1.1x the proposed rate.

The confined rotational study indicated that residues of 479M04/479M08 (determined together) were seen to decline between plant back intervals of 120 to 366 days for samples of wheat forage, straw and chaff.

A simple compartment model for the estimation of soil metabolite peak concentrations, indicated that residues of metabolite 479M04 and 479M08 are likely to peak in soil at about 70 days after application.

The proposed 12 month plant back interval for rotational crops and the 12 week grazing WHP for canola are therefore considered to be acceptable, as it is unlikely that metabolite residues will increase above the primary feed MRL of 2 mg/kg.

4.7 Animal commodity MRLs

Canola forage can be fed at up to 100% in the diet of beef cattle or 40% for dairy cows. Finite residues of metazachlor are expected to be found in treated, dry canola forage, fodder and rotational animal feed crops (dry wheat forage and fodder) therefore an MRL of 2 mg/kg is recommended for metazachlor on Primary feed commodities. The APVMA and OECD guidelines indicate that forage and fodder can be fed at up to 100% in the diet of cattle.

An animal transfer study for metazachlor in dairy cows was submitted, in which cows were dosed with metazachlor twice a day for 28 days, at either 0.8, 2.4 or 8.0 ppm, total dietary dry matter.

Residues of metazachlor found in milk (whole and skim), cream, muscle, fat, kidney and liver after dosing at 0.8 ppm in the diet are tabulated below:

COMPOUND	WHOLE MILK (mg/kg)	SKIM MILK (mg/kg)	CREAM (mg/kg)	MUSCLE (mg/kg)	FAT (mg/kg)	KIDNEY (mg/kg)	LIVER (mg/kg)
Metazachlor	<0.01 (day 28)	<0.01 (day 21)	<0.01 (day 21)	<0.05	<0.05	<0.05	0.06

Given that parent metazachlor is extensively metabolised by plants, the feeding of the major plant metabolites (479M04, 479M08 and 479M16) to livestock was considered.

A metabolism study for the administration of metabolite 479M16 to lactating goats indicated that finite residues are not expected in animal tissues after feeding at 1.63 mg/kg in the feed. Given the highest residue reported for metabolite 479M16 is 0.32 mg/kg in canola forage, finite residues of metabolite 479M16 are not expected in animal commodities as a result of the proposed use of metazachlor on canola.

Animal feeding and animal metabolism studies were not available for metabolites 479M04 and 479M08. It is noted the metabolites are more polar than parent such that metabolite bioavailability is likely to be lower than metazachlor (log Pow = 2.49 for parent, 0.62 for 479M004 and 0.80 for 479M008). For animal metabolism studies involving feeding with parent, metabolite 479M04 was detected at trace amounts in goat and rat urine. Metabolite 479M08 was detected at trace amounts in rat urine. It is likely that metabolites 479M04 and 479M08 follow a similar metabolic pathway to the parent and are intermediates in the metabolic pathway.

The transfer study involving the feeding of parent is therefore considered to be a worst case scenario and can be used to estimate the likely residues of metabolites 479M04 and 479M08 in animal commodities.

The predicted maximum livestock burden is as follows:

Beef and Dairy Cattle 500 kg bw, 20 kg DM/day

COMMODITY	RESIDUE (mg/kg)	BASIS	DM (%)	RESIDUE DW (mg/kg)	MAXIMUM DIET CONTENT (%)	MG/ANIMAL	RESIDUE CONTRIBUTION (ppm)
Primary feed commodities	0.60	HR	100	0.60	100	0.024	0.60
TOTAL					**100**		**0.60**

Primary feed commodities residue for metazachlor = HR of 0.60 mg/kg from rotational study wheat forage and HR of 0.59 mg/kg from primary canola forage.

Predicted residues of metazachlor in tissues and milk as a result of feeding at 0.60 ppm are calculated below:

Beef and dairy cattle

FEEDING LEVEL (PPM)	MILK	MUSCLE	LIVER	KIDNEY	FAT
	METAZACHLOR RESIDUE (mg/kg)				
0.8	<0.01	<0.05	0.06	<0.05	<0.05
0.60–beef and dairy cattle, estimated burden	<0.01	<0.05	<0.05 (0.045)	<0.05	<0.05
Recommended MRLs	*0.01	*0.05	*0.05		*0.01

The likelihood of detectable residues occurring in livestock commodities as a result of the proposed use is very low. It is appropriate to establish animal commodity MRLs at the respective LOQs for metazachlor in the analytical methods. The following MRLs are recommended:

MO 0105 Edible offal (mammalian) *0.05 mg/kg

MM 0095 Meat [mammalian] *0.05 mg/kg

ML 0106 Milks *0.01 mg/kg.

Canola seed can be fed at up to 30% in the diet of poultry. Wheat grain and pulses (i.e. from rotational crops) can each be fed at up to 100% in the diet. Plant protein meal (including those from oilseeds and soya bean) and processed grain fractions (excluding grain dust) can each be fed at up to 20% in the diet of poultry.

Finite residues of metazachlor are not expected in treated canola seed from primary crops or wheat grain and pulses from rotational crops. MRLs at *0.03 mg/kg have been recommended for metazachlor in oilseeds, cereal grains and pulses. Residues of metazachlor above the LOQ are unlikely to be found in poultry commodities as a result of the proposed use on primary crops (canola seed) and resulting rotational crops (cereals, other oilseeds and pulses).

It is appropriate to establish poultry commodity MRLs at the respective LOQs for metazachlor in the analytical methods. The following MRLs are recommended:

PE 0112 Eggs	*0.05 mg/kg
PO 0111 Poultry, Edible offal of	*0.05 mg/kg
PM 0110 Poultry meat	*0.05 mg/kg.

4.8 Estimated dietary intake

The chronic dietary exposure 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 1995 National Nutrition Survey of Australia. 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 metazachlor is equivalent to <5 % of the ADI.

There is no ARfD established for metazachlor by the OCS.

4.9 Bioaccumulation potential

The log Pow value is 2.5 for metazachlor, 0.80 for metabolite 479M08 and 0.62 for metabolite 479M04, indicating that there is a low potential for bioaccumulation of metazachlor and metabolites 479M08 and 479M04 in fat.

MRLs for meat ‘in the fat’ are not recommended at this time.

4.10 Spray drift

The draft label includes a restraint that the product should not be applied by air. The product should also not be applied with smaller than MEDIUM spray droplets according to ASAE S572 definition for standard nozzles.

In the dairy cow transfer study provided with the application, dosing with metazachlor at 0.8 ppm gave highest residues of metazachlor of 0.06 mg/kg in liver. For residues of parent to be at the LOQ (0.05 mg/kg), the maximum feeding level is 0.67 ppm. Assuming pasture consists of 1500 kg DM/ ha this corresponds to a maximum permitted drift of 1.0 g a.i./ha.

For ground application to pre-emergent canola at a maximum rate of 900 g a.i./ha, the standard scenario (low ground boom, medium droplet) indicates that a no-spray zone is not required for protection of international trade.

4.11 Recommendations

The following amendments to the APVMA MRL Standard are required for the current application:

TABLE 5: PROPOSED AMENDMENTS TO MRL STANDARD FOR METAZACHLOR—TABLE 1

COMPOUND	FOOD	MRL (mg/kg)
ADD:		
Metazachlor		
	All other foods	1
GC 0080	Cereal grains	*0.03
PE 0112	Eggs	*0.05
MO 0105	Edible offal (mammalian)	*0.05
MM 0095	Meat (mammalian)	*0.05
ML 0106	Milks	*0.01
SO 0088	Oilseeds	*0.03
PO 0111	Poultry, edible offal	*0.05
PM 0110	Poultry meat	*0.05
VP 0070	Pulses	*0.03

TABLE 6: PROPOSED AMENDMENTS TO MRL STANDARD FOR METAZACHLOR—TABLE 3

COMPOUND	RESIDUE
ADD:	
Metazachlor	Commodities of plant origin for enforcement: Sum of metabolites 479M04 (N-(2,6-dimethylphenyl)-N-(1H-pyrazol-1-ylmethyl)oxalamide), 479M08 (N-(2,6-dimethylphenyl)-N-(1H-pyrazol-1-ylmethyl)aminocarbonylmethylsulfonic acid) and 479M16 (3-[N-(2,6-dimethylphenyl)-N-(1H-pyrazol-1-ylmethyl)aminocarbonylmethylsulfinyl]-2-hydroxypropanoic acid), expressed as metazachlor Commodities of plant origin for dietary exposure assessment: Sum of metazachlor and its metabolites containing the 2,6-dimethylaniline moiety, expressed as metazachlor Commodities of animal origin: Sum of metazachlor and its metabolites containing the 2,6-dimethylaniline moiety, expressed as metazachlor

TABLE 7: PROPOSED AMENDMENTS TO MRL STANDARD FOR METAZACHLOR—TABLE 4

COMPOUND	ANIMAL FEED COMMODITY	MRL (mg/kg)
ADD:		
Metazachlor		
	Primary feed commodities	2

5 ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

5.1 Commodities exported

Canola seed, including derived oils and meals are considered to be major export commodities[2], as are commodities of animal origin, such as meat, offal and dairy products, which may be derived from livestock given feeds produced from treated canola. The risk to trade from rotational crops must also be considered. Residues in these commodities resulting from the use of Butisan Herbicide may have the potential to unduly prejudice trade.

5.2 Destination of exports

Australian exports of canola grain, oil and meal totalled 2445 kt (value $1349 million), 159 kt and 37 kt respectively in 2014–15[3]. The major export markets for canola seed in 2014–15 included China, Belgium, Japan, the Netherlands and France. Destinations for canola oil included China, New Zealand, Malaysia and the Republic of Korea. The major market for Canola meal was New Zealand.

Major export markets for Australian canola grain, oil and seed are presented below.

Table 8: Major destinations for Australian canola grain, oil and seed

COMMODITY	MAJOR DESTINATIONS
Canola seed	China, Belgium, Japan, the Netherlands, France
Canola oil	China, NewZealand, Malaysia, the Republic of Korea
Canola meal	New Zealand

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).

5.3 Overseas registration and approved label instructions

The applicant indicated that Butisan Herbicide is registered in the UK and other European countries.

[2] APVMA regulatory guidelines—data guidelines: agricultural—overseas trade (Part 5B)

[3] Australian Commodity Statistics 2015
data.daff.gov.au/data/warehouse/agcstd9abcc002/agcstd9abcc0022015/ACS_2015_1.0.0.pdf

5.4 Comparison of Australian MRLs with Codex and International MRLs

The following relevant international MRLs have been established for metazachlor:

TABLE 9: CURRENT AND PROPOSED AUSTRALIAN AND OVERSEAS MRLS/TOLERANCES FOR METAZACHLOR

COUNTRY (STATUS)	RESIDUE DEFINITION	COMMODITY	TOLERANCE FOR RESIDUES ARISING FROM THE USE OF METAZACHLOR (mg/kg)
Australia (recommended)	Commodities of plant origin: Sum of metabolites 479M04 (N-(2,6-dimethylphenyl)-N-(1H-pyrazol-1-ylmethyl)oxalamide), 479M08 (N-(2,6-dimethylphenyl)-N-(1H-pyrazol-1-ylmethyl)aminocarbonylmethylsulfonic acid) and 479M16 (3-[N-(2,6-dimethylphenyl)-N-(1H-pyrazol-1-ylmethyl)aminocarbonylmethylsulfinyl]-2-hydroxypropanoic acid), expressed as metazachlor	Cereal grains	*0.03
		Oilseeds	*0.03
		Pulses	*0.03
	Commodities of animal origin: Sum of metazachlor and its metabolites containing the 2,6-dimethylaniline moiety, expressed as metazachlor	Eggs	*0.05
		Edible offal (mammalian)	*0.05
		Meat (mammalian)	*0.05
		Milks	*0.01
		Poultry, edible offal	*0.05
		Poultry meat	*0.05
EU	Commodities of plant origin: Sum of metabolites 479M04, 479M08 and 479M16 expressed as metazachlor	Cereals	*0.02
		Pulses	*0.02
		Rapeseeds/canola seeds	*0.06
	Commodities of animal origin: Sum of metazachlor and its metabolite containing the 2,6-dimethylaniline moiety, expressed as metazachlor	Birds eggs	*0.05
		Poultry (muscle, fat, liver, kidney, other offal)	*0.05
		Mammalian muscle, fat, kidney, edible offal (other than kidney and liver)	*0.05
		Swine liver	0.2
		Bovine liver, sheep liver	0.3
		Milk	*0.01

There are no MRLs established by CODEX, China, Japan or New Zealand.

5.5 Potential risk to trade

Export of treated produce containing finite (measurable) residues of metazachlor 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.

Of the possible major export markets for canola seed, oil and meal, MRLs have not been established by CODEX, China, Japan or New Zealand. The EU has established a relevant MRL at *0.06 mg/kg for canola seed. The proposed residue definition for metazachlor in plant commodities is the same as that established by the EU. An MRL for oilseeds is proposed at the LOQ (*0.03 mg/kg) and finite residues in canola oil and meal are unlikely. The export of treated canola seed, oil and meal is unlikely to result in an undue risk to international trade.

Finite residues are not expected in grains of rotational cereals and pulses therefore the risk to trade of these commodities is not considered undue.

Of the possible major export destinations for livestock, only the EU has established mammalian commodity MRLs including *0.05 mg/kg for muscle, fat and offal except liver. An MRL of 0.2 mg/kg is established for swine liver, 0.3 mg/kg for bovine and sheep liver and *0.01 mg/kg for milks. The proposed residue definition for metazachlor in animal commodities is the same as that established by the EU.

Finite residues in animal commodities are not expected from the proposed use and it is considered that the export of commodities derived from livestock will not pose an undue risk to trade.

Oaten hay is considered to be a major export commodity and an MRL of 2 mg/kg has been recommended for primary feed commodities. The major export destination for hay in 2014 was Japan (160,134 tonnes to the end of November)[4]. For oaten hay, standards for metazachlor are not established in The Ordinance of the Standards of Feed Additives (to March 2015[5]). As such, the risk to trade in oaten hay is not considered undue.

[4] grdc.com.au/Research-and-Development/GRDC-Update-Papers/2015/02/Export-oaten-hay-opportunity-for-grain-growers

[5] www.famic.go.jp/ffis/feed/obj/shore_eng.pdf

6 OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

6.1 Health hazards

The active constituent metazachlor (CAS: 67129-08-2) is currently listed in Safe Work Australia's (SWA) Hazardous Substances Information System (HSIS) Database (SWA, 2016).

Butisan Herbicide is classified as a hazardous substance in accordance with NOHSC Approved Criteria for Classifying Hazardous Substances (NOHSC, 2004).

6.2 Formulation, packaging, transport, storage and retailing

The active constituent metazachlor and the formulated product Butisan Herbicide will be manufactured overseas. Butisan Herbicide will be available in 1 L – 110 L pack sizes in HDPE containers.

6.3 Use pattern

The draft label indicates the product is intended to be diluted in water and applied using conventional boom sprayer with either mechanical or by-pass agitation, at a maximum use rate of 1.8 L product per ha for pre-emergent incorporation by sowing.

6.4 Exposure during use

The product Butisan Herbicide will be professionally used in commercial situations, and farmers and their employees, as well as contract sprayers will be the main users of the product. Workers may be exposed to the product when opening containers, using the product, cleaning up spills, maintaining equipment and entering treated areas. The main routes of exposure to the product/spray will be dermal and inhalation, although ocular exposure is also possible.

An exposure assessment was conducted, and in conjunction with the hazard profile, used to determine whether the proposed use of the product would be an undue health hazard to humans. In the absence of exposure data for the proposed mode of application, the Pesticide Handler Exposure Database (PHED) Surrogate Exposure Guide (1998) was used to estimate exposure.

The toxic endpoint of concern and identified NOEL for risk assessment is derived from a repeat dose study in animals, and in this instance a margin of exposure (MOE) of 100 or above is considered acceptable. The MOE takes into account both potential inter-species extrapolation and intra-species variability. Based on the risk assessment, the proposed use of the product for apples is acceptable without the need for PPE (*i.e.* no clothing), though a precautionary hazard statement notifying users of the acute oral toxicity and slight eye irritation potential of the product is recommended.

Application of Butisan Herbicide by groundboom may lead to unintended bystander exposure *via* chemical spray drift. This may be in the form of a single random exposure or repeat exposures of residents who reside adjacent to areas being treated with the product. Adherence of good agricultural practices will minimise potential risks.

6.5 Exposure during re-entry

The OCS notes that the re-entry risks associated with conducting activities where the product has been applied are expected to be by the dermal route, but the MOEs determined for re-entry activities associated with use of Butisan Herbicide are acceptable on day zero after application. Therefore, a *NIL* re-entry statement is appropriate for this product.

6.6 Recommendations for safe use

Based on the risk assessment, Butisan Herbicide is supported for professional use; users should follow the First Aid Instructions and Safety Directions on the product label.

First aid instructions

If poisoning occurs contact a doctor or Poisons Information Centre. Phone Australia 131126.

Safety directions

Harmful if swallowed. May irritate the eyes. Avoid contact with eyes. Wash hands after use.

6.7 Conclusion

The approval of the active constituent metazachlor and registration of Butisan Herbicide, containing 500 g/L metazachlor, for the control of weeds in canola crops is supported.

Butisan Herbicide can be used safely if handled in accordance with the instructions on the product label and any other control measures described above. Additional information is available on the product Material Safety Data Sheet to be available from the supplier.

7 ENVIRONMENTAL ASSESSMENT

The applicant is seeking the registration of Butisan Herbicide containing a new active constituent metazachlor at 500 g/L. The proposed product is a suspension concentrate (SC) formulation for the control of annual ryegrass, wild oats and wireweed in canola. The maximum rate of application rate is 1.8 L product/ha (= 900 g ac/ha) either for post emergent weeds or for pre-emergent weeds by incorporation by sowing.

In support the applicant has provided environmental fate and effects studies. In addition the APVMA considered results for metazachlor from the European Union Draft Risk Assessment and the European Food Safety Authority to supplement the applicant's supplied data.

7.1 Environmental fate and behaviour

Hydrolysis

Metazachlor is hydrolytically stable.

Photolysis/photodegradation

Photolysis on soils is unlikely to be a major degradation route and metazachlor is not expected to rapidly photodegrade in water.

Fate and behaviour in soil

Metazachlor is readily degradable in soil under both laboratory and field conditions, with DT50 values ranging from 6 to 22.4 days (at 20°C), and 2.53 to 17.0 days, respectively. The mean half-lives from the laboratory and field trials were not statistically significantly different and therefore, the 90th percentile DT50 for the total data set of 17.1 days, was for the risk assessment.

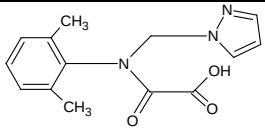
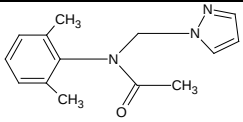
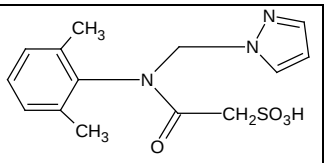
In aerobic soils, the two major metabolites (>10% of parent applied) were BH 479–04 (maximum 16.8% formed) and BH 479-08 (maximum 21.6% formed). Under anaerobic metabolism conditions, BH 479–06 was a major soil metabolite (maximum 18.5% formed). These metabolites are considered very slightly degradable with laboratory DT50 values of 396 days, 249 days and 331 days for BH 479–04, BH 479–06 and BH 479–09 respectively.

Fate and behaviour in water

In two aerobic water/sediment systems, with application to the water column, metazachlor dissipated from the water column with water half-lives of 5.1–12.1 days. Whole system half-lives ranged from 13.4 to 23.0 days. While no metabolite exceeded 10% applied, BH 479–06 was found at a maximum of 8.1%

applied in water at the end of the study in one system without reaching a plateau. This metabolite was present at a maximum of 8.9% applied in sediment. BH 479–04 was found up to 8.4% applied in water without a plateau being reached. Sediment levels of the metabolite were lower with a peak level of 2.8% applied.

Table 10: Major soil and aquatic system metabolites of metazachlor

BH 479-04		BH 479-06		BH 479-08	

Mobility

Metazachlor and its major soil metabolites are mobile in the soil compartment. The study provided was not conducted to contemporary standards, but was still reliable for regulatory prurposes, the data was further supplemented literature report on 18 soils. The Freundlich sorption coefficients (Kf) for metazachlor, has an average 1/n value from all 21 soils of 0.85, as this is close to linearity it is considered a suitable surrogate for a Kd value. Based on regression analysis, a Kd of 1.4 L/kg was predicted for a soil with 1% soil organic carbon. Geometric mean Kd values of 0.10 L/kg, 0.68 L/kg and 0.15 L/kg were calculated for BH 479–04, BH 479–06 and BH 479–09 respectively, with all these metabolites being considerably more mobile than the parent compound. Mobility, particularly for the metabolites, was demonstrated in column leaching studies and lysimeter studies. Additionally, extensive monitoring of wells in Germany and France in metazachlor use areas on oilseed rape consistently show detections of BH 479–4 and BH 479–8. The results across years and between countries show a consistent pattern. The highest number of wells are contaminated with BH 479–08 (up to 50% positive detections) and BH 479–04 (up to ~40% positive detections). The highest detected levels were 16.98 µg/L and 15.7 µg/L respectively, although for BH 479–04, this was considered an anomaly and all other detected levels were <2 µg/L. Modelled values using a USEPA model, were reasonably consistent with the measured values and the predicted groundwater concentration of metazachlor is 0.09 µg ac/L.

Bioaccumulation

Metazachlor is not expected to bioaccumulate due to its moderate water solubility and relatively low octanol/water partition coefficient.

7.2 Environmental effects

Terrestrial organisms

Metazachlor is practically non-toxic to birds on an acute basis and the long term NOEC was determined to be 76.5 mg/kg bw/d. Similarly it is practically non-toxic to mammals and the long term NOEC was determined to be 79 mg/kg bw/d. Bees, non-target arthropods, soil macro-invertebrates and soil micro-invertebrates, were not sensitive to metazachlor; with no demonstrated effects at the highest rates tested.

Terrestrial plants

Greenhouse and subsequent field testing was undertaken on a range of standard terrestrial plants. The most sensitive species were lettuce and ryegrass. Under field conditions the sensitivity of non-target plants was lessened in comparison to that under greenhouse conditions. There was a reduction in plant weight, with the lowest ER50 of 259 g/ha for lettuce. However, there was significant visual injury observed in many plant species in the field that persisted through the study. Lettuce was the most sensitive to visual injury with an ER50 of 56.9 g ac/ha. By applying a standard safety factor of 10, a terrestrial plant regulatory acceptable level (RAL) of 5.69 g ac/ha was determined.

Aquatic organisms

Metazachlor is moderately toxic to fish and slightly toxic to aquatic invertebrates. However as expected for a herbicide, it is highly toxic to algae and aquatic plants. Metazachlor as the active constituent and in formulations was tested, but the toxicity could be attributed to metazachlor alone. As there were numerous studies the APVMA determined a regulatory acceptable concentration for metazachlor based on a species sensitivity distribution which was derived from toxicity data of 14 aquatic plants (monocotyledons and dicotyledons; submersed, emergent and floating) and 9 different algal species. Reliable ER50 or NOER values could not be established for all of these studies and accordingly ER10 values were calculated through non-linear regression analysis of the dose/response data. These ranged from 1.55 µg/L (floating aquatic macrophyte, *Lemna gibba*) to 122 µg/L (aquatic macrophyte; emergent monocotyledon *Sparganium erectum*). Based on these toxicity values the HC5 (95th percentile protection level) was determined to be 2.0 µg/L. This was adopted as the regulatory acceptable concentration (RAC) without any further safety factor. The metabolites were shown to be much less toxic than the parent compound.

The toxicity of metazachlor can be summarised as follows

Table 11: Toxicity of active constituent metazachlor and the product Butisan Herbicide for various organisms

ORGANISM		MEASURE OF TOXICITY OR EFFECT	PARAMETER (TEST PERIOD)	TOXICITY (UNIT)
Terrestrial species				
Mammals	Unspecified	Acute toxicity (oral)	LD50 >2000	mg/kg bw
		Chronic	LC > 79	mg/kg bw/d
Bird	Bobwhite quail	Acute toxicity (oral)	LD50 >2000	mg ac/kg bw
	Bobwhite quail, mallard duck	Short term dietary exposure	LC50 (5 d) >5000	mg/kg diet.
	Bobwhite quail	Reproduction	NOEC	mg ac/kg bw/d
	Honeybee (Apis mellifera)	Oral and contact toxicity	LD50 >72.19	µg/bee
Non-target arthropods	parasitoid (Aphidius rhopalosiphi)	Tier 1 dose/response	LR50 >3750	g ac/ha
	predatory mite (Typhlodromus pyri)			
	Earthworm	Acute toxicity	LC50 >500	mg/kg
Plants*	Lettuce	Seedling emergence test	ER50 56.9	g ac/ha
Aquatic species				
Fish	Rainbow trout	Acute toxicity	LC50 8.5 (96 h)	mg ac/L
	Fathead minnow	Early life stage toxicity	NOEC 1.25	mg ac/L
Aquatic invertebrate	Daphnia magna	Acute toxicity	EC50 33.7	mg ac/L
	Daphnia magna	Reproduction	NOEC 6.25 (21 d)	mg ac/L
	Chironomus riparius	Chronic exposure	7.93 NOEC (28 d)	mg ac/kg dw
Aquatic plants	Lemna gibba	Growth inhibition	EC50 25.6; ErC10 = 1.55	µg ac/L
Algae*	Ankistrodesmus bibraianus	Growth inhibition	ErC50 9.74; ErC10 = 2.18	µg/L

***Most sensitive**

7.3 Risk assessment

The risk to mammals and birds was determined by considering relevant Australian species. This was done on a dose basis by taking into account the species' energy requirements and hence food intake, and the amount of metazachlor predicted to be present on that food. This dose was then compared with the studied acute and chronic effects of metazachlor on birds and mammals. In all cases the risk was found to be acceptable.

The risk to bees, non-target arthropods, soil macro-invertebrates and soil micro-invertebrates, to metazachlor and where relevant its metabolites was found to be acceptable, which is unsurprising given their lack of sensitivity.

The risk to aquatic species from spray drift was determined using the standard APVMA scenario for low boom and MEDIUM spray quality. The downwind no spray zone was determined by calculating the fraction of the proposed spray rate required to achieve a concentration in a 3 m wide 15 cm deep water body, below the RAC.

The risk to aquatic species from run-off water containing metazachlor from treated fields entering the aquatic environment was also considered. The predicted concentration was calculated using an OECD proposed model, which takes into account metazachlor's degradation and mobility from soil characteristics. A refined model prediction was used for the risk assessment, based on real world data for topography, soil type and river flows for the regions in which canola is grown.

Aquatic species are also at risk from resurfacing groundwater containing metazachlor and its metabolites leached from treated fields. Based on screening model predictions and field measurements, the concentrations of metazachlor and its metabolites would be well below the RAC.

The risk to non-target plants from spray-drift was determined in a similar manner to the aquatic risk, excepting that fraction of the spray rate required was based on the regulatory acceptable level (RAL) for plants.

7.4 Conclusions

The risk of Butisan Herbicide, containing 500 g/L metazachlor was found to be acceptable provided label restraints for spray-drift for the protection of the aquatic environment and non-target plants were mandated. Downwind no-spray zones of 50 m and 20 m, are required, respectively.

The use of Butisan Herbicide meets the environmental safety criteria when used in accordance with the instructions on the product label.

8 EFFICACY AND SAFETY ASSESSMENT

The applicant seeks registration of the proposed new pesticide product Butisan Herbicide, a suspension concentrate formulation containing 500 g/L metazachlor, a new active constituent for use to provide pre-emergent control of various weeds in canola.

Metazachlor belongs to the chemical class of chloroacetamides and acts by a complex mode of action involving disruption of fatty acid syntheses. Butisan Herbicide containing metazachlor acts as a pre- and post-emergence herbicide. Butisan Herbicide enters target plants primarily through the roots, the hypocotyl, and the cotyledons of the germinating and emerging weeds.

Butisan Herbicide is active against a broad range of mono- and dicotyledonous weeds. Since it acts via both the roots and the developing shoot, it can be used pre-emergence as well as (early) post emergence. In tolerant crops, metazachlor is rapidly metabolized.

As a Group K herbicide, Butisan Herbicide represents a new mode of action in the canola phase of cropping and as such presents an important residual option for control of a range of weeds and in particular for control of annual ryegrass. Currently, there are only two other modes of action which will provide residual control in this crop phase, being The Group D herbicides trifluralin, pendimethalin and propyzamide and the Group C herbicides in triazine tolerant canola. Resistance to both of these existing modes of action in canola has been widely recorded.

Trial data from 35 replicated field studies conducted in canola crops in NSW, Victoria, South Australia and Western Australia were provided in support of the application. The studies were well designed and appropriately conducted to determine efficacy against weeds present at the trial sites and safety to canola.

The trials were conducted across Australia and in all cases, standard industry herbicide treatments were included, with trifluralin treatments common to all the 2014 and 2015 trials and other alternative herbicides also included. Various potential field rates and application timings were evaluated in 2014, and in 2015 various programs using pesticide combinations via tank mixing or sequential application were also evaluated.

The results indicate that Butisan Herbicide applied as proposed on the label [application immediately before sowing as IBS (incorporation by sowing) at 1.5–1.8 L/ha] is effective against annual ryegrass (*Lolium rigidum*), wild oats (*Avena fatua*) and wireweed (*Polygonum aviculare*). Data was most comprehensive for annual ryegrass, which was evaluated at all 13 sites in 2014 and 11 sites in 2015. For wild oats, data are available from two sites in 2014 and two showing very good efficacy in 2015. While there are only two trials conducted in 2015 for wireweed, the results were very good. Efficacy was similar or better than standard herbicide treatments. Neither existing treatments nor treatment with Butisan alone consistently reached a commercially acceptable level of control (85%) with a single application, thus other measures may be necessary to reach that level of weed control. The trials indicated that IBS was the safest application time, with initial damage occurring to the crop in some cases only being short term. Appropriate instructions have been provided on the draft label to optimise efficacy and minimise the risk of harmful effects to the crop. Based on plant back studies with a range of crops, a re-cropping interval of 12 months was determined.

Based on assessment of the data provided with the application, the APVMA is satisfied that the proposed use of the new product Butisan Herbicide containing the new active constituent metazachlor would be effective and safe when used in accordance with the proposed label instructions.

9 LABELLING REQUIREMENTS

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

BUTISAN HERBICIDE

ACTIVE CONSTITUENT: 500 g/L METAZACHLOR

GROUP	K	HERBICIDE

For the pre-emergent control of annual ryegrass, wild oats, and wireweed in canola as per the Directions for Use Table.

IMPORTANT: READ THE ATTACHED LEAFLET BEFORE USING THIS PRODUCT

CONTENTS: 1 L, 3 L, 5 L, 10 L, 110 L

BASF Australia Ltd ABN 62 008 437 867
Level 12, 28 Freshwater Place Southbank VICTORIA 3006
Website: www.agro.basf.com.au

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APVMA Approval No.: 80664/101359

DIRECTIONS FOR USE

RESTRAINTS

SPRAY DRIFT RESTRAINTS
DO NOT apply with spray droplets smaller than a MEDIUM spray droplet size category according to nozzle manufacturer specifications that refer to the ASAE S572 Standard or the BCPC Guideline.
DO NOT apply when wind speed is less than 3 or more than 20 kilometres per hour as measured at the application site.
DO NOT apply during surface temperature inversion conditions at the application site

Users of this product MUST make an accurate written record of the details of each spray application within 24 hours following application and KEEP this record for a minimum of 2 years. The spray application details that must be recorded are: 1) date with start and finish times of application; 2) location address and paddock/s sprayed; 3) full name of this product; 4) amount of product used per hectare and number of hectares applied to; 5) crop/situation and weed/pest; 6) wind speed and direction during application; 7) air temperature and relative humidity during application; 8) nozzle brand, type, spray angle nozzle capacity and spray system pressure measured during application; 9) name and address of person applying this product. (Additional record details may be required by the state or territory by the state or territory where this product is used.)

MANDATORY NO-SPRAY ZONES
DO NOT apply if there are aquatic or wetland areas including aquacultural ponds, surface streams and rivers downwind from the application area and within the mandatory no-spray zones shown in the table below:

Table 1—No-spray zones for protection of the aquatic environment	
	Downwind Mandatory No-Spray Zone
For ground application	
From 3 to 20 kilometres per hour	50 metres

DO NOT apply if there are sensitive crops, gardens, landscaping vegetation, protected native vegetation or protected animal habitat downwind from the application area and within the mandatory no-spray zones shown in the table below:

Table 2—No-spray zones for protection of the terrestrial environment	
	Downwind Mandatory No-Spray Zone
For ground application	
From 3 to 20 kilometres per hour	20 metres

CROP	WEEDS	RATE L/ha	CRITICAL COMMENTS
Canola	Annual ryegrass	1.5–1.8	Use higher rate when conditions are not optimal or where a heavy grass population is expected. Apply pre-sowing and incorporate by sowing (IBS) using knife points and press wheels. For best results apply just before sowing (refer to Interval between Application and Sowing in GENERAL INSTRUCTIONS). Avoid throwing treated soil into adjacent crop rows when sowing with knife points and press wheels. To reduce the risk of crop effects refer to Crop Safety in GENERAL INSTRUCTIONS. To optimise weed control apply directly to uncultivated soil. Weed control may be greatly reduced where weed seeds have been buried by cultivation prior to sowing. Weed control may be adversely affected by; • uneven application, • application to ridged or cloddy soil, • stubble, plant residue or other ground cover particularly where this exceeds 50%, • germinated and emerged weeds that are not controlled by a knockdown herbicide, • insufficient rainfall within 7 to 10 days after application, • in soils prone to leaching, rainfall which is sufficiently heavy to cause movement of the herbicide out of the weed seed zone. These factors when combined may substantially reduce weed control.
	Wild oats Wireweed	1.8	

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

WITHHOLDING PERIOD:
HARVEST: NOT REQUIRED WHEN USED AS DIRECTED
GRAZING: DO NOT GRAZE OR CUT FOR STOCKFOOD FOR 12 WEEKS AFTER APPLICATION

GENERAL INSTRUCTIONS

BUTISAN HERBICIDE is a residual herbicide that provides pre-emergence control of annual ryegrass, wild oat and wireweed. It is absorbed by the roots of germinating seedlings and translocated primarily by the xylem. Weed control is optimised when BUTISAN HERBICIDE is applied evenly to moist soil just prior to incorporation by sowing and there is sufficient rainfall soon after sowing to ensure activation and uptake of the herbicide by germinating weeds. Weed control may be greatly reduced where weed seeds have been buried by cultivation prior to application. Weed control may also be reduced where there is insufficient soil moisture for herbicide uptake or in soils prone to leaching where rainfall is sufficiently heavy to cause movement of the herbicide out of the weed seed zone. BUTISAN HERBICIDE will not reliably control emerged weeds. A knockdown herbicide should be used to control emerged weeds at sowing.

INCORPORATION BY SOWING

BUTISAN HERBICIDE should be applied prior to sowing, and incorporated by sowing using knife points and press wheels as soon as practicable. Weeds germinating in the seed row may not be controlled. Weeds germinating from depth, weeds just about to emerge, or weeds that have emerged which are not controlled by a knockdown herbicide at sowing may not be controlled by BUTISAN HERBICIDE.

Caution not to throw treated soil from one sowing furrow into an adjacent furrow should be followed as this may result in crop damage.

COMPATIBILITY
BUTISAN Herbicide is compatible with the following herbicides: glyphosate, Sharpen WG Herbicide, propizamide, atrazine, trifluralin, triallate, Stomp 440EC, terbuthylazine

CROP SAFETY
In situations where a concentration of herbicide occurs in the planting row or at the planted crop seed may cause crop damage. Therefore situations such the following may result in potential crop damage:

- Deep planting furrows where soil infills into the planted furrow via such circumstances as wind or rain
- Heavy rainfall after application and before crop emergence particularly in soils with higher potential for leaching

Other stress events on the crop such as frost, waterlogging, disease, insect attack or vigor reductions from other tank mixed herbicides, and vigor reductions from some seed treatments may increase the potential for crop damage.

RECROPPING INTERVAL

Crops	Minimal cropping interval
All crops including Wheat, Durum, Barley, Oats, Field peas, Chickpeas, Lupins	12 months

RESISTANT WEEDS WARNING

GROUP	K	HERBICIDE

BUTISAN Herbicide is a member of the chloroacetamide group of herbicides and has the inhibitor of very long chain fatty acids (VLCFA inhibitors) mode of action. For weed resistance management BUTISAN is a Group K herbicide. Some naturally-occurring weed biotypes resistant to BUTISAN, and other Group K herbicides, may exist through normal genetic variability in any weed population. These resistant individuals can eventually dominate the weed population if these herbicides are used repeatedly. These resistant weeds will not be controlled by BUTISAN or other Group K herbicides. Do not rely exclusively on BUTISAN for weed control. Use as part of an integrated weed management program involving herbicides with other modes of action and non-chemical methods of control. CropLife Australia resistance management strategies are available from your local agricultural chemical supplier or at the CropLife Australia website (www.croplifeaustralia.org.au). Refer to these strategies for details of how to manage the build-up of resistant weeds on your farm. Since occurrence of resistant weeds is difficult to detect prior to use BASF accepts no liability for any losses that may result from the failure of BUTISAN to control resistant weeds.

TIMING
Incorporation by sowing as soon as practicable after application of BUTISAN HERBICIDE, but no later than 3 days after application.

MIXING
Ensure sprayer and nozzle filters are clean before preparing the spray mixture. Half fill the spray tank with water and, with the agitators in motion, add the correct amount of BUTISAN HERBICIDE directly to the spray tank. Complete filling the tank with agitators in motion. Agitation must continue before and during spraying.

APPLICATION

Ground sprayers
Apply BUTISAN HERBICIDE as a broadcast application using a conventional boom sprayer with either mechanical or by-pass agitation. Spray equipment should be properly calibrated to ensure correct and uniform application. Use a spray volume of 80 to 250 litres per hectare. To minimise off-target drift use the lowest pressure and boom height which provides uniform coverage. Ensure complete and even spray coverage of the soil is achieved. Poor spray coverage may result from application to ridged or excessively cloddy soil or in situations of high stubble, plant residue or other ground cover. A significant reduction in weed control may result where stubble, plant residue or other ground cover exceeds 50%, and in situations where a ‘cold’ or incomplete burn of stubble results in a mass of material which can act as a physical barrier between the herbicide and germinating weeds - this can be exacerbated in header trails where there may be greater weed seed numbers and higher levels of plant residue. Weed control can be particularly affected where BUTISAN HERBICIDE is applied to a barrier of stubble, plant residue or other ground cover and there is insufficient following rainfall to transfer the herbicide to the soil surface and the germinating weed seeds.

Aerial sprayers
DO NOT apply BUTISAN HERBICIDE by aircraft.

PROTECTION OF CROPS, NATIVE AND OTHER NON-TARGET PLANTS
DO NOT apply under weather conditions, or from spray equipment, which may cause spray drift onto nearby susceptible plants, adjacent crops, or pastures.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT
Highly toxic to aquatic life. DO NOT contaminate streams, rivers or watercourses with the chemical or used containers.

STORAGE AND DISPOSAL
Store in the closed, original container in a dry, cool, well ventilated area out of direct sunlight. 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.

SAFETY DIRECTIONS
Harmful if swallowed. May irritate the eyes. Avoid contact with eyes. Wash hands after use.

FIRST AID
If poisoning occurs contact a doctor or Poisons Information Centre. Phone Australia 13 11 26.

SAFETY DATA SHEET
For further information refer to the Safety Data Sheet (SDS).

CONDITIONS OF SALE
All conditions and warranties rights and remedies implied by law or arising in contract or tort whether due to the negligence of BASF Australia Ltd or otherwise are hereby expressly excluded so far as the same may legally be done provided however that any rights of the Buyer pursuant to non- excludable conditions or warranties of the Competition and Consumer Act 2010 or any relevant legislation of any State are expressly preserved but the liability of BASF Australia Ltd or any intermediate Seller pursuant thereto shall be limited if so permitted by the said legislation to the replacement of the goods sold or the supply of equivalent goods and all liability for indirect or consequential loss or damage of whatsoever nature is expressly excluded. This product must be used or applied strictly in accordance with the instructions appearing hereon. This product is solely sold for use in Australia and must not be exported without the prior written consent of BASF Australia Ltd.

FOR SPECIALIST ADVICE IN AN EMERGENCY ONLY PHONE 1800 803 440 TOLL FREE-ALL HOURS-AUSTRALIA WIDE

APVMA Approval No: 80664/101359

Batch No:
Date of Manufacture:

BASF
The Chemical Company

BASF Australia Ltd
ABN 62 008 437 867
Level 12, 28 Freshwater Place
Southbank VICTORIA 3006

ABBREVIATIONS

ac	active constituent
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
ARfD	Acute Reference Dose
BBA	Biologische Bundesanalstalt fur Land—und forstwirschaft
bw	bodyweight
d	day
DAT	Days After Treatment
DT_{50}	Time taken for 50% of the concentration to dissipate
EA	Environment Australia
E_bC_{50}	concentration at which the biomass of 50% of the test population is impacted
EC_{50}	concentration at which 50% of the test population are immobilised
EEC	Estimated Environmental Concentration
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
EUP	End Use Product
Fo	original parent generation
g	gram
GAP	Good Agricultural Practice
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GVP	Good Veterinary Practice
h	hour

ha	hectare
Hct	Heamatocrit
Hg	Haemoglobin
HPLC	High Pressure Liquid Chromatography *or* High Performance Liquid Chromatography
id	intradermal
im	intramuscular
ip	intraperitoneal
IPM	Integrated Pest Management
iv	intravenous
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
JMPR	Joint FAO/WHO Meetings on Pesticide Residues
kg	kilogram
K_{oc}	Organic carbon partitioning coefficient
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
LOQ	Limit of Quantitation—level at which residues can be quantified
mg	milligram
mL	millilitre
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
NDPSC	National Drugs and Poisons Schedule Committee
NEDI	National Estimated Daily Intake
NESTI	National Estimated Short Term Intake
ng	nanogram

NHMRC	National Health and Medical Research Council
NOEC/NOEL	No Observable Effect Concentration Level
OC	Organic Carbon
OM	Organic Matter
po	oral
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
Q-value	Quotient-value
RBC	Red Blood Cell Count
s	second
sc	subcutaneous
SC	Suspension Concentrate
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons
TGA	Therapeutic Goods Administration
TGAC	Technical grade active constituent
T-Value	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons
TTR	Total Radioactive Residues
µg	microgram
vmd	volume median diameter
WG	Water Dispersible Granule
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
Leaching	Removal of a compound by use of a solvent
Log Pow	Log to base 10 of octanol water partitioning co-efficient, synonym KOW
Metabolism	The chemical processes that maintain living organisms
Photodegradation	Breakdown of chemicals due to the action of light
Photolysis	Breakdown of chemicals due to the action of light
Subcutaneous	Under the skin
Toxicokinetics	The study of the movement of toxins through the body
Toxicology	The study of the nature and effects of poisons

REFERENCES

Australian Pesticides and Veterinary Medicines Authority 2008, *Ag MORAG: Manual of Requirements and Guidelines*, APVMA, Canberra.

Australian Pesticides and Veterinary Medicines Authority 2008, *Vet MORAG: Manual of Requirements and Guidelines*, APVMA, Canberra.