Australian Government

Australian Pesticides and Veterinary Medicines Authority

PUBLIC RELEASE SUMMARY

on the Evaluation of the New Active Saflufenacil in the Product SHARPEN WG HERBICIDE (Previously Heat Herbicide)

APVMA Product Number 62853

FEBRUARY 2012

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PREFACE

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is an independent statutory authority 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 Aging, Office of Chemical Safety and Environmental Health (OCSEH), Department of the Environment, Water, Heritage and the Arts (DEWHA), and State Departments of Primary Industry.

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 all products containing new active ingredients.

The information and technical data required by the APVMA to assess the safety of new chemical products and the methods of assessment must be undertaken according to accepted scientific principles. Details are outlined in the APVMA's publications *Ag MORAG: Manual of Requirements and Guidelines* and *Vet MORAG: Manual of Requirements and Guidelines*.

This Public Release Summary is intended as a brief overview of the assessment that has been completed by the APVMA and 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 Australian Pesticides and Veterinary Medicines Authority (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
- occupational exposure aspects
- residue and trade aspects
- environmental fate, toxicity, potential exposure and hazard
- efficacy and target crop or animal safety.

Comment is sought from interested persons 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 **SHARPEN WG 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 grounds include **occupational health and safety, chemistry and manufacture, residues, safety and first aid, environmental fate and toxicity, trade** and **efficacy**. Submissions should state the grounds on which they are based. Comments received outside these grounds cannot be considered by the APVMA.

Submissions must be received by the APVMA by close of business on **27 March 2012** 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. A summary of relevant comments and the APVMA's response will be published on the APVMA website.

When making a submission please include:

- Contact name
- Company or Group name (if relevant)
- Postal Address
- Email Address (if available)
- The date you made the submission.

All personal and ***confidential commercial information (CCI)***[1] material 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:

Contact Officer, Pesticides Program
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[1] A full definition of "confidential commercial information" is contained in the Agvet Code.

Further information

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

Copies of full technical evaluation reports covering 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: http://www.apvma.gov.au

1 INTRODUCTION

Applicant

BASF Australia Ltd

Details of Product

It is proposed to register SHARPEN WG Herbicide, containing 700 g/kg saflufenacil as a water dispersible granule (WG) formulation. SHARPEN WG Herbicide is a post-emergence herbicide to be added to Roundup Attack Herbicide containing glyphosate to improve the control of certain broadleaf weeds including fleabane prior to the establishment of fallows, prior to establishing winter and summer broadacre crops and forestry plantations, in commercial, industrial and public service areas, around agricultural buildings, yards and other farm situations.

Saflufenacil is a herbicidal active ingredient new to the Australian market. It is structurally related to an already registered herbicide, butafenacil. It has been classified as a Group G mode of action for weed resistance management. SHARPEN WG Herbicide is a fast acting contact herbicide and aids in control of weeds through a process of membrane disruption. The foliar uptake of SHARPEN WG Herbicide is rapid and plant desiccation can occur within 4 days of application. Application of SHARPEN WG Herbicide is intended to target small actively growing weeds. Subsequent germinations will not be controlled.

The active ingredient saflufenacil will be manufactured overseas, while SHARPEN WG Herbicide will be formulated at either local or overseas facilities.

This submission has been assessed under a joint review arrangement where registrations for the same formulations and uses have been submitted concurrently in Canada, USA, and Australia. Saflufenacil and products containing this active ingredient has already been approved in USA and Canada.

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of SHARPEN WG Herbicide containing the new active ingredient saflufenacil.

2 CHEMISTRY AND MANUFACTURE

2.1 Active Constituent

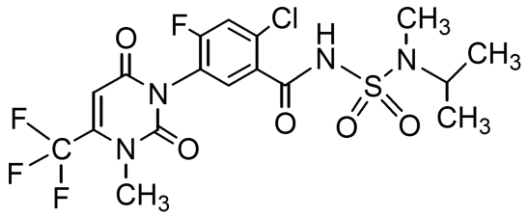
Saflufenacil is a new active constituent, which is a herbicide belonging to the pyrimidindione class of chemical compounds that is for use in field and row crops, groves, orchards, vineyards, forest plantations and in non-crop applications.

Manufacturing Site

The active constituent saflufenacil is manufactured by CBW Chemical GMBH Bitterfeld-Wolfen, Greppiner Strasse 19, D-06766 Bitterfeld-Wolfen, Germany

Chemical Characteristics of the Active Constituent

COMMON NAME:	Saflufenacil
IUPAC NAME:	*N'*-{2-chloro-4-fluoro-5-[1,2,3,6-tetrahydro-3-methyl-2,6-dioxo-4-(trifluoromethyl)pyrimidin-1-yl]benzoyl}-*N*-isopropyl-*N*-methylsulfamide
CAS NAME:	2-chloro-5-[3,6-dihydro-3-methyl-2,6-dioxo-4-(trifluoromethyl)-1(2*H*)-pyrimidinyl]-4-fluoro-*N*-[[methyl(1-methylethyl)amino]sulfonyl]benzamide
CAS REGISTRY NUMBER:	372137-35-4
MANUFACTURER'S CODE:	BAS 800 H
MOLECULAR FORMULA:	$C_{17}H_{17}ClF_4N_4O_5S$
MOLECULAR WEIGHT:	500.85
STRUCTURE:	



APVMA Active Constituent Standard for Saflufenacil Active Constituent

CONSTITUENT	SPECIFICATION	LEVEL
Saflufenacil	Saflufenacil	Not less than 945 g/kg
Dimethyl sulfate	Dimethyl sulfate	Not more than 1 mg/kg

Physical and Chemical Properties of Pure Active Constituent and Technical Material

COLOUR	White powder
PHYSICAL STATE	Solid
ODOUR	Odourless
MELTING POINT	189.9°C
VAPOUR PRESSURE AT 20°C	4.5×10^{-15} Pa
WATER SOLUBILITY AT 20°C	0.21 g/100mL at pH 7 buffer, 0.0014 g/100mL at pH 4 buffer, and degradation in pH 9
SOLUBILITY IN ORGANIC SOLVENTS	Heptane: < 0.005 g/100 mL *n*-Octanol: < 0.01 g/100 mL Toluene: 0.23 g/100 mL Methanol: 2.98 g/100 mL Acetonitrile: 19.4 g/100 mL Acetone: 27.5 g/100 mL Dichloromethane: 24.4 g/100 mL THF: 36.2 g/100 mL
PARTITION COEFFICIENTS (N-OCTANOL/WATER)	2.6

2.2 Product

Distinguishing name: Sharpen WG Herbicide

Formulation type: Water Dispersible Granule (WG)

Active constituent concentration: Saflufenacil 700 g/kg

Physical and Chemical properties of the Product

APPEARANCE	Light brown, extruded granules
PARTICLE SIZE (UPON DILUTION IN WATER)	1.5 – 3.0 μm
ACIDITY/ALKALINITY	pH 5 (1% dilution)
BULK DENSITY	Free fall 0.574 kg/L; packed 0.628 kg/L
DISPERSABILITY	<15 turns
WETTABILITY	< 1 min without swirling
DUST CONTENT	Nearly dust free
FLOWABILITY	100% after 20 drops
ATTRITION RESISTANCE	>98%
PERSISTENT FOAM	Max 60 ml after 1 min
FLASH POINT	Not applicable
FLAMMABILITY	Not flammable
EXPLOSIVE PROPERTIES	Not explosive
OXIDISING PROPERTIES	No oxidising properties
CORROSIVE HAZARD	Not applicable
DIELECTRIC BREAKDOWN VOLTAGE	Not applicable, formulation is not intended for use around electrical equipment.
DANGEROUS GOODS CLASSIFICATION	Not dangerous good according to the Australian Code of Transport of Dangerous Goods by Road and Rail. Poisons Schedule: 5

Recommendation

Based on a review of the chemistry and manufacturing details provided by the applicant, registration of *Sharpen WG Herbicide* is supported.

3 TOXICOLOGICAL ASSESSMENT

3.1 EXECUTIVE SUMMARY

Toxicology Public Health Aspects

Saflufenacil is a herbicidal active ingredient new to the Australian market. It is structurally related to an already registered herbicide, butafenacil. The product Sharpen WG Herbicide is a water dispersible granule formulation containing saflufenacil 700 g/kg. The product is intended for control of broadleaf weeds prior to establishment of crops, or in commercial, industrial and public service areas.

In rats, orally administered saflufenacil was rapidly absorbed, distributed, and excreted. There was a sex dependent difference in the excretion, i.e. the main route of elimination was via the faeces for males, but via the urine for females. Males also showed a significantly higher biliary excretion of saflufenacil. Dermal absorption of undiluted emulsifiable concentrate formulation was high (up to 83%), though it is considered that this high dermal penetration rate of saflufenacil was likely to be the result of skin damage caused by the organic solvent in the emulsifiable concentrate formulation. Dermal absorption of a 1:10 and 1:100 dilution of emulsifiable concentrate formulation was lower (3-9%). In a dermal absorption study with a suspension concentrate formulation (SC) containing 342.2 g/L of saflufenacil, the greatest absorption, approximately 4% of the applied dose, was seen with a 1:100 aqueous dilution of the SC formulation. It is considered that data from the dermal absorption study using the suspension concentrate is more appropriate to use for Sharpen™ WG Herbicide (a water dispersible granule formulation) for risk assessment purposes.

Saflufenacil and Sharpen WG Herbicide were of low acute oral, dermal and inhalational toxicity in rats, and both were slightly irritant to the eyes and skin of rabbits, but were not skin sensitisers in guinea pigs.

In repeat dose studies in mice, rats or dogs, primary effects of saflufenacil were anaemia, increased weight, fatty changes, decreased iron storage, occasional extramedullary haemopoiesis in the liver and spleen, and erythroid hyperplasia in bone marrow. Long term studies indicate that saflufenacil was not carcinogenic in mice and rats. Saflufenacil was not mutagenic or genotoxic *in vitro* and was not genotoxic *in vivo*.

When tested in the rat, saflufenacil did not affect the reproductive performance or the reproductive system. In the rat developmental toxicity study, saflufenacil decreased the body weight gain of the foetuses, and when compared to concurrent and historical control data there was a slightly higher incidence of skeletal malformation involving bent scapula at 20 mg/kg bw/day in the absence of marked maternal toxicity. Adverse developmental effects were only observed in the presence of severe maternal toxicity in a rabbit developmental study.

Saflufenacil was not neurotoxic in an acute and 90-day neurotoxicity study in rats.

Occupational Health and Safety

Farmers and their employees will be the main users of the products. Workers may be exposed to the products when opening containers, mixing/loading, application, and cleaning up spills and equipment. The

main route of exposure to the product/spray will be dermal and inhalation, although ocular exposure is also possible. Workers and the general public may have dermal contact when entering treated areas.

In the absence of exposure data for the proposed mode of application, the Pesticide Handler Exposure Database (PHED) Surrogate Exposure Guide was used to estimate exposure. Exposure to Sharpen WG Herbicide is at an acceptable level when wearing cotton overalls buttoned to the neck and wrist and elbow-length chemical resistant gloves for opening the container and preparing spray.

Based on the risk assessment, First Aid Instructions, Warning Statements, Safety Directions and Re-entry statements have been recommended for the product label.

Conclusion

Based on an assessment of the toxicology, it was considered that there should be no adverse effects on human health from the use of Sharpen WG Herbicide when used in accordance with the label directions.

3.2 EVALUATION OF TOXICOLOGY

The toxicological database for saflufenacil, which consists primarily of toxicity studies conducted in laboratory animals, is quite extensive. 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. From a conservative risk assessment perspective however, 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. Such dose levels as the No-Observable-Effect-Level (NOEL) are used to develop acceptable limits for dietary or other intakes (ADI and ARfD) at which no adverse health effects in humans would be expected.

The toxicology assessment of saflufenacil was conducted jointly by scientists from Canada (PMRA), the United States (EPA) and Australia (OCS). Since the assessment report relies significantly on the international work share assessment, the OCS adopted the no observed adverse effect level (NOAEL) and lowest observed adverse effect level (LOAEL) with scientific justification.

Toxicokinetics and Metabolism

Following oral administration in rats, saflufenacil is rapidly (Cmax 1 h) and completely absorbed, broadly distributed, and fully excreted via the urine (26%/96% for males/females) and faeces (81%/13%) in a sex-specific pattern, with higher biliary excretion in males than females. No significant amount of the parent compound or its metabolites was bound to cellular blood constituents. There are three major transformation steps: demethylation of uracil ring; degradation of the N-methyl-N-isopropyl group; and cleavage of the uracil

ring which forms a sulfonylamide group, resulting predominantly in three main metabolites in addition to the parent compound.

Dermal absorption of undiluted emulsifiable concentrate (EC) formulation was high (up to 83%), though it is considered that this high dermal penetration rate of saflufenacil was likely to be the result of skin damage caused by the organic solvent in the EC formulation. Dermal absorption of a 1:10 and 1:100 dilution of emulsifiable concentrate formulation were lower (3-9%). In a dermal absorption study with a suspension concentrate formulation (SC) containing 342.2 g/L of saflufenacil, the greatest absorption, approximately 4% of the applied dose, was seen with a 1:100 aqueous dilution of the SC formulation. Thus, for risk assessment purpose, it is considered that data from the dermal absorption study using the suspension concentrate is more appropriate to use for the SHARPEN WG Herbicide (a water dispersible granule formulation).

Acute toxicity studies

Saflufenacil was of low acute toxicity in rats, with an oral and dermal LD_{50} greater than 2000 mg/kg bw, and a 4-hr inhalation LC_{50} greater than 5300 mg/m^3. It was a slight skin and minimal eye irritant in rabbits. It did not demonstrate a potential for skin sensitisation in guinea pigs.

SHARPEN WG Herbicide was of low acute toxicity by the oral, dermal, and inhalation routes in rats. It was minimally irritating to the rabbit eye, mildly irritating to the rabbit skin, but was not a skin sensitizer when tested in guinea pigs.

Short term toxicity studies

Saflufenacil is a member of the pyrimidindiones group of herbicides, and its mode of action is through inhibition of the enzyme protoporphyrinogen oxidase (PPO). The inhibition consequently interferes with the biosynthetic pathway of chlorophyll (leaf green) in plants, or the production of heme in mammals. The chemical can be rapidly absorbed by roots and foliage of the plant, and results in membrane damage and eventually plant death by inhibiting the PPO enzyme in the presence of light.

The primary target of saflufenacil was the haematological system. Consistent with its mode of action as a PPO inhibitor, repeat dosing of saflufenacil in rats, mice and dogs caused microcytic hypochromic anaemia (decreased Hb, Hct, MCV, MCH, MCHC, total protein and globulins, increased normoblasts, reticulocytes and polychromasia with or without extramedullary haematopoiesis), porphyria (increased porphyrin in plasma, liver and excretes), changes in clinical chemistry parameters (increased ALT, AST, urea, bilirubin, urobilinogen) and organ weight change and/or histopathology changes in the liver (increased weight, decreased iron storage and porphyrin, extramedullary haematopoiesis, and fatty liver), spleen (increased weight, decreased iron storage and extramedullary haematopoiesis) and bone marrow (hyperplasia). The lowest NOAEL was 4.6 mg/kg bw/day in the 18-month study in mice, based on slight anaemia and increased liver porphyrin observed at the next highest dose level.

The increase porphyrin and bilinogen levels in the plasma, liver and excretions are consistent with the proposed inhibition of protoporphyrinogen oxidase. However, in agreement with Canadian and the US regulatory agencies for the present assessment, increased porphyrins levels observed in animal studies may or may not be considered adverse, depending on the level and duration of the increase, and whether they are associated with relevant histopathological changes. For example, an increased level of porphyrin

(several fold of the control) and bilirubin in the plasma without other histopathological findings were seen in maternal rats at 20 and 60 mg/kg bw/day the rat development study. Hence, an NOAEL for maternal toxicity was established at the highest dose (60 mg/kg bw/day) due to the lack of other treatment-related changes in this study. In fact, in almost all repeat dose toxicity studies in rats, an increased level of porphyrin in the plasma or urobilinogen in the urine was observed at the proposed NOAEL level (usually the lowest dose tested in these studies).

A 4-week dermal toxicity study using 0, 100, 300 or 1000 mg/kg bw/day of saflufenacil in rats showed no skin reactions following daily application of saflufenacil at $\leq$ 300 mg/kg bw/d. The only treatment-related finding was a decrease in the haemoglobin level in males at the high dose of 1000 mg/kg bw/d.

Mice were given saflufenacil at 0, 50, 150, 450, 1350 and 4050 ppm in the daily diet for 28 days. Haematological and clinical chemistry effects and increased liver weight and histopathological changes to the liver were seen in males at 150 ppm, with histopthological changes to the liver seen in females at 450 ppm. The NOAEL was 50 ppm (12.8 mg/kg bw/day) for males and 150 ppm (63.4 mg/kg bw/day) for females.

Rats were given saflufenacil at 0, 50, 150, 450, 1350 or 4050 ppm in the daily diet for 28 days. Anaemia, erythroid hyperplasia in bone marrow, extramedullary haemopoiesis in liver and spleen, increased polychromasia and anisocytosis was seen in males at 450 ppm, with anaemia seen in females at 1350 ppm. The NOAEL was 150 ppm (13.4 mg/kg bw/day) for males and 450 ppm (43.6 mg/kg bw/day) for females.

Dogs received an oral dose of saflufenacil at 0, 30, 100 or 300 mg/kg bw/day daily for 28 days. Haematological findings and histopathological changes in the liver, spleen and bone was seen from 100 mg/kg bw/day. The NOAEL was 30 mg/kg bw/day.

Mice received 0, 15 (males only), 50, 150, 450 or 1350 (females only) ppm of saflufenacil in the daily diet for 90 days. Decreased body weight and body weight gain in males, multiple haematological changes typical of microcytic hypochromic anaemia in both sexes and increased liver weight and histopathological changes to the liver in males only were seen at 150 ppm. The NOAEL was 50 ppm (12.5 / 17.6 mg/kg bw/day for males / females).

Rats received 0, 50, 150, 450 (males only), 1350 or 4050 (females only) ppm of saflufenacil in the daily diet for 90 days. Changes were observed in haematology, clinical chemistry and uranology parameters, along with increased spleen weight and extramedullary haematopoiesis in the spleen of males at 450 ppm and females at 1350 ppm. The NOAEL was 150 ppm (10.5 mg/kg bw/day) for males and 1350 ppm (110.5 mg/kg bw/day) for females.

Dogs were given an oral dose of saflufenacil at 10, 50 or 150 mg/kg bw/day daily for 90 days. The treatment revealed changes in haematology, clinical chemistry and uranology parameters, increased spleen weight and extramedullary haematopoiesis in the spleen of males at 450 ppm and females at 1350 ppm. The NOAEL was 10 mg/kg bw/day.

Long term toxicity and carcinogenicity studies

In the long term (2-year) rat study, porphyrin levels were not measured and no conclusion can be drawn regarding the relationship between increased porphyrin levels and the observed adverse effects. However, considering all the available data, it is concluded that increased urobilinogen and porphyrin levels observed at low doses in the absence of other clinical pathology and histopathological changes should generally not be regarded as an adverse effect. Though, such changes are considered to have toxicological significance, when they are associated with adverse effects (e.g. anaemia) at moderate and high dose levels. Given the adoption of a NOAEL approach in this assessment, the observance of changes in urobilinogen and porphyrin levels at dose levels that are not associated with other clinical pathology and histopathological changes have not been used to set a NOAEL.

In mice given 0, 1 (males only), 5, 25, 75 or 150 (females only) ppm of saflufenacil in the daily diet for 18 months, anaemia and increased total faecal and liver porphyrin levels were observed in males at 75 ppm and in females at 150 ppm. There were no treatment related carcinogenicity findings. The NOAEL was 25 ppm (4.6 mg/kg bw/day) in males and 75 ppm (18.9 mg/kg bw/day) in females.

Rats were given 0, 20, 100, 250 or 500 ppm of saflufenacil in the daily diet for 2 years. The observed findings include decreased body weight and body weight gain, increased incidence of smeared anogenital region, microcytic hypochromic anaemia (decreased Hb, Hct, MCV and MCH) and urobilinogen associated with increased ALT in both sexes at 500 ppm and above. There were no treatment related carcinogenicity findings. The NOAEL was 250 ppm (4.6 mg/kg bw/day) for males, and 100 ppm (6.2 mg/kg bw/day) for females.

Dogs received a daily dose of 0, 5, 20 or 80 mg/kg bw/day for 1 year. Discoloured faeces, lower body weight, body weight gain and food consumption, lower MCV and MHC, increased ALP, lower total protein and albumin, and decreased iron storage in Kupffer cells and hepatocytes were observed in dogs at 80 mg/kg bw/day. The NOAEL was 20 mg/kg bw/day.

Reproduction and Developmental Studies

Increased stillborns and pup mortality during the early phase of lactation, together with reduced pup body weight gains were observed at 50 mg/kg bw/day in a 3-generation reproduction study in rats. However, saflufenacil did not affect reproductive performance or the reproductive system. In a rat developmental study, decreased foetal body weight and increased skeletal malformations (bent scapulae, thick humeri, bent radii, ulnas and femurs, malpositioned and bipartite sternebrae, and wavy ribs) and variations (incomplete ossification in the nasal area) were observed at 20 mg/kg bw/day and/or 60 mg/kg bw/day in the absence of maternal toxicity. In contrast, increased abortion was seen in a rabbit developmental study but only at a dose level that caused severe maternal toxicity (e.g. mortality in dams).

With regard to the rat being significantly more sensitive to the developmental toxicity potential of saflufenacil compared to rabbits, an *in vitro* assay investigating the inhibition of protoporphyrinogen oxidase (PPO) activity in the liver, demonstrated significant inter-species differences in saflufenacil inhibition of PPO. The data indicates that saflufenacil inhibition of PPO is comparable in rabbits and humans, and is significantly less than that seen in rodents (i.e. mouse and rat). However, the MOA for saflufenacil-induced skeletal malformation has not been established.

The lowest NOAEL for developmental toxicity was 5 mg/kg bw/day in the rat developmental study.

Given the occurrence of foetal toxicity in a developmental toxicity study including skeletal malformations in the absence of maternal toxicity, an extra safety factor is consider necessary to protect women of child bearing age. The choice of an appropriate extra safety factor value was undertaken using expert judgement and consideration of the following observations:

- Compared to concurrent controls, there was a statistically significant decrease in mean foetal body weight (both sexes combined) of 8.1 and 16.2% in the mid (20 mg/kg bw/d) and high dose (60 mg/kg bw/day,) groups.
- A statistically significant increase in incomplete ossification of the nasus in the mid (4/106 foetuses i.e. 4%) and high dose (15/98 foetuses i.e. 15%) groups.
- A single incidence of bent scapula at the mid dose and 5 incidences at the high dose (in 3 litters)

Bent scapula and incomplete ossification of the nasus have not been observed in a historical database of 2143 foetuses. However, it is noted and accepted that while the observed decrease in body weight gain is treatment related (i.e. followed a dose response relationship) the decrease of 8.1% at the mid dose was close to the average statistical weight of the testing facility and, thus, may simply reflect biological variation.

Overall, the treatment related findings at the mid dose of 20 mg/kg bw/d are limited and minimal with regards to their incidence and toxicological nature. This suggests that 20 mg/kg bw/d is likely to be close to the NOAEL/LOAEL threshold for developmental toxicity. Furthermore, the NOAEL of 5 mg/kg bw/d for developmental toxicity is 12-fold lower than the identified maternal NOAEL of 60 mg/kg bw/day, at which the observed maternal effects (increased porphyrin and urobilinogen in the plasma) were not considered adverse but are indicators of exposure.

Hence, in consideration of the above, an extra 3-fold safety factor is considered appropriate for derivation of relevant health standard values.

Genotoxicity Studies

No evidence of a mutagenic and/or genotoxic potential for saflufenacil was observed in a battery of *in vitro* and *in vivo* assays.

Neurotoxicity Studies

In an acute neurotoxicity study in rats with a single limit dose of 2000 mg/kg bw, no neurobehavioral or neuropathological changes were seen. A moderately decreased motor activity in high dose males on Day 0 reflected mild and transient general systemic toxicity.

Saflufenacil was not neurotoxic in a 90-day neurotoxicity study in rats. No neurobehavioral or neuropathological changes were seen at dose levels up to and including 1000 ppm for males and 1350 ppm for females. Decreased food consumption, body weight, body weight gain and effects on hematological parameters were seen at the highest dose.

3.3 PUBLIC HEALTH STANDARDS

Poisons Scheduling

The delegate to the Secretary of the Department of Health and Ageing sought advice from the Advisory Committee on Chemical Scheduling (ACCS) on the scheduling of saflufenacil. Saflufenacil was discussed at the June 2011 meeting of the ACCS. The delegate noted and agreed with the ACCS recommendation that saflufenacil be retained in Schedule 7 of the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) though with a cut-off to Schedule 5 for water dispersible granule preparations. This was the interim decision of the delegate. The delegate's finals decision made on 28th September 2011 confirmed the creation of an exception from the Schedule 7 saflufenacil parent entry to Schedule 5 for water dispersible granule preparations. The delegate also decided on an implementation date of 1 January 2012.

NOAEL/ADI /ARfD

The Acceptable Daily Intake (ADI) is that quantity of an agricultural or veterinary chemical which can safely be consumed on a daily basis for a lifetime and is based on the lowest NOAEL obtained in the most sensitive species. This NOAEL is then divided by a safety factor which reflects the quality of the toxicological database and takes into account the variability in responses between species and individuals.

The ADI for saflufenacil was established at 0.017 mg/kg bw/day based on a NOAEL of 5 mg/kg bw/day in a rat developmental study and using a 300-fold safety factor. This 300-fol safety factor consisted of a 10-fold safety factor for interspecies differences, a 10-fold safety factor for intraspecies differences and an additional 3-fold safety factor to account for potential developmental concerns.

The acute reference dose (ARfD) is the maximum quantity of an agricultural or veterinary chemical that can safely be consumed as a single, isolated event. The ARfD is derived from the lowest NOAEL as a single or short term dose which causes no adverse effect in the most sensitive species of experimental animal tested, together with a safety factor which reflects the quality of the toxicological database and takes into account the variability in responses between species and individuals.

The ARfD for saflufenacil was established at 0.017 mg/kg bw/d based on a NOAEL of 5 mg/kg bw/d in a developmental rat study and using a 300-fold safety factor. This 300-fold safety factor consisted of a 10-fold safety factor for interspecies differences, a 10-fold safety factor for intraspecies differences and an additional 3-fold safety factor to account for potential developmental concerns, as it is considered that the potential developmental effects may be caused by a single exposure.

4 RESIDUES ASSESSMENT

Sharpen WG Herbicide is a water dispersible granule formulation containing the new active constituent saflufenacil. The product is intended for application as a tank mix with glyphosate to control a range of broadleaf and grass weeds in cereal, cotton, legume and pulse crops when applied prior to sowing the crop, as well as for weed control in orchards, vineyards, in industrial, commercial and public areas, and when commencing or maintaining a fallow. As part of the residues assessment for saflufenacil, plant and animal metabolism studies, supervised residue trials, crop rotation studies, processing studies, and trade aspects were considered and details are provided below.

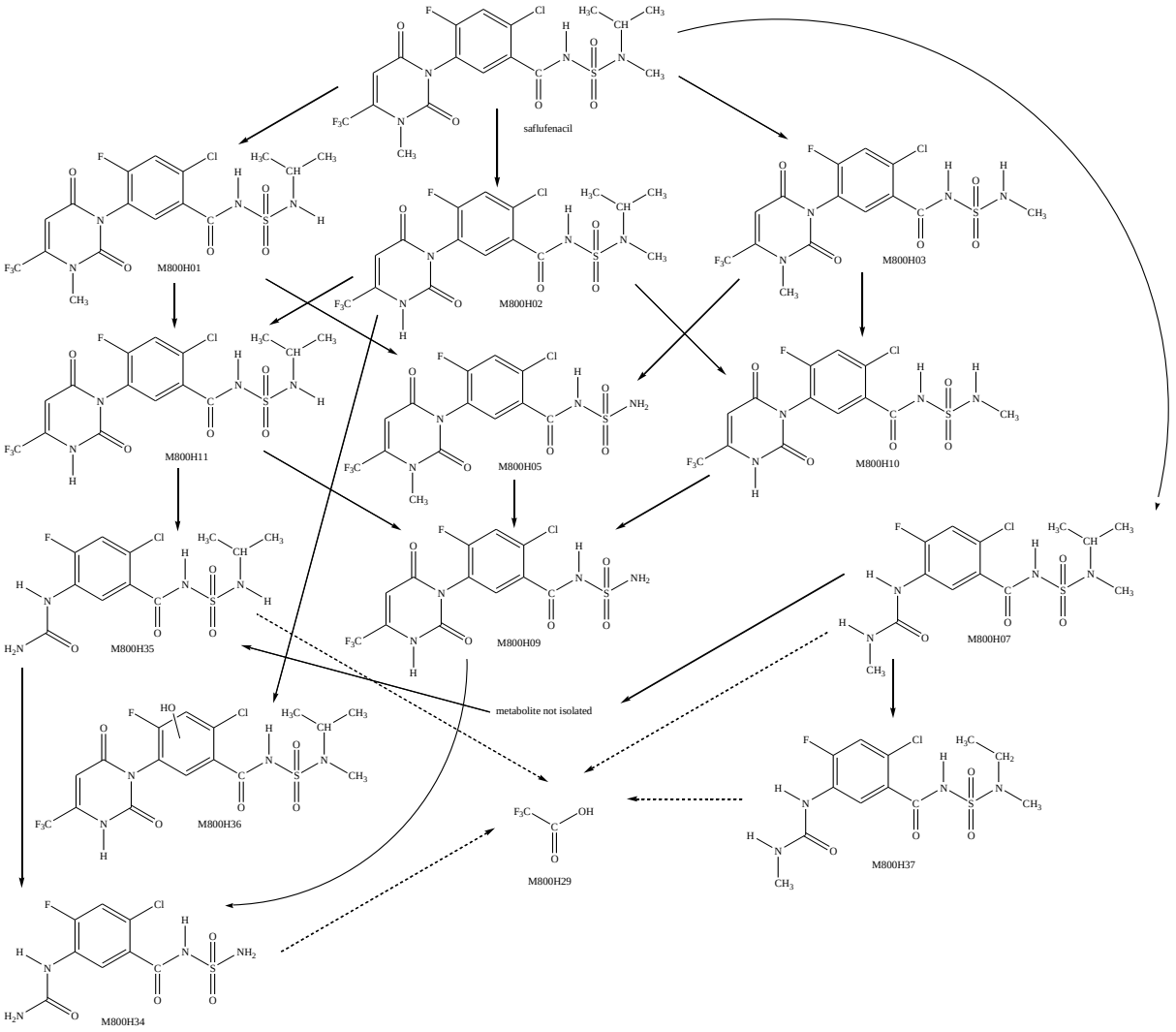
4.1 Metabolism

The applicant provided an extensive plant metabolism package across a range of crop types including cereals (corn and wheat as a confined rotational crop), legumes (soybeans), fruiting vegetables (tomatoes), leafy vegetables (lettuce, as a confined rotational crop) and root vegetables (radish, as a confined rotational crop).

Metabolism of saflufenacil in plants was observed to occur via the following major pathways:

- Demethylation of the 3-position of the uracil ring;
- Dealkylation (loss of either or both of the methyl group and the isopropyl group) of the terminal sulfamide nitrogen; and
- Hydrolytic cleavage of the uracil ring.

Metabolic pathways and metabolites of saflufenacil in plants are summarised in the following figure:



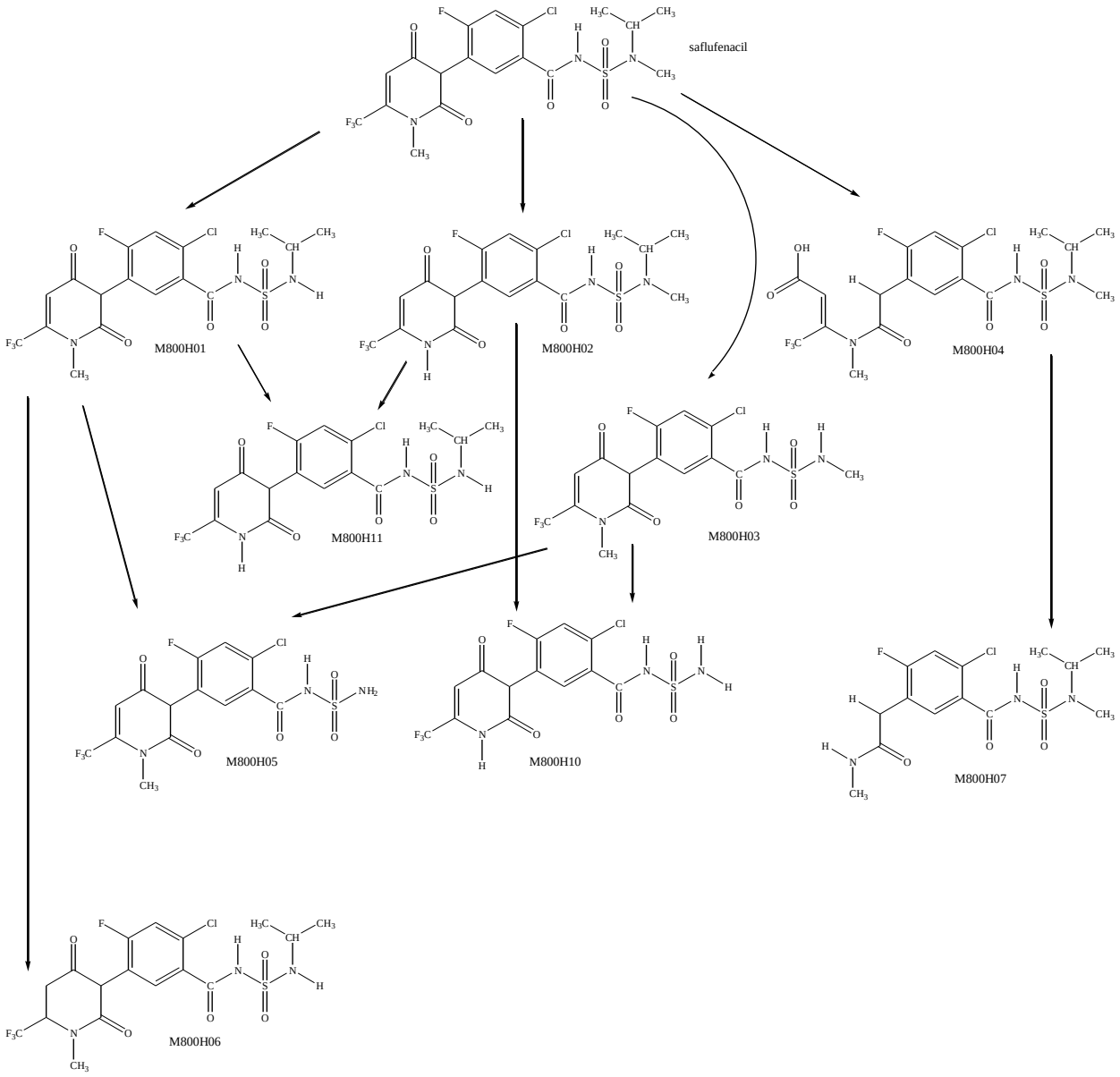
The applicant has proposed that M800H11 (*N'*-{2-chloro-4-fluoro-5-[1,2,3,6-tetrahydro-2,6-dioxo-4-(trifluoromethyl)pyrimidin-1-yl]-benzoyl}-*N*-isopropyl sulfamide) and M800H35 (*N*-[4-chloro-2-fluoro-5-({[(isopropylamino)sulfonyl]amino}carbonyl)phenyl]urea) be included in the plant commodity residue definition together with the parent compound, as these two compounds are present as major components of the residue in a number of plant tissues and across a number of crop groups, and represent three of the observed metabolic pathways (*N*-demethylation of the uracil 3-position in M800H11, *N*-demethylation of the sulfamide nitrogen in both compounds, and hydrolytic cleavage of the uracil ring in M800H35).

Given that residues of any metabolite are not expected to be found in plant tissues above the limit of quantitation and given that the proposed metabolites for inclusion in the residue definition cover the three major metabolic pathways, this proposal is acceptable. The proposed residue definition for saflufenacil in plant commodities is therefore:

Sum of saflufenacil, *N'*-{2-chloro-4-fluoro-5-[1,2,3,6-tetrahydro-2,6-dioxo-4-(trifluoromethyl)pyrimidin-1-yl]-benzoyl}-*N*-isopropyl sulfamide, and *N*-[4-chloro-2-fluoro-5-({[(isopropylamino)sulfonyl]amino}carbonyl)phenyl]urea, as saflufenacil equivalents.

Animal metabolism studies were supplied for lactating goats and laying hens.

The metabolism of saflufenacil in animals is summarised in the figure below:



Metabolism of saflufenacil in animals takes place by two main pathways, demethylation of the 3-position on the uracil ring and dealkylation of the terminal sulfamide nitrogen. In goats, ring opening and cleavage of the uracil moiety was also observed. A minor metabolite in hens suggested a reductive pathway where the double bond of the uracil moiety was hydrogenated. However, the resulting metabolite, M800H06, was only

found in significant quantities in excreta, and furthermore, was not separated from another metabolite, M800H02, by HPLC.

Given that parent compound was found in all animal tissues and was the largest residue component in every tissue except eggs, a residue definition of parent compound only is supported for saflufenacil in animal commodities.

4.2 Analytical methods

Determination of saflufenacil residues in plant commodities

A method was developed and validated for analysis of saflufenacil and the metabolites M800H11 and M800H35 in wheat grain and hay, garbanzo bean, peach, soybean seed, orange, and corn oil. Non-oily matrices (wheat grain and hay, garbanzo bean and peach) were extracted with methanol/water, then cleaned up by liquid-liquid partition. Oily samples (orange and soybean seed) were extracted with methanol/water and cleaned up by liquid/liquid partition, with the incorporation of an additional partition step for removing oily interferents. Corn oil was extracted with acetonitrile, and oily contaminants were removed by a liquid/liquid partition repeated three times. All samples were diluted in an appropriate solvent prior to LC/MS/MS analysis.

The method was validated with limits of quantitation (LOQs) of 0.01 mg/kg for each of the analytes in the representative food commodities, and at 0.025 mg/kg for wheat hay. Recoveries were conducted with fortification at concentrations of 0.01 or 0.1 mg/kg (or 0.025 and 0.25 mg/kg for wheat hay) and ranged from 64-129% for the transition used for quantitation. The vast majority of individual recoveries, and all mean recoveries for this transition were within guideline limits. Method linearity was good.

Determination of residues of saflufenacil in animal tissues

A method was presented for determination of saflufenacil in meat, fat, offal, whole and skim milk, cream and eggs. Samples were extracted using acetonitrile, followed by a clean-up step by liquid/liquid partition. Analyses were conducted using LC/MS/MS. Recoveries were determined by fortification of samples at 0.01 or 0.1 mg/kg, and were, for saflufenacil: 69-88% in whole milk, 77-95% in skim milk, 81-96% in cream, 81-96% in egg, 69-96% in beef muscle, 81-96% in beef fat, 69-88% in beef liver, and 86-99% in beef kidney. The LOQ is 0.01 mg/kg, while the method limit of detection (LOD) was significantly lower at 0.084 µg/kg. Method linearity was good.

Overall, the methods are suitable for the proposed purposes and are acceptable.

4.3 Residue definition

The following residue definition is recommended for saflufenacil for the purposes of dietary exposure assessment and for compliance and monitoring:

Compound	Residue definition
Saflufenacil	Plant commodities:

	Sum of saflufenacil, *N'*-{2-chloro-4-fluoro-5-[1,2,3,6-tetrahydro-2,6-dioxo-4-(trifluoromethyl)pyrimidin-1-yl]benzoyl-*N*-isopropyl sulfamide and *N*-[4-chloro-2-fluoro-5-({[(isopropylamino)sulfonyl]amino}carbonyl)phenyl]urea, expressed as saflufenacil equivalents. Animal commodities: Saflufenacil

4.4 Storage stability

Stability over 18 months storage at -5 °C was tested for residues of saflufenacil and the two metabolites proposed to be included in the plant commodities residue definition in a range of plant matrices, including corn forage, grain and stover, garbanzo bean, orange whole fruit, juice, oil and pulp, radish root, raisins, and soybean forage, hay and seed.

Raw recoveries determined with respect to the initial concentrations were corrected for method recoveries at each time point, plotted against time, fitted by linear regression and analysed for statistical significance of any decline. At the 5% level of significance (P-value = 0.05), statistically significant declines were observed for saflufenacil parent compound in corn forage and corn stover, for M800H11 in corn stover, radish root, soybean forage and soybean seed, and for M800H35 in corn grain and orange juice. Residues of saflufenacil were stable over 18 months in corn grain, chickpea, orange fruit, orange juice, orange oil, orange pulp, radish root, raisin, soybean forage, soybean hay and soybean seed. Residues of M800H11 were stable over 18 months in corn grain, corn forage, chickpea, orange fruit, orange juice, orange oil, orange pulp, raisin, and soybean hay. Residues of M800H35 were stable over 18 months in corn forage, corn stover, chickpea, orange fruit, orange oil, orange pulp, radish root, raisin, soybean forage, soybean hay and soybean seed. All samples in residue trials were stored for less than 18 months prior to analysis, and were generally stored below -18 °C.

It is noted that the reported storage temperature (<-5 °C) is significantly higher than that usually used for sample storage (deep freeze conditions, or <-18 °C). This may have contributed to the residues declines observed on storage for some of the combinations of analytes and commodities. The higher storage temperature used during the trial means that the test samples have been subjected to more adverse conditions, and represent a 'worse case storage scenario' than will typically be experienced.

Even for the sample/analyte combinations for which a statistically significant decline was observed, it should be noted that residues of saflufenacil or its metabolites are not expected to found in any plant commodities above the LOQ in any case.

A storage stability study for saflufenacil in bovine muscle, fat, liver, kidney and whole milk was conducted concurrently with the lactating cattle feeding study. Samples were stored below -18 °C for 31-51 days.

Residues of saflufenacil in whole milk declined by 9% over 51 days storage below -18 °C, in muscle a decline of 8% over 31 days was observed, in fat 9% over 35 days, in kidney 17% over 32 days, and in liver 18% over 32 days. Residues of saflufenacil do not therefore appear to be very stable in animal tissues. However, it should be noted that all whole milk samples were analysed within 63 days. Skim milk and cream were not tested for storage stability, however stability behaviour of saflufenacil in these matrices is not expected to be very different from whole milk, and further, the samples were only stored for 29 days.

Muscle, fat, liver and kidney were stored for between 23 and 34 days. All samples were stored below – 18 °C.

Given that declines in residue levels were <30%, and given that sample storage periods were the same or close to the tested storage stability times, it is not proposed to correct results from the dairy cattle feeding study for decline on storage.

4.5 Residue trials

Broadacre use (cereals, cotton, pulses, and legumes)

Heat Herbicide is proposed for application at rates of 6-24 g ai/ha for control of various broadleaf and grass weeds prior to sowing cereals (wheat, barley, sorghum and oats), or pulses and legumes (chickpeas, faba beans, field peas, lentils, soybeans, cowpeas, clover, and lupins). The products are to be used in a tank mix with glyphosate.

In the Australian cereal residue trials, residues of saflufenacil and the metabolites M800H11 and M800H35 were below their individual LOQs of 0.01 mg/kg in all samples of oat, barley, wheat and sorghum grain and forage, oat, barley and wheat straw and sorghum trash. Correspondingly, overall residues were below 0.03 mg/kg. This was observed for the untreated control samples, and for all samples treated at 0.75X and 2.1X the proposed label rate. In the US and Canadian cereal residue trials, the application rates were around 6X those proposed for Australia. With the exception of two trials for sorghum, where low levels (maximum 0.04 mg/kg) of M800H35 were observed in stover, residues of all three analytes in all wheat, sorghum and corn forage samples, in all grain samples, in all rice and wheat straw samples, in all wheat hay, in all corn and sorghum stover samples, and in all samples of corn kernel plus cob with husk removed were below the LOQ (0.01 mg/kg for grain and corn cobs, and 0.025 mg/kg for forage, straw, hay and stover). Maximum Residue Limits for saflufenacil in cereal grains, forage and fodder are recommended at the limit of quantitation, with no harvest withholding period being required, while a 5-week grazing withholding period is recommended. For cereal forage and fodder, the MRL will be set at the rounded-up combined LOQ of 0.1 mg/kg.

No residues above the limit of quantitation were found in any of the raw cereal agricultural commodities in the processing study (wheat, rice and corn grain, or sorghum stalks). Therefore, the processed commodities were not analysed. Saflufenacil residues are unlikely to be found in cereal raw agricultural commodities given the use pattern. They are also unlikely to concentrate in processed commodities. Establishment of MRLs for processed cereal commodities is therefore unnecessary.

Residues of saflufenacil and the metabolites were below their LOQs in all samples of cotton forage, seed, oil, hulls and meal. Although a limited number of trials have been conducted for cotton, the application rates were considerably above the proposed maximum label rate, and the proposed use pattern in cotton, application to soil prior to sowing, or prior to starting or maintaining a fallow, is the same as the proposed use pattern in cereals, for which an extensive data package is available. Therefore, there is sufficient data for the establishment of an MRL at the combined LOQ (0.03 mg/kg), for saflufenacil in cottonseed. A harvest withholding period is not required when the product is used as directed. As no residues were found above the LOQ in seed, meal, hulls, or oil, the MRL for cottonseed will cover processed commodities, and no separate MRLs for processed cotton commodities are required. Cotton forage and trash are not generally fed to livestock, however since the proposed use is as a pre-emergent herbicide and residues are not

expected in forage or fodder above the LOQ, stockfeed MRLs will be established at the rounded-up combined LOQ of 0.1 mg/kg for cotton forage and cotton fodder. Cottonseed meal and hulls are fed to livestock so a stockfeed MRL at the combined LOQ (0.03 mg/kg) will also be established for saflufenacil in cottonseed meal and hulls.

Residues of saflufenacil and metabolites in all treated and untreated samples of canola seed, straw and forage were below the LOQ (0.01 mg/kg in grain, 0.025 mg/kg in straw and forage). Although a limited number of trials have been conducted for canola, and the application rates were below the proposed maximum label rate (75%), the proposed use pattern in canola, application to soil prior to sowing, or prior to starting or maintaining a fallow, is the same as the proposed use pattern in cereals, for which an extensive data package is available. Therefore, there is sufficient data for the establishment of an MRL at the combined LOQ (0.03 mg/kg), for saflufenacil in rape seed. A harvest withholding period is not required when the product is used as directed. A stockfeed MRL at the rounded-up combined LOQ of 0.1 mg/kg for canola forage and fodder is supported, in conjunction with the 5-week grazing withholding period discussed above for cereal crops.

No processing data was supplied for canola. Canola seed is processed into oil in a similar fashion to cottonseed. No residues were observed in cottonseed oil in the processing study discussed above. It is unlikely that residues would be found in canola oil. Therefore, an MRL for rapeseed oil is not required, and residues in oil will be controlled by the raw commodity MRL.

No residues of saflufenacil or the two metabolites were found above their LOQs (0.01 mg/kg for dry seeds and succulent seeds with or without pods, 0.025 mg/kg for straw, hay or forage) in any of the samples of soybean, chickpea, lupin or pea dry seeds, soybean or pea succulent seeds with or without pods, chickpea or lupin straw, soybean hay, or soybean or lupin forage. The data package is extensive, comprising 39 trials in chickpeas, soybeans and peas from the US and Canada, and 2 trials in lupins and one in chickpeas from Australia. All trials included plots that were treated at rates well above the proposed maximum label rate (between 2.1 and 4.3X the proposed rates). Application methods were in accordance with the proposed label instructions. Further, the trials have been conducted for succulent soybeans and peas, representing two major crops in the legume vegetables group, and for dried peas, soybeans, chickpeas and lupins, representing four major crops in the pulses group.

There is therefore sufficient data to establish group MRLs for both legume vegetables and pulses at the combined LOQ of 0.03 mg/kg. Harvest withholding periods are not required when the product is applied as directed. There is sufficient data for the establishment of a group stockfeed MRL at the rounded-up combined LOQ of 0.1 mg/kg for legume animal feeds. Residues of saflufenacil are not expected above the LOQ in cereal forage at 5 weeks after application based on the cereal trials. Even though the shortest forage harvest interval for legumes was 7 weeks, residue behaviour in legume forage is not expected to be different from cereal forage. Therefore, a 5-week grazing withholding period is sufficient for legume and pulse crops.

As sufficient data has been supplied to establish MRLs at the combined LOQ of 0.03 mg/kg for saflufenacil in cottonseed, rape seed and soybean, a group MRL of 0.03 mg/kg will be recommended for oilseeds. Similarly, group Table 4 entries of 0.1 mg/kg will be established for oilseed forage and oilseed fodder.

As residues were not found above the LOQ in raw soybeans in the soybean processing trial, even when treated at 300 g ai/ha, processed soybean commodity samples were not analysed. Saflufenacil residues are unlikely to be found in soybeans given the use pattern. They are also unlikely to concentrate in processed commodities, as shown by residues of saflufenacil not being found above the LOQ in treated cottonseed or cottonseed oil. Further evidence is provided by the sunflower processing study where sunflowers were treated 2 weeks prior to harvest in order to dessicate the plants. Finite residues were found in sunflower seed (up to 0.32 mg/kg), however residues were below LOQ in sunflower oil, showing that residues did not concentrate in sunflower oil. Establishment of an MRL for soybean oil is therefore unnecessary.

Orchard/vineyard use

Heat Herbicide is proposed for application as a tank mix with glyphosate in citrus, pome fruit, stone fruit or tree nut orchards, or in vineyards, at rates of 6-24 g ai/ha for control of grass and broadleaf weeds.

A large package of orchard crop data was collected in the USA and Canada, including stone fruit (6 cherry trials, 13 peach trials and 10 plum trials), citrus fruit (12 orange trials, 6 grapefruit trials and 5 lemon trials), pome fruit (15 apple trials and 10 pear trials), and tree nuts (5 almond and 5 pecan trials).

No residues of saflufenacil or its metabolites M800H11 and M800H35 were found above the LOQ in any of the treated or untreated control samples from the stone fruit, citrus fruit, pome fruit or tree nut trials. It is noted that no Australian residues trials have been conducted for use of saflufenacil for weed control in orchards or vineyards. However, given that the proposed use pattern is application using ground spraying equipment to the orchard floor, where the spray will make no contact with the trees, residues in Australian orchards are expected to be similar to those observed in US/Canadian orchards. Further, applications have been made at double the maximum rate proposed for Australia. The data package was sufficient to recommend MRLs at the combined limit of quantitation (0.03 mg/kg) for saflufenacil in stone fruit, pome fruit, citrus fruit and tree nuts. A harvest withholding period is not required when the product is used as directed. As no data has been supplied for grazing of treated pasture, a statement to the effect of ‘do not graze treated orchards’ is recommended for inclusion on the label.

Levels of saflufenacil and the two metabolites were below the LOQ in raw grapes from the grape processing trial, even though the orchard floor had been treated three times at more than 10 times the proposed maximum application rate. Because of this, the juice and raisins were not analysed. Given the use pattern and given that, for example, no saflufenacil residues were found above the LOQ in raw plums even when the orchard floor had been treated at 10X the proposed application rate, it is very unlikely that residues of saflufenacil will be found above the LOQ in raw grapes, juice, wine or dried grapes. The data supplied, when considered in conjunction with data for other orchard crops such as stone and citrus fruit, is sufficient to support an MRL at the combined LOQ of 0.03 mg/kg for saflufenacil in grapes. Separate MRLs are not required for processed grape commodities. A harvest withholding period is not required when the product is used as directed. As no data has been supplied for grazing of treated pasture, a statement to the effect of ‘do not graze treated vineyards’ is recommended for inclusion on the label.

Fallow use

The applicant is proposing use of *Heat Herbicide* for control of broadleaf and grass weeds prior to commencing, or during maintenance of, a fallow, and prior to establishing a forestry plantation at rates of 6-

18 g ai/ha. No residue data has been provided in support of this use pattern, which could give rise to residues in the meat and milk of animals grazing the treated areas. It is therefore proposed that a statement prohibiting the grazing of the treated weeds be included on the product labels.

4.6 Processing studies

Processing studies were conducted in cereals (aspirated grain fractions, middlings, flour, shorts, bran and germ of wheat; aspirated grain fractions, grits, meal, flour, oil and starch of corn; hulls, bran and polished rice; and sorghum molasses), cottonseed (refined oil, hulls and meal), soybeans (aspirated grain fractions, hulls, meal, and refined oil), sunflower seed, oranges (juice, oil and dried pulp), apples (juice and pomace), grapes (juice and raisins) and plums (prunes).

Processing study results for cereals, cotton, and sunflower have been discussed above and will be discussed again briefly here. No residues were found above the LOQ in cotton seed, meal, hulls, or oil, therefore the MRL for cottonseed will cover processed commodities, and no separate MRLs for processed cotton commodities are required.

In the cereal study, no residues were found in the wheat, rice, corn or sorghum raw commodities, and the decision was taken by the study authors not to analyse the processed commodities as a result. Given that residues were generally not found above LOQ in any of the raw cereal commodities even when making applications at up to 6X the proposed application rate, it is very unlikely that residues above the LOQ would be observed in any processed cereal commodities in practice. Therefore the MRL for cereal grains will cover processed commodities, and no separate MRLs for processed cereal commodities are required.

No processing data was supplied for canola. Canola seed is processed into oil in a similar fashion to cottonseed. No residues were observed in cottonseed oil in the processing study discussed above. It is unlikely that residues would be found in canola oil. Therefore, an MRL for rapeseed oil is not required, and residues in oil will be controlled by the raw commodity MRL.

As residues were not found above the LOQ in raw soybeans in the soybean processing trial, even when treated at 300 g ai/ha, processed soybean commodity samples were not analysed. Saflufenacil residues are unlikely to be found in soybeans given the use pattern. They are also unlikely to concentrate in processed commodities, as shown by residues of saflufenacil not being found above the LOQ in treated cottonseed or cottonseed oil. Further evidence is provided by the sunflower processing study where sunflowers were treated 2 weeks prior to harvest in order to dessicate the plants. Finite residues were found in sunflower seed (up to 0.32 mg/kg), however residues were below LOQ in sunflower oil, showing that residues did not concentrate in sunflower oil. Establishment of an MRL for soybean oil is therefore unnecessary. Registration in sunflowers is not proposed for Australia at this stage.

In the citrus processing trial, no residues of saflufenacil were found above the LOQ in raw oranges or in orange oil. In the other fruit processing trials (apples, plums and grapes), residues were not found above the LOQ in any of the raw fruit, even though applications were made at around 10 times the proposed maximum application rate. Processed commodities in the apple, grape and plum processing studies were not analysed for this reason, nor were the juice or dried pulp from the citrus processing study. However, given the proposed use pattern and the highly exaggerated application rates used in the field components of the

processing studies, residues of saflufenacil are very unlikely to be found above the LOQ in processed fruit commodities and separate MRLs for these commodities are not required.

4.7 Animal feeds

In the cereal residues trials discussed above, where applications was made at up to 6X the proposed maximum application rate for cereals in Australia, residues were below the LOQs of 0.025 mg/kg for individual residue components, and below the combined LOQ of 0.075 mg/kg in all samples of wheat, sorghum and corn forage, wheat and rice straw, wheat hay, and corn and sorghum stover, with the exception of two samples of sorghum stover from the US 6X trials were low levels (≤0.04 mg/kg) of residue were seen. MRLs at the rounded-up combined LOQ of 0.1 mg/kg for saflufenacil in cereal forage, cereal straw and fodder, sorghum forage, and sorghum straw and fodder are therefore proposed in conjunction with a 5-week grazing withholding period.

In the cotton residues and processing trials, no residues were found above the LOQ of 0.03 mg/kg for food items in cottonseed meal or hulls, or above the LOQ of 0.075 mg/kg for feed items in cotton forage. Therefore, a stockfeed MRL at the combined LOQ (0.03 mg/kg) will be established for saflufenacil in cottonseed meal and hulls. Cotton forage and trash are not generally fed to livestock, however since the proposed use is as a pre-emergent herbicide and residues are not expected in forage or fodder above the LOQ, stockfeed MRLs are supported at the rounded-up combined LOQ of 0.1 mg/kg for cotton forage and cotton fodder, in conjunction with a 5-week grazing withholding period.

In the canola residue trials, no residues were found above the feed item LOQ of 0.075 mg/kg in canola straw or forage. Although a limited number of trials have been conducted for canola, and the application rates were below the proposed maximum label rate (0.75X), the proposed use pattern in canola, application to soil prior to sowing, or prior to starting or maintaining a fallow, is the same as the proposed use pattern in cereals, for which an extensive data package is available. A stockfeed MRL at the rounded-up combined LOQ of 0.1 mg/kg for canola forage and fodder is supported, in conjunction with the 5-week grazing withholding period discussed above for cereal crops.

In the pulse and legume residue trials, no residues were found above the LOQ of 0.075 mg/kg for feed items in chickpea or lupin straw, in soybean hay, or in soybean or lupin forage. There is sufficient data for the establishment of a group stockfeed MRL at the rounded-up combined LOQ of 0.1 mg/kg for legume animal feeds. Residues of saflufenacil are not expected above the LOQ in cereal forage at 5 weeks after application based on the cereal trials. Even though the shortest forage harvest interval for legumes was 7 weeks, residue behaviour in legume forage is not expected to be different from cereal forage. Therefore, a 5-week grazing withholding period is sufficient for legume and pulse crops.

As mentioned above, data has been supplied for a sufficient number of oilseed crops (cotton, canola and soybeans) to establish group Table 4 entries of 0.1 mg/kg for oilseed forage and oilseed fodder.

4.8 Crop rotation

A rotational cropping metabolism study was conducted for wheat, lettuce and radish. A single spray application of radio-labelled (either at the phenyl or the uracil position) saflufenacil was made to soil at 150 g

ai/ha (~6X the proposed maximum application rate in Australia). The nature and levels of radioactive residue were measured in lettuce heads, radish roots and leaves, and wheat forage, straw, chaff and grain from crops planted 30, 120, or 365 days after application. Additionally, radish and lettuce were planted 58 days after application.

No residues were found above the LOQ in radish or lettuce, or in wheat grain or forage, for any of the components of the proposed residue definition. In wheat straw planted 30 days after application, residues of M800H35 were found at levels up to 0.045 mg/kg. In wheat straw planted 120 days after application, levels of M800H35 reached 0.030 mg/kg, while in straw from wheat planted 365 days after application, residues reached 0.031 mg/kg. In chaff, residues reached a maximum of 0.029 mg/kg for M800H11 and 0.162 mg/kg for M800H35 in wheat planted at 30 days, 0.026 mg/kg for M800H35 in wheat planted at 120 days, and 0.035 mg/kg M800H35 in wheat planted at 365 days. Scaling these residues for the expected maximum application rate (24 g ai/ha), the residues of all components in straw and chaff are expected to be well below the individual feed component LOQ (0.025 mg/kg), with the exception of 30 day chaff for which the scaled residue is 0.026 mg/kg, just above the LOQ. However, given that metabolism studies are conducted in protected cropping systems and residues are therefore higher than those observed in field systems, residues above the LOQ are not expected in practice in cereal crops planted in rotation with a treated crop. Further, the residue trials discussed in the sections above showed an essentially complete absence of residues in any raw or processed commodity derived from cereal, pulse, legume or oilseed crops which were treated at the time of sowing.

A field rotational study was conducted in NAFTA Growing Region 2 (3 trials in Georgia) and 10 (three trials in California). Saflufenacil was applied as a single pre-emergence application to the soil, after planting of the primary crop wheat, at 148-154 g a.i./ha. The representative rotational crops radish, lettuce, and wheat (spring and winter) were grown at plantback intervals (PBIs) of 4 months (119-125 days), 6 months (180-183 days) and 9 months (270-274 days). All rotational crop samples were harvested at commercial maturity, 34-169 days after planting (DAP) for radish, 39-187 DAP for lettuce, 59-147 DAP for forage and hay and 121-223 DAP for grain and straw. All collected samples were promptly frozen on the date of harvest.

The crop samples were analyzed for residues of saflufenacil (BAS 800 H) and its metabolites M800H11 and M800H35 using a validated liquid chromatography/mass spectroscopy/mass spectroscopy (LC-MS/MS) method.

Residues of saflufenacil and its metabolites M800H11 and M800H35 were all below the LOQ in rotated wheat (<0.025 ppm for wheat forage, hay and straw, <0.01 ppm for grain), radish (<0.01 ppm, top and roots) and lettuce (<0.01 ppm, leaves).

The field rotational crop study shows residues in following cereal crops, root vegetables, and leafy vegetables are unlikely to exceed the LOQ. Given that residues observed in the rotational crop trials, as well as in the residue trials for broadacre and orchard crops were all below the LOQ, regardless of the harvest interval, neither plant-back intervals nor MRLs in respect of rotational crops are required for saflufenacil.

4.9 Animal commodity MRLs

A feeding study was supplied for lactating dairy cattle. Three cattle were assigned to the untreated control group, three were assigned to the 0.1 mg/kg group, three to the 0.3 mg/kg group and five to the 1 mg/kg

group. The treated cattle were given the equivalent of the designated concentration of saflufenacil in feed daily for 28 days. Milk was collected twice daily and analysed. On one day, milk was separated into skim milk and cream to determine if there was any partitioning into milk fat. On day 29 the control cattle, and all treated cattle except two from the 1 mg/kg group were sacrificed, and samples of muscle, fat, liver and kidney were collected for analysis. The two remaining cattle were assigned to a depuration study and were placed on clean feed. One beast was sacrificed after two days depuration, while the second was slaughtered after 7 days. Tissue samples were collected for analysis as before.

In the dairy cattle feeding study, feed consumption, body weights and milk production were not adversely affected by daily oral administration of saflufenacil to dairy cows for 28-29 consecutive days at the target dose rates of 0.1, 0.3, and 1.0 mg/kg feed. The actual residue intakes (mean) in the diets were 0.118, 0.363, and 1.386 ppm. Residues of saflufenacil in all whole milk, muscle and fat samples were below the LOQ. There was no concentration of milk residues into skim milk or cream. Residues in kidney at the 0.1 mg/kg feeding level were below the LOQ, rising to 0.02 mg/kg for the 0.3 mg/kg dose group, and 0.04 mg/kg for the 1.0 mg/kg group. In liver, residues ranged up to 0.26, 0.88 and 3.49 mg/kg for the low, mid and high dose groups, respectively. The relationship between the feeding level and residues was linear (r^2 = 0.8859-0.9062). Clearance of saflufenacil residues from liver and kidney during the depuration period was relatively rapid, with half lives of 2.5 and 4.0 days in liver and kidney, respectively. Residues in kidney were below the LOQ by the end of the 7-day depuration period.

It should be noted from the goat metabolism study that saflufenacil parent compound was by far the most significant residue in both liver and kidney (71-80% of TRR), in which the highest residues are expected. No metabolism studies were conducted for the other components of the plant residue definition, M800H11 and M800H35. It is very unlikely that animal metabolism of M800H11 and M800H35 will lead to the synthesis of saflufenacil parent compound, which is the proposed animal commodity residue definition. Therefore, only the parent compound is of dietary significance in livestock when considering residues from feed intake. MRLs have been proposed at the rounded-up combined LOQ of 0.1 mg/kg for a number of key feed commodities, including cereal forage and fodder, cereal grains and legume animal feeds. Residues in livestock feed commodities have been measured on a fresh weight basis in the residues trials. However, given the results of the residues studies, residues of saflufenacil are not expected to be found in livestock feed in practice.

Therefore, MRLs of *0.01 mg/kg are recommended for saflufenacil in milk, mammalian meat, and mammalian edible offal.

A poultry feeding study was not provided. In the poultry metabolism study, two groups of eight hens were dosed with saflufenacil labelled with ^{14}C in either the phenyl ring or the uracil ring at a dose of 0.83-0.84 mg/kg bw/day, or 12.6-12.7 mg/kg in feed for 10 consecutive days. At sacrifice, the following levels of saflufenacil parent compound were found in tissues and eggs:

Residues of saflufenacil parent compound in hen tissues after 10 days dosing at 12.6-12.7 mg/kg (0.83-0.84 mg/kg bw/day)

Tissue	Saflufenacil residues (mg/kg)	
	Phenyl label	Uracil label
Muscle	0.006	0.005
Fat	0.002	0.002
Liver	0.029	0.028

Eggs (2-10 days pooled sample)	0.002	0.002

The only feed commodities relevant to the current application that are significant poultry feeds are cereal and pulse grains, and cottonseed meal. MRLs in these commodities have been established at the combined LOQ of 0.03 mg/kg. However, residues are not expected to be detected in these commodities in practice.

Therefore, MRLs for saflufenacil in poultry meat, poultry (edible offal of), and eggs are recommended at 0.01 mg/kg.

4.10 Spray drift

Aerial application of *Heat Herbicide* is not proposed. Ground application was modelled using AgDrift. The highest application rate proposed is 24 g ai/ha. It was considered that livestock will not simply graze at a single distance from the edge of a treated field, but will graze over the whole paddock, and will therefore sample a range of concentrations of drifted chemical on a pasture. Using the model parameters suited to a coarse spray application, with the maximum proposed application rate, the minimum practical pasture density of 1500 kg dry matter per hectare, and the transfer factor into liver of 1.78 calculated from the feeding study, the residue in liver for cattle grazing over a distance of 1 metre (the closest an animal is likely to get to an adjacent treated area) to 300 metres (the limit of the AgDrift model) from the edge of the sprayed area was calculated. This gave an expected liver residue of 0.068 mg/kg.

Given that the model parameters represent a worse case (a minimum pasture density and assuming that the wind was blowing onto the entire grazing paddock during the entire application), since residues are only likely to be observed in liver, and given that the short half life of the residue in liver (2.5 days) would mean that residues at the maximum likely concentration in liver of 0.068 mg/kg would drop below 0.01 mg/kg within 7 days of application, a buffer zone is not required on the label for the purposes of ensuring compliance with domestic or overseas MRLs for saflufenacil.

Separate modelling for orchard application was not conducted. As saflufenacil is a herbicide to be applied to the orchard floor, it will be applied by ground rigs not using airblast sprayers. Therefore, due to the trapping effect of the canopy, drift from orchard applications would be expected to be no more than from broadacre applications.

4.11 Bioaccumulation potential

The octanol/water partition coefficient ($\log_{10}P_{OW}$) of saflufenacil is 2.6. The animal transfer study showed no evidence of preferential partitioning of residues into fat. Therefore, saflufenacil is not considered fat soluble and has a low potential for bioaccumulation.

RISK ASSESSMENT CONCLUSIONS

4.12 Estimated dietary intake

The chronic dietary intake risk for saflufenacil has been assessed. The ADI for saflufenacil is 0.017 mg/kg bw/day, based upon a NOEL of 5 mg/kg bw/day and a 300-fold safety factor. The NEDI calculation is made

in accordance with WHO Guidelines[2] and is a conservative estimate of dietary exposure to chemical residues in food. The NEDI for saflufenacil is equivalent to 2.5% of the ADI. DIAMOND Modelling[3] of chronic dietary exposure is also performed on new chemicals, and chemicals with estimated dietary exposure greater than 90% of the ADI. The DIAMOND model estimated the chronic dietary exposure of saflufenacil as 1.96% of the ADI for the general population (mean consumption for all respondents), and 3.99% for the 90th percentile consumers.

The acute dietary intake risk for saflufenacil has been assessed. The ARfD for saflufenacil is 0.017 mg/kg bw/day, based upon a NOEL of 5 mg/kg bw/day and a 300-fold safety factor. The highest acute dietary intake was estimated at 14.2% of the ARfD, for 2-6 year olds consuming grapes. These calculations used the LOQ for the residue level in all food items, however residue data indicates that no residues are expected in practice.

It is concluded that the dietary exposure to saflufenacil is low and the risk from residues in food is acceptable when *Heat Herbicide* is used according to label directions.

4.13 Recommendations

The following amendments to the MRL Standard are recommended in relation to the proposed use of *Heat Herbicide*:

Table 1

Compound	Food		MRL (mg/kg)
ADD:			
Saflufenacil	GC 0080	Cereal grains	*0.03
	FC 0001	Citrus fruit	*0.03
	MO 0105	Edible offal (mammalian)	*0.01
	PE 0112	Eggs	*0.01
	FB 0269	Grapes	*0.03
	VP 0060	Legume vegetables	*0.03
	MM 0095	Meat (mammalian)	*0.01
	ML 0106	Milks	*0.01
	SO 0088	Oilseeds	*0.03
	FP 0009	Pome fruit	*0.03
	PO 0111	Poultry, edible offal of	*0.01
	PM 0110	Poultry meat	*0.01
	VD 0070	Pulses	*0.03
	FS 0012	Stone fruit	*0.03
	TN 0085	Tree nuts	*0.03

2 Guidelines for predicting dietary intake of pesticide residues, WHO, 1997.
3. DIAMOND: The DIamond Modelling Of Nutritional Data is a computer dietary modelling program based upon statistical software that is used by FSANZ.

Table 3

Compound	Residue
ADD: Saflufenacil	Plant commodities: Sum of saflufenacil, *N'*-{2-chloro-4-fluoro-5-[1,2,3,6-tetrahydro-2,6-dioxo-4-(trifluoromethyl)pyrimidin-1-yl]benzoyl-*N*-isopropyl sulfamide and *N*-[4-chloro-2-fluoro-5-({[(isopropylamino)sulfonyl]amino}carbonyl)phenyl]urea, expressed as saflufenacil equivalents. Animal commodities: Saflufenacil

Table 4

Compound	Animal feed commodity		MRL (mg/kg)
ADD: Saflufenacil		Almond hulls	*0.1
	AF 0081	Forage of cereal grains (green) [fresh weight]	*0.1
	AL 0157	Legume animal feeds [fresh weight]	*0.1
		Oilseed fodder	*0.1
		Oilseed forage (green) [fresh weight]	*0.1
	AF 0651	Sorghum forage (green) [fresh weight]	*0.1
	AS 0651	Sorghum straw and fodder (dry)	*0.1
	AS 0081	Straw and fodder (dry) of cereal grains	*0.1

The following withholding periods are required in conjunction with the above MRLs:

HARVEST WITHHOLDING PERIOD

Not required when used as directed. However, refer also to the withholding period of product/s mixed with Heat Herbicide.

GRAZING WITHHOLDING PERIOD

Do not graze treated broadacre crops or cut for stock food for 5 weeks after application.

Do not allow stock to graze treated orchards or vineyards.

Do not allow livestock to graze treated weeds.

5 ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

5.1 Commodities exported and main destinations

Some of the commodities of interest in connection with the proposed products, namely cereal grains, cereal hay, pulses, cotton, canola, pome fruit, stone fruit, citrus fruit, grapes (including dried grapes and wine), mammalian and poultry meat and offal, eggs, and dairy produce are considered to be major Australian export commodities.

Cereal grains

The total exports of Australian wheat and wheat flour were 13705 kilotonnes in 2009/10, at a total value of $3.686 billion. Key wheat export destinations are Indonesia, Japan, Korea, Malaysia, China and the Middle East.

Total exports of coarse grains (barley, oats, sorghum, maize and triticale) were 4995 kilotonnes, worth $1.286 billion, in 2009/10 (Australian Commodities Statistics 2010). This included 4256 kilotonnes of barley ($1.098 billion), 216 kilotonnes of oats ($53 million), 487 kilotonnes of sorghum ($116 million), and 36 kilotonnes of maize ($19 million).

Cotton

Total exports of raw cotton in 2009/10 were 395.4 kilotonnes, at a value of $754.6 million. Key export destinations for Australian raw cotton are P.R. China, Taiwan, Indonesia, Thailand and Korea (Australian Commodity Statistics 2010).

Oilseeds

Total exports of oilseeds (canola, cottonseed, linseed, peanuts, safflower, sunflower and soybean) were 1357 kilotonnes in 2009/10, at a total value of $652.83 million (Australian Commodities Statistics 2010). Exports of oils were 117.65 kilotonnes, worth $211.69 million, while meals exports were 61.08 kilotonnes ($28.38 million). Canola comprised the largest share of seed and oil exports, while cottonseed made up most of the meal exports. Major destinations for canola seed and oil exports were Japan, Pakistan, Bangladesh and New Zealand, while for cottonseed and cottonseed meal, the major markets were Japan and Korea.

Pulses and legumes

Australian legume exports in 2009/10 were 1578.7 kilotonnes, at a value of $774.7 million (Australian Commodities Statistics 2010). This included 360.8 kilotones of lupin ($116.5 million), 167.3 kilotonnes of field peas ($62.4 million), and 454.7 kilotonnes of chickpeas ($252.1 million).

Grapes and wine

Total Australian wine exports in 2009/10 were 775.47 megalitres, with a value of $2.1725 billion. Major export destinations for Australian wine include the USA, the UK, Canada, P.R. China, and New Zealand (Australian Commodities Statistics 2010).

Exports of dried vine fruits in 2009/10 were 4.0 kilotonnes, worth $13 million.

Citrus fruit

Total Australian citrus exports in 2009/10 were 159.36 kilotonnes at a value of $186.716 million. Most citrus exports were navel oranges, followed by mandarins (Australian Commodities Statistics 2010).

Pome fruit

In 2007/08, Australian apple exports were worth $7.13 million, with major destinations including the UK, Indonesia and Papua New Guinea. Pear exports were worth $6.64 million, with major destinations including New Zealand, Indonesia, Fiji, New Caledonia and Papua New Guinea.

Stone fruit

Australian cherry exports in 2007/08 were worth $15.23 million; major destinations included Thailand, Hong Kong, Singapore, Malaysia and the United Arab Emirates. Peach exports in 2007/08 were worth $3.46 million. Major destinations were Hong Kong, Malaysia, Singapore and the United Arab Emirates. Plum exports were worth $10.87 million, again with Hong Kong, Singapore and Malysia being major destinations.

Meat and dairy products

Total exports of dairy products in 2009/10 were worth $2.0342 billion, with key export destinations being Japan, Singapore, China, the Philippines, Thailand and the USA. Total exports of beef and veal were worth $4.144 billion in 2009/10, with the major destinations being Japan, the USA, Korea, Indonesia and Taiwan. Total exports of lamb and mutton were worth $1.4555 billion in 2009/10, with the top destinations being the USA, the European Union, Japan, and the Middle East.

5.2 Overseas registration status

Codex MRLs have not been determined for saflufenacil.

The following overseas residue MRLs/tolerances have been established in plant commodities:

Country/status	Commodity	Tolerance, mg/kg (expiry date)	Reference
Canada	Cereal grains	*0.03	List of Maximum Residue Limits Regulated Under the Pest Control Products Act (last update, 18/5/11)
	Citrus fruit	*0.03	
	Undelinted cotton seed	*0.03	
	Legume vegetables (succulent or dried)	*0.03	
	Pome fruit	*0.03	
	Grapes	*0.03	
	Tree nuts	*0.03	
	Stone fruit	*0.03	
	Sunflower seeds	1	
USA	Almond hulls	0.1	Electronic Code of Federal Regulations, Title 40: Protection of Environment, Part 180, Subpart C, section 180.649, 22 July 2010
	Cotton gin byproducts	0.1	
	Cotton, undelinted seed	0.03	
	Fruit, citrus, group 10	0.03	
	Fruit, pome, group 11	0.03	
	Fruit, stone, group 12	0.03	
	Grain, cereal, forage, fodder and straw, group 16	0.1	
	Grain, cereal, group 15	0.03	
	Grape	0.03	
	Nut, tree, group 14	0.03	
	Pistachio	0.03	
	Sunflower seed	1	
	Vegetable, foliage of legume, group 7	0.1	
	Vegetable, legume, group 6	0.03	

The following overseas animal commodity MRLs /tolerances have been established:

Country	Commodity	Tolerance, mg/kg (expiry date)	Reference
Canada	Fat of cattle, goats, hogs, horses and sheep	*0.01	List of Maximum Residue Limits Regulated Under the Pest Control Products Act (last update, 18/5/11)
	Meat of cattle, goats, hogs, horses and sheep	*0.01	
	Meat by-products (except liver) of cattle, goats, hogs, horses and sheep	0.02	
	Liver of cattle, goats, hogs, horses and sheep	0.8	
	Milk	*0.01	
USA	Cattle, fat	*0.01	Electronic Code of Federal Regulations, Title 40: Protection of Environment, Part 180, Subpart C, section 180.649, 22 July 2010
	Cattle, liver	0.8	
	Cattle, meat	*0.01	
	Cattle, meat byproducts, except liver	0.02	
	Goat, fat	*0.01	
	Goat, liver	0.8	
	Goat, meat	*0.01	
	Goat, meat byproducts, except liver	0.02	
	Hog, fat	*0.01	
	Hog, liver	0.8	
	Hog, meat	*0.01	
	Hog, meat byproducts, except liver	0.02	
	Horse, fat	*0.01	
	Horse, liver	0.8	
	Horse, meat	*0.01	
	Horse, meat byproducts, except liver	0.02	
	Milk	*0.01	
	Sheep, fat	*0.01	
	Sheep, liver	0.8	
	Sheep, meat	*0.01	
	Sheep, meat byproducts, except liver	0.02	

Australian MRLs in plant commodities are the same as those recommended in the USA and Canada, with the exception of an MRL of 1 mg/kg for saflufenacil in sunflower seeds, to cover a proposed pre-harvest dessication use. This use is not proposed for Australia, hence there is no need for the MRL.

Australia has proposed MRLs for poultry commodities, including poultry meat, poultry offal and eggs; the USA and Canada have not proposed or established MRLs for these commodities. However, Australian MRLs are at the LOQ. Australian MRLs for milk and mammalian meat are the same as those proposed by the USA and Canada, at the LOQ of 0.01 mg/kg. Unlike the USA and Canada, Australia has not established a separate MRL for mammalian fat, due to saflufenacil not being fat soluble. The proposed Australian MRL for edible mammalian offal, 0.01 mg/kg, is lower than that proposed for the USA and Canada for mammalian

liver (0.8 mg/kg); this is thought to be due to the pre-harvest dessication use in sunflowers in the US and Canada, which results in finite residues in sunflower meal.

The APVMA is not aware of any established or proposed MRLs in countries other than Australia, the USA or Canada at this stage.

5.3 Potential risk to trade

Australian MRLs in plant commodities are the same as those recommended in the USA and Canada, with the exception of an MRL of 1 mg/kg for saflufenacil in sunflower seeds, to cover a proposed pre-harvest dessication use. This use is not proposed for Australia, hence there is no need for the MRL.

It should be noted that since saflufenacil is a very new chemical, there are no established MRLs in other countries. However, all proposed Australian MRLs for plant commodities are at the limit of quantitation (LOQ). Based on the use patterns, detectable residues in plant commodities are not likely. Therefore, although most of the proposed use patterns are for major export crops (pome fruit, stone fruit, citrus fruit, cereals, cotton, legumes and oilseeds), there is unlikely to be any significant risk to trade in those commodities as a result of these products.

The overall risk to export trade in animal commodities is considered to be low. MRLs for saflufenacil in mammalian meat, mammalian edible offal, milk, poultry meat, poultry offal and eggs have been recommended at the limit of quantitation (0.01 mg/kg), so there is unlikely to be a risk to trade in those commodities.

The relevant industry groups should be given the opportunity to comment on the proposed application.

CONCLUSIONS

Cereal grains, oilseeds, pulses, legumes, citrus fruit, pome fruit, stone fruit and grapes*:** The available residues trial data, including extensive processing studies, show that residues are not expected in any of these commodities above the limit of quantitation (LOQ). MRLs are therefore proposed at the LOQ (0.03 mg/kg) in all cases. ***The risk to Australian exports of any of the relevant plant commodities is considered to be low, however APVMA welcomes any comments on this assessment.

Animal commodities*:** The overall risk to export trade in animal commodities is considered to be moderate. MRLs for saflufenacil in mammalian meat, mammalian edible offal, milk, poultry meat, poultry offal and eggs have been recommended at the limit of quantitation (0.01 mg/kg), so there is unlikely to be a risk to trade in those commodities. ***The risk to Australian exports of any of the relevant animal commodities is considered to be low, however APVMA welcomes any comments on this assessment.

6 OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

6.1 Health hazards

Saflufenacil (CAS No: 372137-35-4) is currently listed in Safe Work Australia's Hazardous Substances Information System (HSIS) Database (2011) as a hazardous substance. With the available toxicology information and according to NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004), OCS supports the current HSIS entry which classifies saflufenacil with the following risk phrases:

Xn; R63 (Repr. Cat. 3)	Possible risk of harm to the unborn child

The following cut-off concentrations apply for saflufenacil:

Conc. ≥ 5%	Xn; R63

Based on the product toxicology information, OCS has determined that SHARPEN WG Herbicide is classified as a hazardous substance according to the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004) with the following risk phrases:

Xn; R63 (Repr. Cat. 3)	Possible risk of harm to the unborn child

6.2 Formulation, packaging, transport, storage and retailing

The active ingredient saflufenacil will be manufactured overseas. SHARPEN WG Herbicide will be formulated in Australia or in overseas & imported to Australia as water dispersible granules packed in 1 kg and 5 kg high density polyethylene (HDPE) packages.

Transport workers and store persons will handle the active ingredient and/or packaged products, and could only become contaminated only if packaging were breached.

6.3 Use pattern

The product SHARPEN WG Herbicide is used prior to the establishment of fallows in winter and summer for broadacre and horticultural crops (barley, oats, wheat, chickpeas, faba beans, field peas, lentils, lupins, sub clover, cotton, cowpeas, sorghum and soybeans) or in young or established citrus, treefruits, nuts and grapevines. It is also used to assist in weed control in commercial, industrial and public service areas, around agricultural buildings, yards and other farm situations. SHARPEN WG Herbicide can also be used alone with a suitable adjuvant for control of volunteer cotton seedlings including Roundup Ready cotton.

The product is mixed with glyphosate herbicides (at a rate recommended on the label), 1% Bonza (an oil spray adjuvant) or 1% Hasten and water to a spray volume of 50 to 250 L/ha (minimum 80 L/ha for volunteer cotton). It is applied to weeds which are at an early growth stage (2-10 leafs) in winter or summer prior to sowing. It is recommended to apply SHARPEN WG Herbicide as a broadcast application using a conventional boom sprayer with either mechanical or by-pass agitation.

6.4 Exposure during use

Farmers and their employees will be the main users of the products. Workers may be exposed to the products when opening containers, mixing/loading, application, and cleaning up spills and equipment. The main route of exposure to the product/spray will be dermal and inhalation, although ocular exposure is also possible.

There are no worker exposure studies on saflufenacil or the product (SHARPEN WG Herbicide) available for assessment. In the absence of worker exposure data, the OCS used the Pesticide Handler Exposure Database (PHED) Surrogate Exposure Guide (1998) to estimate worker exposure during mixing/loading and application based on the maximum product use rate according to the Australian use pattern. The toxic endpoint of concern and identified NOAEL is derived from a developmental toxicity study in animals, and in this instance a margin of exposure (MOE) of 300 or above is acceptable. The MOE takes into account both interspecies extrapolation, intraspecies variability and to account for potential developmental concerns.

The MOE for worker exposure to SHARPEN WG Herbicide is at an acceptable level when wearing cotton overalls buttoned to the neck and wrist and elbow-length chemical resistant gloves for opening the container and preparing spray.

6.5 Exposure during re-entry

Do not allow entry into treated areas until the spray has dried, unless wearing cotton overalls buttoned to the neck and wrist (or equivalent clothing) and chemical resistant gloves. Clothing must be laundered after each day's use.

6.6 Recommendations for safe use

Users should follow the First Aid Instructions, Warning Statement, Safety Directions and Re-entry statement on the product label.

6.7 Conclusion

The registration of SHARPEN WG Herbicide a water dispersible granule formulation containing saflufenacil 700 g/kg for control of broadleaf weeds prior to establishment of crops, or in commercial, industrial and public service areas, is supported.

SHARPEN WG 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.

7 ENVIRONMENTAL ASSESSMENT

7.1 Introduction

BASF Australia Ltd is seeking registration from the Australian Pesticides and Veterinary Medicines Authority (APVMA) of a new active constituent, saflufenacil (BAS 800H), together with the associated end use product SHARPEN WG Herbicide (BAS 800 01H), a 700 g saflufenacil/kg WG formulation.

7.2 Environmental fate summary

Saflufenacil was stable in sterile aqueous solutions at pH 5, degraded slowly at pH 7, and was rapidly hydrolysed at pH 9 in experiments conducted at 25°C. The DT50 at pH 7 was estimated to be 248 days, while that at pH 9 was 4.9 days. The major products found at pH 9 were M800H04, M800H07, M800H15 and M800H33 (trifluoroacetone), and resulted from opening of the uracil ring. No major transformation products were isolated at pH 7. Under environmental conditions, hydrolysis is not expected to be a significant route of saflufenacil degradation, except at higher pH.

Saflufenacil degraded in pH 5 buffer under continuous photolytic conditions with a half-life of 28.0 days or 55.9 days based on a 12-hour light/12-hour dark cycle and was stable in the dark control. Since the intensity of the artificial light used was roughly equivalent to natural sunlight, the environmental phototransformation half-life of saflufenacil is ca. 56 days. In natural pond water (pH 7.1), the phototransformation half-life of saflufenacil is 10.8 days based on continuous irradiation used in the study and the environmental phototransformation half-life of saflufenacil is about 22 days. The half-life was 44.6 days in the dark controls with this value relatively uncertain since it is extrapolated beyond the duration of the study. In the pH 5 buffer solution no metabolites were found at levels greater than 10% of the total added radioactivity (TAR) at the end of the photolysis period. In the natural water system, hydrolysis appeared to contribute to the degradation, and M800H07, trifluoroacetone, and trifluoroacetic acid (TFA) were identified at levels approaching or exceeding 10% TAR. Aqueous photolysis in natural neutral and slightly basic water systems may be an environmental degradation mechanism for saflufenacil.

Saflufenacil degraded on the soil surface during irradiation in a 12 hour light/dark cycle with a calculated DT50 of 29.3 days with a dark control DT50 of 52.8 days. No degradation products were found at levels greater than 10% TAR, but several minor components were observed. Two major transformation products, M800H07 and M800H08 were isolated in the dark controls. The phototransformation half-life for saflufenacil is 65.9 days based on the 12 hour light/12 hour dark cycle used in the study and the estimated environmental phototransformation half-life of saflufenacil is ca. 66 days. Under continuous irradiation, saflufenacil had half-lives of 19.0 days in the irradiated samples and 34.4 days in dark controls. DT50s were not observed in the irradiated samples or dark controls. The estimated environmental phototransformation half-life of saflufenacil is ca. 83 and 87 days. The only major transformation product in the irradiated sample was not identified but characterized as a compound with an intact methyl group on the uracil ring and an intact isopropyl side chain that degraded to M800H01. M800H08 was the only major transformation product in the dark controls. Soil photolysis can be a contributing factor to the degradation of saflufenacil under field conditions.

Saflufenacil is expected to undergo ready atmospheric degradation based on its calculated hydroxyl radical interaction atmospheric half-life of 0.307 days (12 hour day) and its 6.55 days ozone interaction half-life.

Under aerobic conditions saflufenacil degraded in four different North American soils (sandy loam, silty clay loam, silt loam and loamy sand) at 25°C with DT50 values ranging from 8.6 to 26 days. DT90s ranged from 38 to 153 days. Seven transformation products were identified and quantified as being present at 10% or more of the TAR at certain times during the study: M800H01, M800H02, M800H07, M800H08, M800H22, M800H26 and M800H31. M800H02 and M800H08 were major transformation products in every soil type. All the other identified degradates were present as a major transformation product in at least one soil type. In soil treated with [14C-Uracil] saflufenacil, CO2 was found at levels up to 15.3% TAR, demonstrating further degradation. Bound residues reached maximum levels of 15-35% TAR by the end of the study. In a separate experiment a single soil was dosed with M800H08 and a DT50 was calculated to be 433 days with M800H22 the only transformation product identified.

Under reasonably maintained, anaerobic soil conditions, degradation of parent saflufenacil and formation of degradation products over a 92 day period were both slowed compared to the rates of degradation seen in aerobic soil conditions. Three major non-volatile transformation products, M800H08, M800H01, and M800H02, and four minor products, M800H15-ketohydrate, M800H22, M800H07, and trifluoroacetic acid were detected with the first five of these transformation products detected with both labels. M800H07 was detected in phenyl-label treated systems and trifluoroacetic acid in uracil-label treated systems. In the soil, calculated linear and non-linear single first order (SFO) DT50s for the combined labels, were 47 days and 11 days respectively. In the total system, non-linear SFO DT50 and DT90 (combined labels) values were, respectively 217 and 721 days.

Saflufenacil degraded in an aerobic pond water-sediment system incubated in the dark and in additional samples irradiated on a 12 hour light/dark cycle. In the dark, saflufenacil dissipated with half-lives of 71 days in the total system and 56 days in the water layer. Half-lives were not calculated for the sediment because of insufficient dissipation. In the 12 hour light/dark cycle, saflufenacil degraded in the total system with the following respective DT50 and DT90 values: water, 2.8 and 9.5 days; sediment, 4.9 and 16 days and total system, 3.6 and 12 days. In both systems, three transformation products were identified - M800H07, trifluoroacetone and trifluoroacetic acid. M800H07 and trifluoroacetone were major transformation products in the total system and water. M800H07 was a minor transformation product in sediment, and trifluoroacetone was not detected in the sediment. Trifluoroacetic acid was a minor transformation product in the water and sediment and was a major transformation product in the total system because it continued to accumulate until study termination. Saflufenacil remained primarily in the water phase and aerobic aquatic metabolism is considered to be an important degradation route for saflufenacil, especially in the presence of light.

Saflufenacil degraded in an anaerobic aquatic water-sediment system, such that by 91 DAT essentially none remained in either phase although the test conditions appear to have varied throughout the 364-day incubation with conditions being reducing to strongly reducing based on redox potentials in the sediment. Dissolved oxygen concentrations at the water/sediment interface indicated that anaerobic conditions were not completely maintained. Saflufenacil dissipated with half-lives of 29 days in the total system, 24 days in the sediment layer, and 26 days in the water layer. Half-lives are uncertain in the sediment layer because of the pattern of dissipation; sediment concentrations were 11.1-15.8% of the applied at 3 through 30 days post-treatment, then dropped by >80% between 30 and 62 days. M800H07, M800H15-ketohydrate,

trifluoroacetic acid, trifluoroacetone, and trifluoro-2-propanol were major transformation products in the water and total system. M800H07 was the only major transformation product in the sediment. Degradation occurred mainly through hydrolysis of the uracil ring to produce several metabolites which remained predominantly in the water phase. From the phenyl labelled test substance, the major metabolite was the urea M800H07, which comprised approximately 67% of the TAR at the end of the study. In the total systems, the major transformation product, M800H15-ketohydrate, declined with time from its maximum at 91 DAT.

Saflufenacil is very slightly volatile, moderately soluble expected to show only very slight volatility from water.

The sorption of saflufenacil and metabolites M800H01, M800H02, M800H07, M800H08, M800H15, and M800H22 was determined in six US soils with a range of characteristics. Freundlich isotherm adsorption values for saflufenacil (Koc, mL/g) ranged from 9.3 to 55 and potential mobility in soil is indicated. Saflufenacil desorption Koc values ranged from 10 to 51. The saflufenacil metabolites also had low KOC values that ranged from 3.3 to 111. The respective ranges for the metabolites were: 4.8-27, 6.7-41, 3.3-111, 4.8-20, 9.6-57 and 5.2-25. The equivalent desorption Koc values were: 4-26, 6-39, 3-107, 4-20, 9-57 and 4-22. Koc values indicate that these degradates can be expected to be weakly adsorbed to soils.

Three studies with total of five sites in the United States of America and two sites in Canada were designed to evaluate the field behaviour of saflufenacil and its degradates in soils supporting uses in pine/vegetation management, orchards/vineyards, and field/row crop production. The saflufenacil field dissipation DT50 values ranged from 1.4 to 35.5 days and DT90 values, from 4.5 to 118 days. Field results for M800H08 indicate that it is more persistent than saflufenacil, with DT50 values of between 33.6 and 149 days and respective DT90 values of 112 and 494 days. Residues of saflufenacil were generally restricted to the top soil and not greater than the 45-60 cm soil depth with this result occurring in one soil only at the limit of determination (0.01 ppm) following application at a rate approximately 17-times that proposed for Australia. Transformation products were generally restricted to the top soil and present in low concentrations. Saflufenacil is expected to degrade readily in the field environment with a variety of transformation products, particularly M800H08, expected to form. The degradation of saflufenacil should limit its mobility in the soil profile. Expected soil metabolite products also have low soil sorption values and have some potential for mobility depending on the rate of degradation.

Bioaccumulation of saflufenacil in bluegill sunfish was negligibly low. The uptake reached steady state conditions at very low residue levels within 14 days of a 28 day exposure period and the bioconcentration factor at steady state in whole fish was 3.91 exposed to 1.0 µg saflufenacil/L) and bioaccumulation of saflufenacil is not to be expected in aquatic systems. The low BCF value did not trigger any metabolism investigations on fish or tank water samples. Following 16 days of depuration, [14C] saflufenacil residues in the whole fish decreased by a mean of 70.5%, contrasting with no significant depuration after 16 days in fish exposed to 10 µg saflufenacil/L.

7.3 Environmental toxicity summary

Acute toxicity studies showed that saflufenacil is practically non-toxic to birds. The oral and dietary acute toxicity values were LD_{50} >2000 mg/kg and LC_{50} >5275 mg ac/kg diet, respectively, for both bobwhite quail and mallard duck. The reproductive toxicity studies showed that saflufenacil is not toxic to birds with NOECs for bobwhite and mallard duck being 96 mg and 279 mg ac/kg diet, respectively.

Acute fish toxicity studies showed that saflufenacil is practically non-toxic to fish. The tests showed the 96 h LC_{50} of the most sensitive species, sheephead minnow, being >98 mg ac/L. In addition, a 33-day chronic toxicity study on the fish early life stage showed that saflufenacil is very slightly toxic to fathead minnow (LC50 >9.63 mg ac/L).

Acute toxicity of saflufenacil to aquatic invertebrates varies from practically non-toxic to moderate toxicity. Daphnia is the least sensitive species with LC_{50} > 98.2 mg ac/ha, while mysid shrimp and eastern oyster with LC_{50}= 8.5 mg ac/L and EC_{50} >6.08 mg ac/L respectively, are the most sensitive aquatic species. In addition, a 21 day chronic toxicity study showed that saflufenacil is very slightly toxic to daphnia. Further, the acute aquatic toxicity of the metabolite M07 showed that this metabolite is also practically non-toxic to mysid shrimp (>98 mg ac/L).

A toxicity study on chironomids showed that saflufenacil is very slightly toxic to these sediment dwelling organisms. The 28 day LC_{50} for sediment and overlying water were found to be >7.68 mg ac/L and >5.18 mg ac/L, respectively. Due to its solubility, saflufenacil dissipates quickly from sediment into water.

Saflufenacil is highly to very highly toxic to duckweed (EC_{50} frond count = 87 µg ac/L), green algae (E_rC_{50} = 120 µg ac/L) and saltwater diatoms (700 µg ac/L). However, it was found to be at worst moderately toxic to freshwater diatoms (E_rC_{50} >9.2 mg ac/L) and slightly toxic to blue-green algae (E_rC_{50} >63.6 mg ac/L). The toxicity studies on the metabolites M07 and M08 showed that these are at worst slightly toxic to duckweed and green algae. The lowest endpoint of these metabolites was that of M08 to duckweed (EC_{50} = 12 mg/L).

Acute toxicity studies of saflufenacil to terrestrial invertebrates showed that it is very slightly toxic to these organisms. Studies on honey bees found acute contact LD_{50} >100 µg ac/bee and acute oral $LC_{50\ is}$ >121 µg ac/bee; for parasitic wasps (*A. rhopalosiphi*) and predatory mites (*T. pyri*) the acute contact LR_{50} were 567 g ac/ha and 453 g ac/ha, respectively. Studies on earthworms, found that the LC_{50} of saflufenacil and M08 were both >1000 mg ac/kg,

Toxicity at the proposed application rates saflufenacil is not expected to have a significant effect on soil microbes.

Saflufenacil was found to be very highly toxicity to terrestrial plants. The effects were shown in terms of emergence, survival and growth (dry weight and plant heights). The biggest effect in terms of plant survival (i.e. mortality) was found in lettuce with LC_{50} = 0.403 g ac/ha shown in vegetative vigour tests. In terms of growth, the biggest effect found was also on the vegetative vigour test where tomato was the most sensitive species with EC_{50} dry weight = 0.26 g ac/ha. The two major metabolites M07 and M08 are moderately, and possibly highly, toxic to terrestrial plants with NOEC = 0.0481 mg/ha and EC_{50} >0.3840 mg/kg dw.

7.4 Risk Assessment

BASF Australia Ltd has applied for registration of a new herbicide - Sharpen WG Herbicide, containing 700 g/kg of the new active constituent saflufenacil for the control of a broad range of weeds in a wide range of field crops and orchards. It is proposed that the product would be routinely tank mixed with glyphosate; the latter is a widely used herbicide and will be used at recommended label rates, which are normally substantially higher than the rates of saflufenacil. Only ground application is proposed.

The risk assessment of both saflufenacil and glyphosate also showed that at the maximum recommended rate they will not pose an unacceptable risk to terrestrial vertebrates and invertebrates. Given that Q values are generally very low for each individual herbicide, the expected risk of the tank mix is also expected to be acceptable.

Saflufenacil is very slightly toxic to fish and aquatic invertebrates, but it is highly toxic to aquatic plants and some algae. However, the risk assessment of saflufenacil showed that even with a 10% spray drift the risk to aquatic environments is acceptable. Despite the larger dose of glyphosate, the risk is also acceptable and considering its properties, expected to be acceptable for the tank mix as well.

The risk to aquatic environments that could result from the runoff was considered only for saflufenacil, because it is the mobile active constituent of the tank mix. Calculations of risk associated with the runoff of saflufenacil under the worst case scenario showed that, when 5% of the applied product is washed into aquatic environments, the risk is expected to be acceptable.

Given the broad pattern of use and its very high toxicity to terrestrial plants, spray drift of saflufenacil can pose an unacceptable risk to nontarget plants. In addition, because of the frequency of its use as a mandatory tank mix with glyphosate, the risk to non-target terrestrial plants was assessed for each herbicide using a ground spray drift model (AgDRIFT).

The results of the individual risk calculations for each herbicide indicate that in terms of spray free zone for a given spray quality, the risk of saflufenacil is slightly higher than that of glyphosate. It is noted again that glyphosate is a widely used herbicide and no buffer zones are established. Therefore, this risk assessment referred to the use of saflufenacil alone and to its use in tank mix with glyphosate.

In regard to the tank mix with glyphosate, recent studies suggest that there is an increased effect when the two herbicides are combined. This increase can be up to 65% (in biomass reduction) when the rates of saflufenacil (25 g ac/ha) and glyphosate (2.25 kg ac/ha) are similar to the proposed application (~24 g ac/ha and 2.16 kg ac/ha respectively), compared to when the saflufenacil is applied alone.

The increase in the combined effect of the herbicides is a measure of increased phytotoxicity of the tank mix. Due to the lack of appropriate joint toxicity data, DSEWPaC used this as one of the criteria in this assessment to estimate the risks of the combined toxicity of the tank mix, by assuming an increase of 65% in the combined toxicity for the tank mix. The resulting spray free zone of the tank mix was estimated to be beyond the limits of AgDRIFT model (i.e. >300 m) for medium and fine spray qualities. However, the model showed that for coarse spray quality, a spray free zone of 250 m must be kept to the nearest non-target vegetation for an acceptable risk.

The APVMA has considered the findings of the DSEWPaC and accepts these conclusions.

8 EFFICACY AND SAFETY ASSESSMENT

The applicant seeks to register SHARPEN WG Herbicide, containing 700 g/kg saflufenacil in water dispersible granule formulation (WG) formulation as a post-emergence herbicide to be added to Roundup Attack Herbicide to improve the control of certain broadleaf weeds including fleabane prior to the establishment of fallows, prior to establishing winter and summer broadacre crops and forestry plantations, in commercial, industrial and public service areas, around agricultural buildings, yards and other farm situations.

SHARPEN WG Herbicide containing the new active ingredient Saflufenacil is a fast acting contact herbicide and aids in control of weeds through a process of membrane disruption. SHARPEN WG Herbicide is rapidly absorbed through the foliage of plants. Within a few hours following application, the foliage of susceptible weeds will show signs of desiccation, and in subsequent days necrosis and death of the plant. Saflufenacil has been classified as a Group G mode of action for weed resistance management.

8.1 Proposed use pattern

SHARPEN WG Herbicide is a post-emergence herbicide to be added to glyphosate herbicide (Roundup Attack Herbicide) at a rate of 9 -34 g/ha to improve the control of certain broadleaf weeds (at a rate of 9 -26 g/ha) including fleabane (at a rate of 17 -34 g/ha) prior to the establishment of fallows, prior to establishing winter and summer broadacre crops, in commercial, industrial and public service areas, around agricultural buildings, yards and other farm situations. SHARPEN WG Herbicide may be used alone with a suitable adjuvant for control of volunteer cotton seedlings including Roundup Ready Flex cotton. The foliar uptake of SHARPEN WG Herbicide is rapid and plant desiccation can occur within 4 days of application. SHARPEN WG Herbicide is intended to target small actively growing weeds. Subsequent germinations will not be controlled.

8.2 Summary of Evaluation of Efficacy and Crop Safety

Australian data were derived from 35 trials, including 6 for crop safety. All trials were for broadacre farming except for one wine grape efficacy trial. All data presented were derived from small plot randomised complete block replicated trials. All US data were for crop safety on grain sorghum (4 trials) and cotton (11 trials). Canadian data were derived from 104 efficacy trials and 150 crop safety trials for ‘winter crops’ and 37 and 55 efficacy and safety trials for soybeans and maize respectively.

Trial designs, location, timing, formulations tested were accurately targeted at gaining registration for Saflufenacil formulations (BAS 800). In all three countries, trials were located widely covering a range of soil types and environments. Timings were aimed at pre-sowing and fallow applications in Australia with and without glyphosate. Canadian data were generated to evaluate pre-sowing and chemical fallow applications, but also looked at residual suppression of weeds post-sowing.

Australian trials targeted the major pre-plant/fallow weed problems in both southern and northern farming systems, particularly those species that have tolerance or resistance to glyphosate. These species include capeweed, Indian hedge mustard, volunteer lupins, small flowered mallow, muskweed, Paterson’s curse, sowthistle, emex, wild radish, cowvine, bladder ketmia, small fleabane, volunteer cotton and barnyard grass.

Sufficient Australian data were presented to prove the equivalence of Saflufenacil formulations and the benefit of using an oil adjuvant.

The claims, directions for use and label instructions of Sharpen WG Herbicide label are largely supported by the data package presented. Minor modifications recommended by the efficacy reviewer in regard to - dropping the mallow size to 6 leaf, adding Roundup Ready™ canola and *Fallopia convolvulus*, tightening 'Critical Comments' regarding crop tolerance and the method of sowing the crop and suggesting higher application volumes are used if applying in coarse droplets in stubble, have been incorporated to amend the label.

8.3 Assessment of trial results

All Australian data presented were included in the assessment. Crop safety data for grain sorghum and cotton from the USA were also included. The Canadian data package was also utilised.

Australian Data

Thirty five trials were presented, with 29 trials primarily evaluating efficacy and six trials for crop safety. A range of soil types and environments has been tested. Dry conditions in southern Australia in 2005 and 2006 may have reduced the levels of crop damage. Most trials were conducted in randomised complete block designs replicated three or four times, with two exceptions where a more complex factorial design was required.

Analysis of variance was used and evaluated at a 95% confidence interval. Trials were conducted by qualified technical staff or contractors.

Saflufenacil herbicides improved early burndown of many broadleaf species and improved the control of certain species over glyphosate alone. These species include glyphosate resistant and conventional volunteer cotton, cowvine, dwarf amaranth, bladder ketmia, sowthistle, capeweed, small fleabane, prickly lettuce, Paterson's curse, spiny emex, subterranean clover, wild radish, turnip weed, muskweed, *Vulpia* spp and barnyard grass and liverseed grass.

In regards to crop safety, wheat, barley, oats, lupins, chickpeas appear unaffected when applied up to sowing at the proposed rates. Lentils, faba beans, soybean, cotton, cowpea, sorghum exhibit a narrow safety margin, while canola and sunflowers are susceptible. Addition of a crop oil improved early burndown.

USA Data

Data from four sorghum trials and 11 cotton trials were presented. Replicated small plot trails were used for both conventional and no-till. Qualified technical staff conducted these trials. The WDG formulation was tested at 18, 36 and 72 g ai ha^{-1} pre-plant and postsowing pre-emergent. A range of soil types and localities were tested. Soil texture influences crop tolerance.

Canadian Data

Canadian efficacy and crop safety data was also assessed. The frequency distribution tables were used to present results from 104 efficacy and 150 crop safety trials for small grain crops, 37 efficacy and tolerance trials for soybean and 55 efficacy and tolerance trials for maize.

Small plots trials conducted in randomised complete block design with 4 replicates. The investigated rates used at 12.5, 18, 25, 38 and 50 g ai/ha, with and without glyphosate at 450 and 900 g ai/ha. A range of soil types was tested – sandy loam to clay; pH 5.8-8.4; organic matter – 2-10%; Evaluations were conducted at 3-12; 13-28; 29-42; and 43+ DAT. The investigation looked into formulation bridging, weed burndown (pre-sowing and chemical fallow) and residual suppression. Qualified technical staff conducted these trials.

The emulsifiable concentrate and water dispersible granule formulations of Saflufenacil were found to be biologically equivalent. Use of Saflufenacil herbicides with glyphosate improved the control of the following weeds up to the 8 leaf stage - conventional and herbicide resistant canola, Fallopia *convolvulus, Chenopodium album*, small *Kochia scoparia, Malva pusilla, Sinapis arvensis, Thlaspi arvense*, and *Amaranthus retroflexus*. A 50 g ai/ha pre-sowing application showed suppression of the re-establishment of *S. arvensis, T. arvense, F. convolvulus*, and *A. retroflexus*. The herbicide application appeared to be safe pre-sowing on spring & winter wheat, durum, barley, oats canary seed and chickpeas up to 50 g ai ha^{-1}. Lentils and soybeans were safe up to 18 and 25 g ai ha^{-1} respectively pre-plant, while maize can tolerate 50 g ai ha^{-1}.

Conclusion

The trial data presented substantiates the claims on the proposed labels for Sharpen WG Herbicide. The Directions for use, restraints, situations, weeds and weed stage and advice or critical comments on crop safety, application techniques, withholding periods, resistance weeds warning all appears to be appropriate.

Therefore, in terms of the evidence for the efficacy of the product and its safety to target and non-target species, the application by BASF Australia Pty Ltd for the registration of SHARPEN WG Herbicide is supported whin used in accordance with the proposed label instructions and Good Agricultural Practice (GAP).

9 LABELLING REQUIREMENTS

CAUTION

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

SHARPEN® WG HERBICIDE

ACTIVE CONSTITUENT: 700g/kg SAFLUFENACIL

GROUP	G	HERBICIDE

For improvement in the control of specified broadleaf and grass weeds - prior to establishment of crops and forestry plantations; fallows; in commercial, industrial and public service areas; around agricultural buildings and yards - in tank mixture with Roundup® Attack™ Herbicide and control of volunteer cotton seedlings including Roundup Ready Flex® cotton as per the Directions For Use Table.

IMPORTANT: READ THE ATTACHED LEAFLET BEFORE USING THIS PRODUCT

POWERED BY KIXOR™

NET CONTENTS: 1 & 5 kg

Distributed by:
Nufarm Australia Limited
ACN 004 377 780
103-105 Pipe Road
Laverton North Victoria 3026
Tel: (03) 9282 1000
Fax: (03) 9282 1001

® Registered trademark of BASF

APVMA Approval No: **62853/44119**

STORAGE AND DISPOSAL
Store in the closed, original container in a dry, cool, well ventilated area out of direct sunlight. Triple or preferably pressure 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 bury empty containers in a local authority landfill. If no landfill is available, bury the containers below 500 mm 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 and Territory government regulations. Empty containers and product should not be burnt.

SAFETY DIRECTIONS
May irritate the eyes and skin. Avoid contact with eyes and skin. When opening the container, mixing and loading and preparing spray, wear cotton overalls buttoned to the neck and wrist and elbow length chemical resistant gloves. Wash hands after use. After each days use wash gloves and contaminated clothing.

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

ADDITIONAL USER SAFETY INFORMATION
WARNING: DO NOT use if pregnant.

MATERIAL SAFETY DATA SHEET
For further information refer to the Material Safety Data Sheet (MSDS), which can be obtained from your supplier or the Nufarm website - www.nufarm.com.au)

In case of emergency: Phone 1800 033 498
Ask for shift supervisor. Toll free 24 hours.

Conditions of sale
Any provisions or rights under the Competition and Consumer Act 2010 or relevant state legislation which cannot be excluded by those statutes or by law are not intended to be excluded by these conditions of sale. Subject to the foregoing, all warranties, conditions, rights and remedies, expressed or implied under common law, statute or otherwise, in relation to the sale, supply, use or application of this product, are excluded. Nufarm Australia Limited and/or its affiliates ("Nufarm") shall not accept any liability whatsoever (including consequential loss), or howsoever arising (including negligence) for any damage, injury or death connected with the sale, supply, use or application of this product except for liability which cannot be excluded by statute.

SHARPEN is a registered trademark of BASF.

APVMA Approval No: **62853/44119**

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BN:

DOM:

CAUTION

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

SHARPEN® WG HERBICIDE

ACTIVE CONSTITUENT: 700g/kg SAFLUFENACIL

GROUP	G	HERBICIDE

For improvement in the control of specified broadleaf and grass weeds - prior to establishment of crops and forestry plantations; fallows; in commercial, industrial and public service areas; around agricultural buildings and yards - in tank mixture with Roundup® Attack™ Herbicide and control of volunteer cotton seedlings including Roundup Ready Flex® cotton as per the Directions For Use Table.

IMPORTANT: READ THIS LEAFLET BEFORE USING THE PRODUCT

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Laverton North Victoria 3026
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Fax: (03) 9282 1001

DIRECTIONS FOR USE

RESTRAINT
DO NOT apply by aerial application.

SPRAY DRIFT RESTRAINTS
DO NOT apply with spray droplets smaller than a **COARSE** spray droplet size category according to "*APVMA Compliance Instructions for Mandatory COARSE or Larger Droplet Size Categories"* located under this title in the GENERAL INSTRUCTIONS section of this label.
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 WHEN NOT USED IN TANK MIX
DO NOT apply if there is non-target vegetation downwind from the application area and within the mandatory no-spray zone shown in the table below.

Coarse Spray Quality (ASAE S572 definition for standard nozzles)	
Wind Speed Range at Time of Application	**Downwind No-Spray Zone**
3 to 20 kilometres per hour	100m

MANDATORY NO-SPRAY ZONES WHEN USED IN TANK MIX WITH GLYPHOSATE
DO NOT apply if there is non-target vegetation downwind from the application area and within the mandatory no-spray zone shown in the table below.

Coarse Spray Quality (ASAE S572 definition for standard nozzles)	
Wind Speed Range at Time of Application	**Downwind No-Spray Zone**
3 to 20 kilometres per hour	250m

Situation	Weeds	Weed Stage	Rate	Critical Comments
Prior to sowing the following **Winter** broadacre crops Cereals - Barley - Oats - Wheat Pulses - Chickpeas - Faba beans - Field peas - Lentils - Lupins Legumes - Sub clover Prior to starting a fallow, fallow maintenance and prior to establishment of Forestry Plantations	Amsinckia *Amsinckia spp.,* Annual ryegrass *Lolium rigidum,* Barley grass *Hordeum spp.,* Brome grass *Bromus spp,* Capeweed *Arctotheca calendula,* Indian hedge mustard *Sisymbrium orientale,* Lupins (volunteer) *Lupinus angustifolius* Marshmallow / Small flowered mallow (max 6 leaf) *Malva parviflora,* Medics *Medicago spp.,* Muskweed *Myagrum perfoliatum,* Paterson's curse *Echium plantagineum,* Sowthistle *Sonchus oleraceus*, Spiny emex / Doublegee / Three-cornered Jack *Emex australis,* Storksbill - long *Erodium botrys,* Sub. clover *Trifolium subterraneum,* Turnip weed *Rapistrum rugosum,* Volunteer canola (max 4 leaf) including Roundup Ready® varieties *Brassica napus,* Wild oats *Avena spp.,* Wild radish *Raphanus raphanistrum*	Apply as a tank mix with Roundup® Attack™ Herbicide to weeds at growth stage 2 leaf to 10 leaf Note: and small flowered mallow, maximum 6 leaf; Volunteer canola, maximum 4 leaf	9 – 26g/ha plus Bonza at 1% plus recommended label rate of Roundup Attack Herbicide	**DO NOT apply post-sowing pre-emergent** **ALWAYS apply SHARPEN WG Herbicide with an oil adjuvant such as Bonza.** Use of SHARPEN WG Herbicide with Roundup® Attack™ Herbicide with IQ inside™ will increase the speed at which specified broadleaf and grass weeds develop visible symptoms (compared to results achieved with Roundup Attack applied alone). The use of SHARPEN WG Herbicide with Roundup Attack may improve final control of broadleaved weeds including certain less sensitive weeds such as bladder ketmia, cowvine and marshmallow. Refer also to the Roundup Attack label for information on handling and use. Use the lower rates on younger plants or plants growing under good conditions and the higher rates on older plants or plants growing under less optimum conditions. Apply only as a tank mix with recommended rates of Roundup Attack. Refer to the appropriate label for weed sizes and follow all label directions. Bonza at 1% v/v must be added when applying SHARPEN WG Herbicide with glyphosate herbicides. If one of the listed weeds is the dominant weed, and there is no specific rate for it on the Roundup Attack label, consult the label's annual-weed rate-range. Select from within this range to suit the weed-stage, weed-density, conditions (etc) of your situation. To ensure uptake of SHARPEN WG Herbicide, DO NOT sow crops for at least 1 hour after application. Crop tolerance to SHARPEN WG Herbicide by the IBS sowing method is very good and is maximised if the seeder is fitted with knifepoints and press wheels to remove treated soil from above the seed. Sow crops with a seeder that will move treated soil away from crop row. This is particularly important with lentils and faba beans. Use of seeders, or planting under conditions that do not move treated soil from the crop row may increase the level of early crop damage. Refer to the plant-back interval table on this label and also refer to the appropriate companion product label, in case a longer re-crop sowing period is required.
Prior to sowing the following **Summer** broadacre crops Cotton Cowpeas Sorghum Soybeans Prior to starting, or maintaining a fallow. To assist in weed	Weeds as above if appropriate and in addition: Bladder ketmia (max 6 leaf) *Hibiscus trionum,* bindweed/climbing buckwheat (*Fallopia convolvulus*), Cowvine (Peachvine) *Ipomoea lonchophylla,* Marshmallow / Small flowered mallow (max 6 leaf) *Malva*	Apply as a tank mix with Roundup Attack Herbicide. Weed growth stage 2 leaf to 10 leaf Note: Bladder ketmia and small flowered mallow, maximum 6 leaf	9 – 26g/ha plus Bonza at 1% plus recommended label rate of Roundup Attack Herbicide	Refer to Critical Comments above and in addition: Cotton, sorghum, maize, cowpeas and soybeans can be sown 1 day after application of SHARPEN WG Herbicide. Sow crops with a seeder that will move treated soil away from the crop row. This is particularly important with cotton, cowpeas, sorghum and soybeans. Use of seeders, or planting under conditions that do not move treated soil from the crop row may increase the level of early crop damage. Minor transient reduction in plant height may be observed in cotton where moist conditions prevail after germination but the crop will soon recover and will not affect yield. Also be careful when applying SHARPEN to fields just prior to sowing that will be soon after irrigated as soil water may move herbicide into crop row resulting in injury.

Situation	Weeds	Weed Stage	Rate	Critical Comments
control in Commercial, Industrial and Public Service areas, around Agricultural buildings, yards	*parviflora,* Sowthistle *Sonchus oleraceus* , Turnip weed *Rapistrum rugosum,* Wild oats *Avena spp.,* Wild radish *Raphanus raphanistrum*			Reduction of glyphosate activity on summer grasses may occur from the tank mix, which may result in reduced control of certain grass weeds. If grass weeds are present and their control is important, it is recommended that a full rate of 1.9L/ha of Roundup Attack is used. If grass weeds recover, a follow up application of a knockdown herbicide with another mode of action may be required. Refer also to the product label for the knockdown herbicide used. Use the lower rates on younger plants or plants growing under good conditions and the higher rates on older plants or plants growing under less optimum conditions. Refer to the plant-back interval table on this label and also refer to the appropriate companion product label, in case a longer re-crop sowing period is required.
	Volunteer cotton seedlings (2-6 leaf), including Roundup Ready Flex® varieties plus weeds above when tank mixed with Roundup Attack	Apply to seedling cotton at 2- 6 leaf stage	9 – 26g/ha plus Bonza at 1% **or** 9 – 26g/ha plus Bonza at 1% plus recommended label rate of Roundup Attack Herbicide	Refer to Critical Comments above and in addition: The following rates of SHARPEN WG Herbicide are recommended for volunteer cotton control: 9g/ha from cotyledon up to 2 leaf. 17g/ha from cotyledon up to 4 leaf. 26g/ha from cotyledon up to 6 leaf.
Situations as Above	Fleabanes *Conyza spp.*	maximum 6 leaf	17-34g/ha plus Bonza at 1% plus Roundup Attack Herbicide	Refer to Critical Comments above and in addition: Use the higher rate in situations where conditions are less favourable for control and for control of fleabane above 4 leaf up to 6 leaf. Fleabane can germinate in Autumn and Spring and it is important to establish size and age (check tap root as an indication) to ensure control. Fleabane that appears small may in fact be older and have an established tap root and may not be completely controlled. Depending on the other weed species present, adjust the rate of Roundup Attack

Situation	Weeds	Weed Stage	Rate	Critical Comments
				accordingly. A minimum rate of 1.15L/ha is recommended. Refer also to the Critical Comments in relation to summer grass control.

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 FOR SHARPEN WG HERBICIDE WHEN USED AS DIRECTED HOWEVER, REFER ALSO TO THE WITHHOLDING PERIOD OF PRODUCT/S MIXED WITH SHARPEN WG HERBICIDE.
GRAZING: DO NOT GRAZE OR CUT FOR STOCKFOOD FOR 5 WEEKS AFTER APPLICATION. DO NOT ALLOW LIVESTOCK TO GRAZE TREATED WEEDS.

GENERAL INSTRUCTIONS

SHARPEN WG Herbicide is a post-emergence herbicide to be added to Roundup Attack Herbicide to improve the control of certain broadleaf weeds including fleabane prior to the establishment of fallows, prior to establishing winter and summer broadacre crops, in commercial, industrial and public service areas, around agricultural buildings, yards and other farm situations. SHARPEN WG Herbicide may be used alone with a suitable adjuvant for control of volunteer cotton seedlings including Roundup Ready Flex cotton. SHARPEN WG Herbicide is a fast acting contact herbicide and aids in control of weeds through a process of membrane disruption. The foliar uptake of SHARPEN WG Herbicide is rapid and plant desiccation can occur within 4 days of application. Application of SHARPEN WG Herbicide should target small actively growing weeds. Subsequent germinations will not be controlled.

SYMPTOMS

SHARPEN WG Herbicide is rapidly absorbed through the foliage of plants. Within a few hours following application, the foliage of susceptible weeds will show signs of desiccation, and in subsequent days necrosis and death of the plant.

COMPATIBILITY

SHARPEN WG Herbicide should always be used with Bonza Spray Adjuvant.
For most uses as per the Directions for Use SHARPEN WG Herbicide should always be tank mixed with Roundup Attack. It is also compatible with Roundup® DST, Roundup Ready® Herbicide with Plantshield®, Credit® + Bonus® or Roundup PowerMAX. SHARPEN WG Herbicide is also compatible with partner herbicides commonly used with knockdown herbicides including, Amicide Advance 700, Amicide 625, Nufarm Surpass® 475, Estercide® Xtra 680, Nugran (triasulfuron), Rifle® 440, Stomp® 440, Stomp Xtra and Triflur X® (trifluralin). Other compatible products include Revolver®, Nuquat®, Alliance®, Amitrole T, Nu-trazine™ 600 and Nu-trazine 900DF. This compatibility claim is restricted to a three-way mix of SHARPEN WG Herbicide with any one of the above partner herbicides plus Roundup Attack (provided the Roundup Attack Herbicide label includes a claim of compatibility with that partner herbicide).

RESISTANT WEEDS WARNING GROUP **G** HERBICIDE

SHARPEN WG Herbicide is a member of the pyrimidindiones group of herbicides. Its mode of action is through a process of membrane disruption, which is initiated by the inhibition of the enzyme protoporphyrinogen oxidase. This inhibition interferes with the chlorophyll biosynthetic pathway. For weed resistance management SHARPEN WG Herbicide is a Group G herbicide.
Some naturally occurring weed biotypes resistant to SHARPEN WG Herbicide and other Group G herbicides may exist through normal genetic variability in any weed population and increase if these herbicides are used repeatedly. These resistant weeds will not be controlled by SHARPEN WG Herbicide or other Group G herbicides.
Since the occurrence of resistant weeds is difficult to detect prior to use, Nufarm Australia Limited accepts no liability for any losses that may result from the failure of SHARPEN WG Herbicide or other Group G herbicides.

TIMING

Application should be made to small, actively growing weeds up to 10 leaf in stage (Note: Fleabanes, Small flowered mallow, Bladder ketmia and Volunteer cotton, maximum 6 leaf; Volunteer canola, maximum 4 leaf). As SHARPEN WG Herbicide is a contact herbicide, best control is achieved when weeds are exposed and are not shielded by other weeds and/or stubble.

MIXING

Add half the required volume of water to spray tank and start agitation. Add the measured amount of SHARPEN WG Herbicide and allow product to disperse. Add any partner SC or WG herbicide next if it should be added, before an EC, followed by Roundup Attack Herbicide (if required). Add balance of water to tank and add Bonza adjuvant at 1% or any additive if recommended for use with the Roundup Attack herbicide. Maintain good agitation at all times until spraying is completed.

APPLICATION

The best application conditions are when soil is moist, weather fine and rain unlikely within one hour or as specified for the knockdown herbicide. SHARPEN WG Herbicide is rainfast one hour after application. Burndown activity may be reduced if rain or irrigation occurs within one hour of application. Extremes in environmental conditions eg. temperature and moisture, soil conditions and/or cultural practices may affect the activity of SHARPEN WG Herbicide.

SHARPEN WG Herbicide is a light activated herbicide and under intense light, warm and moist conditions, herbicide symptoms may be accelerated. Under very dry conditions, the expression of herbicidal symptoms is delayed and weeds hardened off by drought are less susceptible to SHARPEN WG Herbicide.

Stubble loads will interfere with coverage and could affect the performance of SHARPEN WG Herbicide. Reduced performance may also occur where weeds are covered with dust or silt.

Ground sprayers

Apply SHARPEN WG Herbicide as a broadcast application using a conventional boom sprayer with either mechanical or by-pass agitation.

Nozzles

Spray equipment should be properly calibrated to ensure correct and uniform application. Use a spray volume of 80 to 250 litres per hectare (minimum 80 L/ha for volunteer cotton). Increase water volume if weed infestation is dense and/or tall. To minimise off-target drift use the lowest pressure and boom height which provides uniform coverage.

Use only COARSE spray quality or greater according to the ASAE S572, when used in tank mix with Roundup Attack .

APVMA Compliance Instructions for Mandatory COARSE or Larger Droplet Size Categories

Important Information

These instructions inform users of this chemical product how to lawfully comply with the requirement of a COARSE or larger spray droplet size category for spray application.

Spray droplet size categories are defined in the ASAE S572 Standard (newer name may also be shown as ASABE) or the BCPC guideline. Nozzle manufacturers may refer to one or both to identify droplet size categories, but for a nozzle to comply with this requirement, the manufacturer must refer to at least one.
In the following instructions, Section 1 is for ground application.

Complying with the label requirement to use a specific droplet size category means using the correct nozzle that will deliver that droplet size category under the spray operation conditions being used. The APVMA has approved only the following specific methods for choosing the correct nozzle. Use one of the methods specified in these instructions to select a correct nozzle to deliver a COARSE or larger droplet size category.

SECTION 1 Instructions for **Ground Application – for COARSE droplet size or larger categories**

Mandatory Instructions for Ground Applications

USE ONLY nozzles that the nozzles' manufacturer has rated to deliver a COARSE, a VERY COARSE or an EXTREMELY COARSE droplet size category as referenced to ASAE S572 or BCPC. Choose a nozzle specified to provide the droplet size category required in the label Spray Drift Restraints.
DO NOT use a higher spray system pressure than the maximum the manufacturer specifies for the selected nozzle to deliver the droplet size category required in the label Spray Drift Restraint.

Sections 2 and 3 are not applicable to this label.

SPRAYER CLEAN OUT

After SHARPEN WG Herbicide is applied the following process should be followed to clean the spray equipment.

1. Completely drain the spray tank, rinse the sprayer thoroughly, including the inside and outside of the tank and all in-line screens.
2. Fill the spray tank with clean water and flush hoses, spray boom and lines, screens, filters and nozzles.
3. Add a detergent such as Omo or Spree or similar at a rate of 100 g per 100 L water or Nufarm Tank & Equipment cleaner or similar at recommended rates and circulate through sprayer for 5 minutes, then flush all hoses, spray boom, screens, filters and nozzles for a minimum of 15 minutes.
4. Drain tank completely.
5. Add enough clean water to the spray tank to allow all hoses, spray boom, screens, filters and nozzles to be flushed for 2 minutes.
6. Remove all nozzles and screens and rinse them in clean water.

Residues of SHARPEN WG Herbicide remaining in the sprayer may cause injury to the following treated crop

Properly dispose of all cleaning solution and rinsate safely in accordance with Federal, State, and local regulations and guidelines.

DO NOT apply sprayer cleaning solutions or rinsate to sensitive crops.

CROP PLANT BACK & ROTATION RECOMMENDATIONS

SHARPEN WG Herbicide does not provide long-term residual activity; however, certain crops show sensitivity to soil residues. Refer to the following table for application-to-sow intervals applicable to the maximum label rate.

1 hour	1 day	6 weeks	16 weeks
Barley Wheat Oats Chickpea Faba bean Field pea Lentil Lupin Sub clover	Cowpea Sorghum Soybean	Cotton	Canola Sunflower Other crops

Check the label of any product mixed with SHARPEN WG Herbicide, to determine any plant back periods or restrictions on use.

RE-ENTRY

DO NOT allow entry into treated areas until the spray has dried, unless wearing cotton overalls buttoned to the neck and wrist (or equivalent clothing) and chemical resistant gloves. Clothing must be laundered after each day's use.

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.

Off-target drift of SHARPEN WG Herbicide onto foliage and green stems of cotton and grapevines and other sensitive plants will cause marked damage.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT

DO NOT contaminate streams, rivers or waterways with SHARPEN WG Herbicide or used container.

STORAGE AND DISPOSAL

Store in the closed, original container in a dry, cool, well ventilated area out of direct sunlight. Triple or preferably pressure 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 bury empty containers in a local authority landfill. If no landfill is available, bury the containers below 500 mm 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 and Territory government regulations. Empty containers and product should not be burnt.

SAFETY DIRECTIONS

DO NOT use if pregnant. May irritate the eyes and skin. Avoid contact with eyes and skin. When opening the container, mixing and loading and preparing spray, wear cotton overalls buttoned to the neck and wrist and elbow length chemical resistant gloves. Wash hands after use. After each days use wash gloves and contaminated clothing.

FIRST AID

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

ADDITIONAL USER SAFETY INFORMATION

WARNING: DO NOT use if pregnant.

MATERIAL SAFETY DATA SHEET
For further information refer to the Material Safety Data Sheet (MSDS), which can be obtained from your supplier or the Nufarm website - www.nufarm.com.au)

In case of emergency: Phone 1800 033 498
Ask for shift supervisor. Toll free 24 hours.

Conditions of sale
Any provisions or rights under the Competition and Consumer Act 2010 or relevant state legislation which cannot be excluded by those statutes or by law are not intended to be excluded by these conditions of sale. Subject to the foregoing, all warranties, conditions, rights and remedies, expressed or implied under common law, statute or otherwise, in relation to the sale, supply, use or application of this product, are excluded. Nufarm Australia Limited and/or its affiliates ("Nufarm") shall not accept any liability whatsoever (including consequential loss), or howsoever arising (including negligence) for any damage, injury or death connected with the sale, supply, use or application of this product except for liability which cannot be excluded by statute.

APVMA Approval No: 62853/44119

ABBREVIATIONS

ac	active constituent
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
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
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
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
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
SUSDP	Standard for the Uniform Scheduling of Drugs 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
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 an absorbed material from 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	Water repelling
Leaching	Removal of a compound by use of a solvent
Log Pow	Log to base 10 of octonol water partitioning co-efficient
Metabolism	The conversion of food into energy
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

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