Australian Government

Australian Pesticides and Veterinary Medicines Authority

PUBLIC RELEASE SUMMARY

on the Evaluation of the New Active Constituent **Sulfoxaflor**

in the Product **Transform Insecticide**

APVMA Product Number 64101

JULY 2013

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

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PREFACE

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

In undertaking this task, the APVMA works in close cooperation with advisory agencies, including the Department of Health and Ageing, Office of Chemical Safety (OCS), Department of Sustainability, Environment, Water, Population and Communities (DSEWPaC), and State Departments of Primary Industries.

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

The information and technical data required by the APVMA to assess the safety of new chemical products, and the methods of assessment, must be consistent with accepted scientific principles and processes. Details are outlined 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 conducted by the APVMA and of the specialist advice received from its advisory agencies. It has been deliberately presented in a manner that is likely to be informative to the widest possible audience thereby encouraging public comment.

About this document

This is a Public Release Summary.

It indicates that the 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
- the residues and trade assessment
- occupational exposure aspects
- environmental fate, toxicity, potential exposure and hazard
- efficacy and target crop or animal safety.

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

Making a submission

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

Submissions must be received by the APVMA by close of business on **Wednesday July 30, 2013** and be directed to the contact listed below. All submissions to the APVMA will be acknowledged in writing via email or by post.

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

When making a submission please include:

- Contact name
- Company or group name (if relevant)
- Email or postal address (if available)
- The date you made the submission.

All personal information, and confidential information judged by the APVMA to be ***confidential commercial information (CCI)***[1] contained in submissions will be treated confidentially.

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

Contact Officer
Pesticides Program
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
Kingston ACT 2604

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

Phone: + 62 2 6210 4748
Fax: + 62 2 6210 4776
Email: pesticides@apvma.gov.au

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

Dow AgroSciences Australia Limited

Details of Product

It is proposed to register Transform Insecticide, a suspension concentrate (SC) formulation containing 240 g/L. Sulfoxaflor is a new insecticide for the control of a number of piercing/sucking insects including aphids, plant bugs, whiteflies, planthoppers, mealybugs, and scales. Sulfoxaflor is being developed for use on cotton, soybeans, cereals, citrus, leafy and fruiting vegetables, cole crops, grapes, apples and a variety of other crops.

It is proposed that the product be applied at rate of up to 400mL/ha (for control of greenhouse whitefly on a range of vegetable crops) and as low as 10mL/ha (to control a range of aphids in stone fruit).

Sulfoxaflor is the first member of a new class of insecticides, the sulfoximines. The sulfoximines are a novel class of insecticides which act through a unique interaction with the nicotinic acetycholine receptor in insects. Sulfoxaflor displays translaminar movement (moves to the opposite leaf surface) when applied to foliage and has been shown to be move through the xylem of treated plants. Sulfoxaflor acts through contact action and ingestion and provides both knockdown and residual control. The length of residual control is dependent on rate of application, the pest and its population level. Sulfoxaflor generally provides from 7 to 21 days of residual control. Sulfoxaflor is proposed for use on crops where plant bugs, whiteflies, aphids, planthoppers, and scale insects are economic problems.

Sulfoxaflor is currently registered in products in the USA and Canada for the control of sucking and piercing pests on cotton, oilseeds, cereal grains and a range of fruits, vegetables and nuts

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of Transform Insecticide, and approval of the new active constituent Sulfoxaflor.

This submission has been assessed under a joint review arrangement where registrations for the same formulations and uses have been submitted concurrently in Australia, Canada, and the USA.

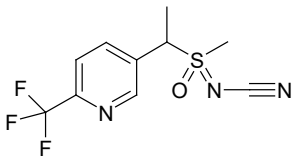
2 CHEMISTRY AND MANUFACTURE

2.1 Active Constituent

Manufacturing Site

The Dow Chemical Company, 2030 Dow Centre, Midland, MI, 48674 USA

Chemical Characteristics Of The Active Constituent

COMMON NAME:	Sulfoxaflor
IUPAC NAME:	[methyl(oxo){1-[6-(trifluoromethyl)-3-pyridyl]ethyl}-λ^6-sulfanylidene]cyanamide
CAS NAME:	N-[methyloxido[1-[6-(trifluoromethyl)-3-pyridinyl]ethyl]-λ^4-sulfanylidene]cyanamide
CAS REGISTRY NUMBER:	946578-00-3
MANUFACTURER'S CODES:	XDE-208
MINIMUM PURITY:	950 g/kg
MOLECULAR FORMULA:	$C_{10}H_{10}F_3N_3OS$
MOLECULAR WEIGHT:	277.27
STRUCTURE:	
CHEMICAL FAMILY:	Sulfoximines
MODE OF ACTION:	Acts through a unique interaction with the nicotine acetylcholine receptor in insects

APVMA Active Constituent Standard for Sulfoxaflor Active Constituent

CONSTITUENT	SPECIFICATION	LEVEL
Sulfoxaflor	Sulfoxaflor	Not less than 950 g/kg

Physical and Chemical Properties of Active Constituent

PHYSICAL STATE	White to off white crystalline powder		
ODOUR	Sharp		
MELTING POINT	112.9 °C (99.7% pure active)		
BOILING POINT	No boiling point at atmospheric pressure. It decomposes at approximately 167.7°C for 99.7% pure active		
DENSITY	1.5191 g/cm^3 @ 19.6°C for 99.7% pure active ; 1.5378 g/cm^3 @ 19.7°C for 95.6% pure active		
pH OF 1%	5.82 (1% suspension in distilled water at 24ºC for 95.6% pure active)		
SOLUBILITY IN WATER (AT 20 °C FOR 99.7% PURE ACTIVE)	670 mg/L (unbuffered) 1380 mg/L (pH 5) 570 mg/L (pH 7) 550 mg/L (pH 9)		
SOLUBILITY IN VARIOUS SOLVENTS (AT 20 °C FOR ACTIVES WITH DIFFERENT PURITIES)	Solvent	g/L (95.6% pure AC)	g/L (99.7% pure AC)
	Acetone	217	256
	Ethyl Acetate	95.2	49.5
	Methanol	93.1	36.0
	1,2-Dichloro-ethane	39.6	40.1
	n-Octanol	1.66	n/a
	Xylene	0.743	0.791
	n-Heptane	2.42 × 10^{-4}	1.54 ×10^{-4}
VAPOUR PRESSURE (FOR 99.7% PURE ACTIVE)	≤ 2.5 × 10^{-6} Pa @ 25 °C ≤ 1.4 × 10^{-6} Pa @ 20 °C		
HENRY'S LAW CONSTANT (AT 20 °C FOR 99.7% PURE ACTIVE)	5.8 x 10^{-7} Pa m^3/mol (unbuffered) 2.8 x 10^{-7} Pa m^3/mol at pH 5 6.8 x 10^{-7} Pa m^3/mol at pH 7 7.1 x 10^{-7} Pa m^3/mol at pH 9		
N-OCTANOL/WATER PARTITION COEFFICIENT	Log K_{ow} = 0.8 (pH 5, pH 7 and pH 9 at 20°C)		
HYDROLYSIS	Hydrolytically stable under acidic, neutral and alkaline conditions		
PHOTO-STABILITY IN WATER	Real lifetime: DT_{50} >1000 days for all seasons and latitudes		
DISSOCIATION CONSTANT (PKA)	No measureable ionization constant within environmentally relevant pH ranges (pH 2 – 10)		

UV/VIS ABSORPTION (AT 25°C FOR 99.7% PURE ACTIVE)	Conditions	λmax (nm)	ε (L/mol·cm)
	Neutral	192	10.2×10^3
		211	8.0×10^3
		260	3.1×10^3
	Acidic	210	7.8×10^3
		260	3.1×10^3
	Basic	218	5.9×10^3
		260	3.1×10^3
FLAMMABILITY	Not a highly flammable solid		
AUTO- FLAMMABILITY	None before melting at approximately 110°C		
EXPLOSIVE PROPERTIES	Not explosive		
OXIDISING PROPERTIES	Not oxidizing		

2.2 Transform Insecticide

FORMULATION TYPE:	Suspension Concentrate (SC)
ACTIVE CONSTITUENT CONCENTRATION:	Sulfoxaflor (240 g/L)

The product Transform Insecticide will be manufactured overseas and imported into Australia in 1, 5, 10 or 20 L high density polyethylene (HDPE) jerry can containers.

PHYSICAL AND CHEMICAL PROPERTIES OF THE PRODUCT

APPEARANCE	Tan liquid with a mild odour
PH	4.67 @ 23.9°C (1% aqueous dilution)
SPECIFIC GRAVITY	1.1066 g/mL at 20 ºC
SURFACE TENSION	47.0 mN/m after dilution at 0.05 g ai/L 42.0 mN/m after dilution at 0.75 g ai/L
VISCOSITY	1209 mPa.s at 1.5 rpm using Brookfield (spindle SC4-18) @ 20°C; 463.8 mPa.s at 6 rpm
PERSISTENT FOAM	0 mL after 12 min at max use rate of 2.1% w/v
SUSPENSIBILITY	98% (at max use rate of 2.2% w/v) 97% (at min use rate of 0.0008% w/v)
SPONTANEITY OF DISPERSION	95% (at max use rate of 2.2% w/v)
POURABILITY	2.14% residue 0.13% rinsed residue
LOW TEMPERATURE STABILITY	No sediment or noticeable changes
EXPLOSIVE PROPERTIES	Not explosive
OXIDISING PROPERTIES	No oxidising properties
FLAMMABILITY	Not flammable
CORROSIVE HAZARD	Not corrosive to HDPE containers
PACK SIZES	1, 5, 10, or 20 L
PACKAGING MATERIAL	High density polyethylene (HDPE)
PRODUCT STABILITY	The product should remain within specifications for at least 2 years under normal conditions in HDPE packaging

3 TOXICOLOGICAL ASSESSMENT

The toxicological database for sulfoxaflor, which consists primarily of toxicity tests conducted using animals, is 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 generally 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 sulfoxaflor was conducted jointly by scientists from Canada (PMRA), the United States (US EPA) and Australia (OCS). The US EPA was the primary reviewer for all the toxicity studies, and the PMRA and OCS were secondary reviewers. Since this report relies significantly on the international work share assessment, the OCS adopted the no observed adverse effect level (NOAEL) and low observed adverse effect level (LOAEL) approach using scientific justification for their adoption. Additional reconsideration of the findings in the two-generation reproductive study and the developmental neurotoxicity study has been undertaken by OCS nationally (i.e. outside of the GJR).

Chemical Class

Sulfoxaflor is the first member of a new class of insecticides, the sulfoximines. It is a novel class of insecticides which act through a unique interaction with the nicotine acetylcholine receptor in insects. Sulfoxaflor displays translaminar movement (mover to the opposite leaf surface) when applied to foliage and has been shown to be xylem-mobile. Sulfoxaflor acts through contact action and ingestion and provides both knockdown and residual control.

3.1 Toxicokinetics and Metabolism

Following oral administration sulfoxaflor is readily absorbed through the gastrointestinal tract of rats and rapidly excreted in the faeces and urine. The highest tissue levels of sulfoxaflor were found in the kidney, liver and red blood cells following single and repeat-dose administration in rats. Absorbed sulfoxaflor was nearly completely excreted un-metabolised, with only low levels of metabolites identified in urine samples. Only parent sulfoxaflor was detected in rat plasma. Following repeated oral doses, a total of seven radiolabeled components were identified in rat urine and/or faecal samples. Parent sulfoxaflor was the primary component in urine and faeces (>93%).

There were no metabolites identified in the metabolism studies as being toxicologically significant. Sulfoxaflor was rapidly excreted in rats and mice with 87 - 98% and 80-85% (respectively) of the administered oral dose eliminated within 24 h. Faecal elimination accounted for only 5-8% in rats and 13% in mice, mostly apparently representing unabsorbed dose due to its recovery in faeces within the GI transit time of 24 hours. The elimination half-life ($T_{1/2}$) in male rats from the plasma and RBC was 9 and 11 hours, and in females rats was 7 and 8 hours, respectively. Faecal excretion was slightly higher than urinary excretion in male rats, and faecal and urinary excretion were roughly equal in female rats. Bile is a major route of faecal excretion in rats.

In summary, administered sulfoxaflor was rapidly absorbed following oral administration, widely distributed without metabolism, with the highest levels in portal of entry and excretory tissues. Test material-derived radioactivity in tissues (other than portal of entry and excretory) tracked that of blood and did not indicate potential for bioaccumulation.

The dermal absorption of sulfoxaflor was determined to be low when tested in an aqueous suspension concentrate formulation in in vitro human and rat assays and in an in vivo rat study. As data were available, the triple-pack formula for estimating human in vivo dermal exposure was applied, and it was estimated that an in vivo human dermal absorption of 1.0% (rounded up) would occur upon exposure to a 240 g/L sulfoxaflor formulation, and 1.94% and 3.4% to a 1:20 and 1:100 dilution of the sulfoxaflor formulation respectively.

Acute Studies

Sulfoxaflor has low oral (LD_{50} = 1000 mg/kg bw in female rats, 1405 mg/kg bw in male rats and 750 mg/kg bw/d in male mice), dermal (LD_{50} > 5000 mg/kg bw in male and female rats, no deaths) and inhalational toxicity (4hr LC_{50} > 2.09 mg/L in male and female rats the maximum obtainable concentration, no deaths). Sulfoxaflor was not a skin irritant in rabbits, but was a slight irritant in the same species. Sulfoxaflor was not a skin sensitiser in mice (local lymph node assay).

Transform Insecticide (containing 240 g/L sulfoxaflor) was of low oral (LD_{50} > 5000 mg/kg bw in male and female rats, no deaths) and dermal toxicity (LD_{50} > 5000 mg/kg bw in male and female rats, no deaths). The formulated product was not a skin irritant in rabbits, but was a slight irritant in the same species, and was not a skin sensitiser in mice (local lymph node assay). Due to the inability to generate a sustainable respirable aerosol (e.g. 1-4 µm MMAD) at any concentration, an inhalation study in rats was not conducted, however, Transform Insecticide is assumed to have low acute inhalational toxicity given the product constituents.

Systemic Effects

In short-term studies (28-day and 90-day) dietary toxicity studies in rats and mice indicated that the main target organ was the liver. Males were affected more than females, which may in part have been related to the initial longer half-life of elimination in males. In all of these studies the main effects observed at the LOAEL comprised of a consistent pattern of increased liver weight with histopathological effects such as hepatocellular hypertrophy with altered tinctorial properties. In rats, single cell necrosis was detected at 90-days with fatty changes in males.

In mice these effects were seen at 28 days in males, together with mitotic figures. Cholesterol levels were increased in rats but not in mice, which had increased triglyserides in females. Mice also had hypertrophy/vacuolisation of the zona fasciculate of the adrenal gland of both sexes. In the 1-year chronic toxicity study in rats, the effects were decreased body weight gain in females and increased blood cholesterol and liver effects comprising increased weight, hepatocellular hypertrophy, fatty change, single cell necrosis and increased aggregates of macrophages at the high doses in both sexes. In the 1-year chronic toxicity study in dogs, gavage administration of sulfoxaflor gave the highest achievable doses but the only effects observed were decreases in feed consumption and body weight gain at the highest dose tested.

The 28-day dermal toxicity study in rats showed no treatment related toxicity effects in females. In males serum cholesterol levels and liver weights were marginally increased at the limit dose of 1000 mg/kg bw/d but were within the normal range and therefore considered incidental to treatment. The only histopathological effect was slight hepatocellular hypertrophy with altered tinctorial properties at the high dose. This finding was considered indicative of enzyme induction and an adaptive response of no toxicological significance. Therefore, it was considered that no treatment related toxicologically significant findings were seen at the highest dose tested (the limit dose of 1000 mg/kg bw/d) in either sex.

Carcinogenicity and Genotoxicity

The comprehensive battery of in vitro and in vivo genotoxicity tests for sulfoxaflor did not indicate any mutagenic or genotoxic potential in vitro with or without metabolic activation, or genotoxic potential in vivo in somatic cells.

Carcinogenicity was assessed in a 2-year dietary study in F344 rats and an 18-month dietary study in CD1 mice. Liver tumours were identified at the highest dose in male rats at 500 ppm (21.3 mg/kg bw/d) and mice at 750/1250 ppm (79.6/176 mg/kg bw/d M/F) which were considered treatment related. Rodent liver MoA studies were conducted, which included separate in vivo MoA studies in F344 and CD1 mice as well as MoA assessment of liver for cellular proliferation from regulatory toxicity studies. Finally, studies were conducted in transgenic knockout and humanized mice. Results of these studies taken together demonstrated that sulfoxaflor induces hepatocellular tumours in rodents by a phenobarbital-like MoA (i.e. constitutive androstane receptor-mediated) which would be of low relevance to humans (i.e. liver findings are not considered to provide evidence of a carcinogenic hazard). In F344 rats, testes weights of mid and high dose males given 100 and 500 ppm (4.24 and 21.3 mg/kg bw/d) were increased due to the increased size of Leydig cell tumours (LCT, benign adenomas). The incidence of animals with singular or bilateral (i.e. total) LCT was not increased at any dose level but the incidence of high dose animals with only bilateral LCT effects significantly increased ($P<0.05$).

Effects considered secondary to the larger LCT comprised severe atrophy of testicular seminiferous tubules (100 and 500 ppm), decreased amount of sperm in the epididymides (100 and 500 ppm), decreased secretory material in the accessory sex glands (500ppm) and an increase in the incidence of preputial gland carcinomas (500 ppm). These effects were considered to be associated with the overwhelming size of the LCT compromising normal testicular function (and OCS notes the absence of an adverse effect on reproductive function in the rat dietary 2-geneeration study). It should be noted with regard to the preputial gland tumours that humans do not have an anatomical correlate and therefore, they are considered to have no relevance to humans. The relevance of LCT to humans, on the other hand is undisputable. However, the F334 strain of rat is uniquely predisposed to LCT formation, with spontaneous incidences of up to 100% at 24 months being reported. In contrast, Sprague-Dawley rats have a background incidence of 1-5% and CD1 mice 1-2.5%. Estimates of human LCT incidences are orders of magnitude lower ranging from 0.01 – 0.00004%. Noting there is a detection bias towards animal studies, as they use histopathological examination compared to human diagnoses based on palpable tumours confirmed by biopsy.

The variance in spontaneous LCT incidences between F334 rats and humans are thought to arise from a quantitative difference in proliferative response of Leydig cells to lutenising hormone (LH). Initially, a proliferative response results in Leydig cell hyperplasia which with chronic stimulation may grow to form a LCT, typically a benign adenoma. Rats are more prone to LCT because their Leydig cells have more LH receptors than humans, which convey a greater sensitivity to slight changes in LH levels. In addition, in rats but not human, Leydig cells have GnRH receptors and prolactin receptors on their surface. Stimulation of rat Leydig cells through these receptors is a rat-specific mechanism by which Leydig cell tumour formation can also occur.

In conclusion, the interstitial cell tumours (Leydig cells) and male reproductive effects identified in rats at 100 ppm were not considered treatment related due to lack of dose-response relationship, lack of statistical significance and high background rate for this kind of tumours in F344/DuCrl rats (and the incidence was only slightly above the laboratory historical control data). While the preputial gland tumours could be a secondary effect to disturbed endocrine balance of treated animals to Leydig cell tumours and therefore preputial gland tumours are considered of low relevance to humans.

Reproductive and Developmental Toxicity

In addition to standard regulatory studies, comprising a two-generation reproduction study in rats and a developmental study in rats and rabbits, a series of studies was conducted to understand the mode of action (MoA) for two effects seen in rats. They were:

1) fetal abnormalities (primarily forelimb flexure and bent clavicle plus hindlimb rotation); and

2) neonatal pup loss at birth.

Apart from a slight delay in balano-preputial separation (BPS) in high doses level F1 male CD rats in the dietary 2-generation study (balano-preputial separation was not determined in F2 males), these were the only treatment related reproduction effects of sulfoxaflor. However, this external marker of male puberty onset is androgen dependent, but the underlying reason for how sulfoxaflor induced this finding is not known. Nevertheless, OCS notes that there were no other indications of androgenic or anti-androgenic effects. This included no treatment-related effects on anogenital distance, no effects on testis or accessory sex gland (i.e., prostate, seminal vesicle, and epididymis) weight or histopathology, no evidence of malformations like hypospadias or ectopic testes, no effects on mating, fertility, time to mating, or gestation length, and no treatment-related effects on preputial separation at the same dose level in a developmental neurotoxicity study with sulfoxaflor. Taken together, the weight of evidence across androgen-sensitive endpoints led to the conclusion that the data do not support any other sulfoxaflor -mediated anti-androgenic effects. Thus the PPS finding was not considered to demonstrate a toxicologically significant reproductive toxicity potential.

The proposed developmental MoA program and related tests were based on a hypothesis that both effects had a single MoA associated with sulfoxaflor's agonism to the fetal rat muscle nicotinic acetylcholine receptor (nAChR). A series of studies in rats and rabbits and in vitro studies using recombinant rat and human nAChRs demonstrated that the developmental target for sulfoxaflor is the fetal rat muscle nicotinic acetylcholine receptor. Prolonged activity (agonism) at this receptor in rats causes striated muscle contracture and reduced muscle responsiveness, considered responsible for the fetal abnormalities and neonatal death in rats. All the morphological effects in fetal rats listed above in point 1 were shown to be reversible after birth, and sulfoxaflor was also shown not to be an agonist to the corresponding human receptors. Therefore these were shown to be pharmacological effects mediated via in utero exposure from the mother at the end of gestation. These findings in rats, but not rabbits, were not considered relevant to humans.

For the hypothesis given above, the authors carried out an experiment in which they mimicked the fetal abnormalities via sulfoxaflor dose-dependent muscle contracture. The effects observed in the MoA study, limb and shoulder grindle contracture effects were similar to skeletal findings in the rat developmental study supporting the above hypothesis. The human relevance framework analysis considered that the limb and shoulder girdle contracture effects as data gaps. These effects have been demonstrated to be reversible in live offspring, however, experimental amelioration or prevention of the effects had not been demonstrated to date. Direct assessment of fetal type nAChR inhibition or neuronal nAChR agonism by sulfoxaflor could be considered a data gap. However, neither of these was conducted as they are inconsistent with the repeatable and robust observations in neonatal offspring for sulfoxaflor developmental effects. It is concluded that there is sufficient evidence to exclude the suggested plausible alternative MoAs for the observed neonatal offspring limb abnormalities and death.

In the standard guideline compliant dietary teratogenic study, additional observed skeletal (fused sternebrae), and visceral findings (convoluted ureter, hydroureter), were seen in the presence of marked maternal toxicity (e,g. decreases in body weight [8%] and body weight gain [22%]) and are considered a secondary non-specific consequence of such. Further, an observed increase in post-implantation loss compared to concurrent controls was not only seen in the presence of marked maternal toxicity but was within the historical control range. No developmental toxicity was seen in a rabbit dietary study at dose levels producing marked maternal toxicity. Thus, overall, there is no robust evidence from the rat and rabbit developmental studies that sulfoxaflor is a hazard to humans for developmental toxicity, or robust evidence from the rat 2-generation study that sulfoxaflor is a hazard to humans for reproductive toxicity.

Neurotoxicity

Neurotoxicity endpoints were assessed for sulfoxaflor in rats following acute gavage and repeated dietary exposure in a 90-day toxicity study and in a dietary developmental neurotoxicity study. The acute gavage neurotoxicity study showed decreased motor activity on the day of dosing at >75 mg/kg sulfoxaflor and signs of cholinergic toxicity on the day of dosing at 750 mg/kg. Motor activity is an apical endpoint and may not indicate a specific neurotoxic effect but the cholinergic signs indicate transient effects on the nervous system. The 90-day rat dietary study did not show any treatment-related effects on neurotoxicity endpoints, which included functional observational battery endpoints, motor activity and neuropathology evaluation of both the central and peripheral nervous systems. The developmental neurotoxicity study indicated reduced neonatal survival and pup body weights in response to gestational exposure to 400 ppm sulfoxaflor. However, there was no evidence of neurotoxicity in pregnant/lactating dams or in F1 offspring assessed for nervous system structure and function from the pre-weaning period through adulthood.

Immunotoxicity

In a rat 90-day dietary study, assessment of immunotoxicity was measured by immune responsiveness in the sheep red blood cell antibody-forming cell assay. Compared to controls, a non-statistically significant immune response (26% lower) was seen in the high dose male group but coincided with considerable general toxicity, including decreased body weights and liver toxicity. Therefore, the lower AFC response in the high dose males was considered secondary to systemic toxicity and thus does not reflect a primary immunotoxic potential for sulfoxaflor.

Studies with Metabolites

Sulfoxaflor has 6 known primary metabolites, one of which has two plant conjugates. All are formed by metabolism of the parent’s ethyl-sulfanylidene-cyanamide side chain and/or the side chain of its metabolites.

Sulfoxaflor-related metabolites, in general have low acute toxicity by the oral route. Metabolite X11719474, considered the major metabolite, was rapidly absorbed, mostly un-metabolized and eliminated very quickly from the rat following oral administration. X11719474 has low acute oral toxicity in rats and was not a skin sensitizer in mice (LLNA). A non-guideline compliant screening study investigated skin and eye irritation, though the study results were not considered reliable for regulatory purposes. X11719474 lacks mutagenic and clastogenic activity in vitro with and without metabolic activation. It also lacks the developmental effects of the parent. It has the same target organ as sulfoxaflor, liver, with the same phenobarbital-like mode of action. In all respects, it is less toxic than the parent molecule.

X11519540 is a minor animal metabolite and also found as an impurity of the manufacturing process. The oral LD50 for X11519540 (565.7 mg/kg bw in female rats) is approximately half of the LD50 for sulfoxaflor (1000 mg/kg bw in female rats). Repeat-dose studies in the rat showed that the primary target organ is the liver. In addition, X11519540 resulted in a dose-dependent increase in the adrenal gland weight. The LOAEL of 244 mg/kg bw/d in the 28-day dietary rat study for X11519540 is 10-fold lower than the LOAEL for sulfoxaflor (79.4 mg/kg bw/d in a 28-day dietary rat study). The same study showed that X11519540 has a longer half-life (24-35 h) than sulfoxaflor (4-8h). Therefore, it is apparent that X11519540 is more potent than sulfoxaflor, though as stated it is a minor metabolite.

The rest of the tested metabolites, X11721061, X11596066, X11579457 and X11718922 were of low magnitude compared to/in the parent compound. They had low acute oral toxicity in the rat and/or no mutagenic and/or genotoxic potential in vitro with and without metabolic activation.

3.2 Public Health Standards

Poisons Scheduling

On the 28th May 2013 the delegate to the Secretary of the Department of Health and Aging made an interim decision that sulfoxaflor be listed in Schedule 6 of the SUSMP with a cut-off to Schedule 5 for products containing 25% or less of sulfoxaflor, along with an implementation date of 1st September 2013.

NOEL/ADI

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.

OCS considers that the most appropriate long term study for establishing the ADI is the 2-year combined toxicity and carcinogenicity dietary study in the rat. Noting that the observed tumours in rats were of low relevance to humans, OCS considers that a default safety factor of 100 (to account for potential intra- and inter-species differences) should be applied to the NOAEL of 4.24 mg/kg bw/d based on increased serum cholesterol concentrations, and histopathological liver effects in males at 21.3 mg/kg bw/d to derive an ADI value of 0.04 mg/kg bw/d.

Acute Reference Dose

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.

An acute reference dose (ARfD) was established since sulfoxaflor was considered likely to present an acute hazard to humans. Adverse findings in animal species are assumed to represent potential effects in humans, unless convincing evidence of species specificity is available.

The lowest appropriate NOAEL from single dose and short-term studies is 25 mg/kg bw in male and female rats in the acute neurotoxicity study. This NOAEL is based on transient neurotoxicity (changes in the motor activity) seen on day 1 only at 75 mg/kg bw, with cholinergic signs indicative of transient effects on the nervous system seen at 750 mg/kg bw. Noting the weak neurotoxic potential observed in rats and the absence of histopathological changes to the nervous system in either sex, OCS considers that a default safety factor of 100 is sufficient to establish an ARfD value.

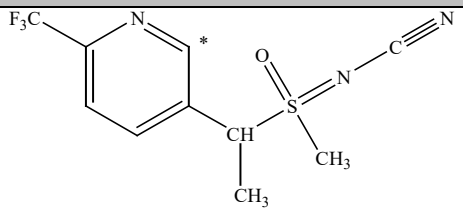
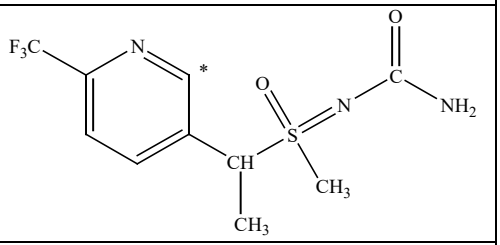
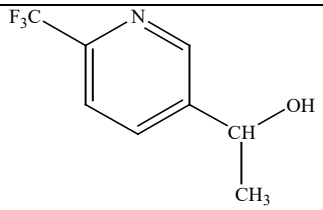
Therefore, the ARfD is established at 0.25 mg/kg bw based on a NOAEL of 25 mg/kg bw in rats in an acute neurotoxicity study for transient effects on the nervous system and applying a default 100-fold uncertainty factor to take into account potential inter- and intra-species variation.

4 RESIDUES ASSESSMENT

Transform Insecticide is a suspension concentrate formulation containing the new active constituent sulfoxaflor. The product is intended for control of various aphid species, green mirid, and greenhouse whitefly in canola, wheat, barley, cotton, soybeans, brassica vegetables, leafy vegetables, fruiting vegetables (both cucurbits and non-cucurbits), and root vegetables, and various mealybug, thrip, scale insect and aphid species in citrus, pome and stone fruit, and wine and table grapes. As part of the residues assessment for sulfoxaflor, plant and animal metabolism studies, supervised residue trials, processing studies, feeding studies, and trade aspects were considered and details are provided below.

4.1 Metabolism

Metabolism data for ^{14}C-labelled sulfoxaflor in tomatoes, peas, rice, lettuce, rotational crops (lettuce, wheat and radish), lactating goats and laying hens was provided. Metabolism studies for the ^{14}C -labelled plant metabolite X11719474 in lactating goats and laying hens were also supplied.

COMPONENT	CHEMICAL NAME	STRUCTURE
Parent	[1-(6-Trifluoromethylpyridin-3-yl)ethyl](methyl)oxido-λ4-sulfanylidenecyanamide	
X11719474	1-{1-[(6-Trifluoromethyl-3-pyridyl)ethyl](methyl)oxido-λ4-sulfanylidene}-urea	
X11721061	1-(6-Trifluoromethyl-3-pyridyl)ethanol	

*Indicates position of carbon-14 label in test substance used in the metabolism studies.

In the plant metabolism studies, after foliar application, parent compound was usually the most significant residue component in edible portions, at 27-59% of the total radioactive residue (TRR). The exception was lettuce, where X11719474 was present at 31% of the TRR, with parent at 17% of TRR. After soil application, X11719474 was the largest component, from 37-90% of the TRR in the edible portions. Similarly, in rotational crops, X11719474 was the largest component of the residue in all matrices (38-88% of TRR), with parent being present only at <5% of TRR.

The identified metabolic pathways in the different plant groups (and rotational crops) were similar, with metabolism of sulfoxaflor proceeding through oxidation of the cyano-carbon to yield X11719474 and loss of

the sulfur side-chain to produce the metabolite X11721061. X11721061 is then conjugated with glucose, which in turn may be conjugated with a malonyl group. Metabolism continues through natural incorporation of the radiolabelled carbon into natural plant constituents, such as lignin.

All proposed use patterns are for foliar application, so parent is expected to be the most significant residue for most crop groups and matrices. This expectation was confirmed in the residue trials, where parent was generally the most significant residue. The metabolites X11719474 and X11721061 are around seven times less toxic than parent compound, so their inclusion in the residue definition for dietary risk assessment purposes is not required.

A residue definition of parent only is therefore proposed for sulfoxaflor in plant commodities, for both compliance with MRLs and for dietary risk assessment purposes.

A study of the hydrolysis of radiolabelled sulfoxaflor under conditions simulating industrial food processes such as pasteurisation, baking, brewing, boiling and sterilisation showed that sulfoxaflor was not hydrolysed to a significant extent. A residue definition of parent compound only will therefore cover residues arising in processed plant commodities.

Metabolism of sulfoxaflor in lactating goats and laying hens was not extensive, with parent comprising 60-97% of the TRR in tissues, milk and eggs. Metabolism proceeds through successive cleavage of the cyanamide and sulfone moieties, followed by reduction of the hydroxy group to give 5-ethyl-2-trifluoromethylpyridine (X11596066) as the terminal metabolite. Much smaller amounts of the three metabolites X11519540, X11721061, and X11596066 were found (maximum 18% TRR, 0.095 mg/kg). The plant metabolite X11719474 was not metabolised at all by lactating goats or laying hens, with only X11719474 being found in the excreta, milk, eggs and tissues.

Although both parent and X11719474 are found largely unchanged in tissues, eggs and milk of livestock fed those compounds, parent is generally a more significant residue in livestock feeds. Parent compound has around 7 times greater toxicological significance than X11719474.

It is therefore proposed to establish a residue definition of parent compound only for sulfoxaflor in animal commodities, for both compliance with MRLs and dietary risk assessment purposes.

Analytical methods

Determination of sulfoxaflor residues in plant commodities

The analytical methods for plant matrices involve extraction of the samples with acetonitrile/water, followed by addition of stable isotope internal standards, hydrolysis of base-labile conjugates with dilute sodium hydroxide, and hydrolysis of glucose conjugates with glucosidase. The sample extracts were then cleaned up by solid phase extraction (on- or off-line), before LC/MS/MS analysis. The method limit of quantitation (LOQ) is 0.01 mg/kg for each analyte, with limits of detection (LODs) of 0.003-0.005 mg/kg. Good method recoveries (mean values in the range 70-120%) and precisions (RSD values <20%) were achieved for the three analytes in a range of sample types (dry commodities such as wheat grain, wheat and barley straw and dry beans, high water and/or high acid samples such as citrus, apples, potato, peach, grape and tomatoes, and high oil content samples such as rape seed, soybean and almond).

Determination of residues of sulfoxaflor in animal tissues

The animal commodity analytical methods involve extraction of homogenised samples with acetonitrile/water, followed by clean-up with solid phase extraction (on- or off-line) and analysis by LC/MS/MS. The method LOQ is 0.01 mg/kg and the LOD is 0.003 mg/kg. With very few exceptions, good recoveries (mean values in the range 70-120%) and precisions (RSD <20%) were achieved for the three analytes in milk, skim milk, cream, eggs, muscle, liver, kidney and fat.

The methods are suitable for the proposed purposes and are acceptable.

Residue definition

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

Compound	Residue definition
Sulfoxaflor	Sulfoxaflor

Storage stability

Stability over 24 months storage at -20 °C was tested for residues of sulfoxaflor and X11719474 and X11721061 in orange, peach, wheat grain and soybean seed, covering high water, high acid, dry and oily commodities. Residues of the analytes were stable in these matrices for at least 24 months. As part of the animal feeding studies, testing of the stability of parent, X11719474 and X11721061 in animal matrices was conducted. Residues were stable for up to 42 days in whole milk, skim milk and cream, and in muscle, fat, liver and kidney for up to 56 days, which covers the storage periods for the cattle feeding study. Residues were stable for up to 64 days in eggs, and chicken muscle, liver and fat, which covers the storage period for the poultry feeding study.

4.2 Residue trials

Canola

The proposed GAP in canola is a maximum of two applications at 25-50 g ai/ha up to full flowering (BBCH growth stage 65), with a harvest withholding period not being required when the product is used as directed, and no grazing withholding period being specified by the applicant.

Six Australian trials in canola conducted in accordance with the proposed GAP were provided to the APVMA. After two applications at 25 g ai/ha of sulfoxaflor to canola (prior to BBCH growth stage 65), residues of sulfoxaflor in canola seed were all ND (6). An MRL of *0.01 mg/kg is proposed for sulfoxaflor in rape seed [canola], with a harvest withholding period not being required when the product is used as directed.

Residues of sulfoxaflor in canola forage and canola stuble, on dry weight basis, 14 days after the second of two applications at 50 g ai/ha, were 0.08, 0.13, 0.21, 0.22, 0.46, 0.54, 1.0, 1.2, and 1.7 mg/kg. A Table 4 entry of 3 mg/kg is proposed for sulfoxaflor in canola forage and fodder, in conjunction with a 14-day grazing withholding period.

The canola processing study showed that residues of sulfoxaflor (parent compound) do not concentrate in crude or refined canola oil, while concentrating slightly in cleaned seeds (1.1X), mechanically extracted meal (1.9X), and solvent extracted meal (2.2X). Given that residues were undetectable in seed treated in accordance with the proposed GAP for canola, establishment of MRLs for processed canola commodities is not required.

Cereals

The proposed GAP in wheat and barley is a maximum of two applications at 12.5-25 g ai/ha up to flag leaf stage (BBCH growth stage 39), with a harvest withholding period not being required when the product is used as directed.

Residue trials including two applications at 25 g ai/ha to cereals were carried out in Australia and New Zealand (four trials in barley and eight trials in wheat). Residues of sulfoxaflor in wheat and barley grain collected at normal harvest after two applications at GAP were ND (12) mg/kg. Based on the combined data set for wheat and barley, an MRL of *0.01 mg/kg is recommended for cereal grains, with a harvest withholding period not being required when the product is used as directed.

The processing study for barley shows that residues of sulfoxaflor (parent compound) do not concentrate significantly in any processed commodity, and only slightly in malt sprouts (1.3X). The wheat processing study shows that sulfoxaflor (parent compound) concentrates significantly in aspirated grain fractions (21X), but not in other fractions. MRLs will not be established for processed wheat commodities.

Due to there being insufficient forage and fodder data for the Australia/New Zealand residue trials, forage and hay data from wheat and barley trials conducted in Australia, New Zealand, the USA and Canada, and Europe at the proposed global GAP (two applications at 50 g ai/ha, with a 14-day harvest withholding period) will be considered, which represents 2X the proposed Australian GAP.

Residues in wheat forage, at a 14-day interval, after the second of two applications at 50 g ai/ha (2X GAP), on a dry weight basis, are: <0.02, <0.04, 0.04 (2), 0.08, 0.16 (2), 0.19, 0.20, 0.28, 0.32, 0.48, and 0.87 mg/kg (STMR = 0.16 mg/kg).

Based on this data set, a Table 4 entry of 2 mg/kg is recommended for forage of cereal grains (green), determined on a dry weight basis. These are in conjunction with a 14-day grazing withholding period.

The combined data set for sulfoxaflor in wheat and barley hay (dry weight basis), 14 days after the last of two applications at 50 g ai/ha, is: <0.01, 0.02 (2), 0.03 (2), 0.05 (2), 0.06, 0.07 (3), 0.10, 0.11, 0.15, 0.17, 0.23, 0.27 and 0.68 mg/kg (STMR = 0.07 mg/kg).

As the hay data set represents a worst case for residues in fodder, this will be used to establish a Table 4 entry for straw and fodder of cereal grains (dry) of 1 mg/kg, in conjunction with a 14-day grazing withholding period.

Cotton

The proposed GAP in cotton is a maximum of four applications at up to 100 g ai/ha, with a harvest withholding period of 14 days.

At a 14-day harvest interval after four applications of sulfoxaflor at a target rate of 100 g ai/ha per application (1X the proposed GAP), residues of sulfoxaflor in cottonseed were <0.01 (2), 0.01 (4), 0.02 (4), 0.03 (2), 0.04 (2), 0.05 (3), 0.06, 0.07, 0.08 (2), and 0.18 mg/kg (STMR = 0.03 mg/kg). Residues of sulfoxaflor in cotton trash (gin by-products) at the same interval were 0.04, 0.06, 0.07, 0.19, 0.26, 0.33, 0.40, 0.49, 0.53, 0.54, 0.57, 0.65, 0.73, 0.90, 1.0, 1.4, 1.5, 1.6, 4.1, 4.7, and 5.6 mg/kg (on a dry weight basis).

An MRL of 0.3 mg/kg is therefore proposed for sulfoxaflor in cottonseed, in conjunction with a 14-day harvest withholding period.

Residues of sulfoxaflor (parent compound) concentrate slightly in hulls (processing factor = 1.8X) but not in meal (processing factor 0.8X).

The calculated HR-P value for sulfoxaflor in cottonseed hulls is 0.32 mg/kg. The calculated STMR-P value for sulfoxaflor in cottonseed hulls is 0.054 mg/kg.

It is therefore proposed to establish an MRL (Table 4) of 0.5 mg/kg for sulfoxaflor in cottonseed meal and hulls.

Soya bean

The proposed GAP in soya bean is a maximum of four applications at up to 100 g ai/ha, with a harvest withholding period of 14 days.

A package of 19 residue trials for sulfoxaflor in soya bean, including four in Brazil and 15 in the USA was provided. Residues of sulfoxaflor in soybeans at at a 7-day harvest interval after 4 × 100 g ai/ha applications were: <0.01 (8), 0.01, 0.02 (3), 0.03 (2), 0.04 (3), 0.09, and 0.21 mg/kg (STMR = 0.02 mg/kg). Residues of sulfoxaflor in soybeans at a 14-day harvest interval were: <0.01, 0.03, 0.04, and 0.09 mg/kg.

As insufficient data are available at a 14-day interval, the 7-day harvest interval data set was used for establishing the MRL. An MRL of 0.3 mg/kg is recommended for sulfoxaflor in soybeans, in conjunction with a 14-day harvest withholding period.

Residues of sulfoxaflor in forage on a dry weight basis at a 7-day interval after 4 × 100 g ai/ha applications were: 0.05, 0.07, 0.21, 0.23, 0.30, 0.34, 0.38, 0.39 (3), 0.55, 0.64, 0.70, 0.71, 0.77, 0.84, 1.0, 2.3, and 3.0 mg/kg (STMR = 0.39 mg/kg). Residues of sulfoxalfor in hay on a dry weight basis at a 7-day interval were: 0.11, 0.15, 0.16, 0.29, 0.31, 0.55, 0.72, 0.82, 0.85, 0.86, 1.1 (3), 1.2, 1.3 (3), 1.5, and 1.6 mg/kg (STMR = 0.86 mg/kg).

Table 4 entries of 5 mg/kg are proposed for sulfoxaflor in soya bean forage (green) and soya bean fodder, in association with a 7-day grazing withholding period.

The soybean processing study shows that residues of sulfoxaflor (parent compound) concentrate significantly in aspirated seed fractions (95X), and slightly in meal/press cake (1.1-1.3X), and hulls (1.5X).

Calculated HR-P values for soybean aspirated seed fractions, meal and hulls are 20, 0.27, and 0.32 mg/kg respectively. Calculated STMR-P values for soybean aspirated seed fractions, meal and hulls are 1.9, 0.026, and 0.03 mg/kg respectively.

A Table 4 entry of 0.5 mg/kg is proposed for sulfoxaflor in soya bean hulls.

Fruiting vegetables, Cucurbits

The proposed GAP in fruiting vegetables, cucurbits (field grown only) is a maximum of four applications, at rates up to 100 g ai/ha, with a harvest withholding period of 1 day. A substantial global residue data package was supplied, including residue data for zucchini/summer squash (two Australian trials and three US trials), winter squash/pumpkin (three trials in the USA), cucumber (twelve trials in Europe, and six trials in the USA) and melons (four trials in Brazil, and six trials each in the USA and Europe. Trials were conducted in accordance with the proposed global GAP, with 4 × 100 g ai/ha applications at a target re-treatment interval of 7 days, and with a target harvest interval of 1 day after the last application for the magnitude of residue trials.

The combined data set for cucurbit fruiting vegetables is: <0.01 (6), 0.01 (2), 0.02 (7), 0.03 (6), 0.04 (3), 0.05 (4), 0.06, 0.07, 0.08 (2), 0.09, 0.11 (3), 0.12, 0.13 (2), 0.14, 0.17, and 0.30 mg/kg (STMR = 0.035 mg/kg).

An MRL of 0.5 mg/kg is recommended for sulfoxaflor in fruiting vegetables, cucurbits.

Fruiting vegetables, other than Cucurbits

The proposed GAP in fruiting vegetables other than cucurbits (both field and greenhouse grown) is a maximum of four applications, at rates up to 100 g ai/ha, with a harvest withholding period of 1 day.

A substantial residue data package was presented, including residue trial data for field grown tomatoes (six trials in Australia, four trials in Brazil, eight trials in the USA (four of these were in cherry tomatoes), and 18 trials in Europe (six of these were in cherry tomatoes)), greenhouse grown tomatoes (four trials in Europe), capsicum/sweet pepper (two trials in Australia, six trials in Europe, and four trials in the USA) and chilli peppers (four trials in Australia and four trials in the USA).

Residues of sulfoxaflor in fruiting vegetables other than cucurbits after 1 day after the last of 4 × 100 g ai/ha applications are: <0.01 (2), 0.01 (4), 0.02 (8), 0.03 (7), 0.04 (3), 0.05 (3), 0.06 (4), 0.07 (2), 0.08 (6), 0.09 (3), 0.10 (4), 0.11 (4), 0.12, 0.14, 0.16, 0.17, 0.22, 0.23, 0.26, 0.28 (2), 0.36, 0.41, 0.43, 0.44, 0.46, 0.59, and 0.77 mg/kg (STMR = 0.075 mg/kg).

Residues of sulfoxaflor appear to be slightly higher in indoor grown tomatoes compared with outdoor grown tomatoes, although all values for indoor grown tomatoes were within the span of the outdoor grown tomato data set. Similarly, residues of sulfoxaflor appear to be slightly higher in cherry tomatoes compared with large tomatoes, although again, all residue values for cherry tomatoes were within the range of the large tomato data set.

An MRL of 1 mg/kg is recommended for sulfoxaflor in fruiting vegetables (other than cucurbits).

The tomato processing study showed that residues of sulfoxaflor concentrated in ketchup (2.1X), puree (2.0X) and paste (4.4X). The HR-P values for ketchup, puree and paste are 1.6, 1.5, and 3.4 mg/kg respectively. The STMR-P values for ketchup, puree and paste are 0.11, 0.10, and 0.22 mg/kg respectively.

No processing data was generated for tomato pomace. The residues in dry tomato pomace were calculated on the basis of the typical dry matter content of tomatoes (6%). The HR-P and STMR-P values for tomato pomace, dry are 13 and 0.83 mg/kg respectively. A Table 4 entry of 20 mg/kg is recommended for tomato pomace, dry.

Leafy vegetables

The proposed GAP in leafy vegetables is a maximum of four applications, at rates up to 100 g ai/ha, with a harvest withholding period of 3 days.

A substantial global residue data package was presented, including trials conducted head lettuce (four trials in Australia, six trials in Europe and four trials in the USA), leafy lettuce (four trials in Australia, six trials in Europe and eight trials in the USA), spinach (one trial in Australia and six trials in the USA), Swiss chard/silverbeet (one trial in Australia), Chinese cabbage (two Australian trials) and mustard greens (eight trials in the USA).

Residues of sulfoxaflor in head lettuce at a 3-day harvest interval after 4 × 100 g ai/ha applications were: <0.01, 0.01 (2), 0.02 (2), 0.04 (2), 0.07, 0.17, 0.18, 0.30, 0.38, 0.50, and 0.53 mg/kg (STMR = 0.055 mg/kg).

An MRL of 1 mg/kg is recommended for sulfoxaflor in head lettuce, in conjunction with a 3-day harvest withholding period.

The combined residue data set for the other leafy vegetables at a 3-day harvest interval after 4 × 100 g ai/ha applications is: 0.04, 0.05, 0.06, 0.18, 0.19, 0.22, 0.27, 0.29, 0.33, 0.41, 0.43, 0.44, 0.45, 0.48, 0.52, 0.57, 0.60, 0.61, 0.66, 0.72, 0.79, 0.83 (2), 0.93, 0.95, 0.97, 1.1 (3), 1.2, 1.4, 1.6, 1.7, 2.1, 3.1, and 3.3 mg/kg (STMR = 0.635 mg/kg).

An MRL of 5 mg/kg is recommended for sulfoxaflor in leafy vegetables except head lettuce, in conjunction with a 3-day harvest withholding period.

The processing studies in head and leafy lettuce showed that residues of sulfoxaflor are lower in washed heads with the wrapper leaves removed and in washed leafy lettuce (processing factors of 0.2X and 0.7X respectively). The calculated HR-P values for washed lettuce heads with wrapper leaves removed and washed leafy lettuce are 0.11 and 2.2 mg/kg respectively. The calculated STMR-P values for washed lettuce heads with wrapper leaves removed and washed leafy lettuce are 0.01 and 0.36 mg/kg respectively.

Root and tuber vegetables

The proposed GAP in root and tuber vegetables is a maximum of four applications, at rates up to 75 g ai/ha, with a harvest withholding period of 3 days. A large package of residue trials in root and tuber vegetables was presented, including data in carrots (eight trials in Europe and four trials in the USA), potatoes (eight trials in Europe, and ten trials in the USA and Canada), radish (six trials in the USA) and sugar beet (eight trials in Europe and five trials in the USA). Trials were conducted with 4 × 100 g ai/ha applications (1.33X the proposed GAP).

There are insufficient data to support a 3-day harvest interval. Given that most data were generated at a 7-day harvest interval, the data at that interval was considered for the purposes of determining an MRL.

At a 7-day harvest interval, residues of sulfoxaflor in potatoes were <0.01 (18) mg/kg. An MRL of 0.01 mg/kg in conjunction with a 7-day harvest withholding period is therefore recommended for sulfoxaflor in potatoes.

At a 7-day harvest interval, the combined data set for carrots, radish and sugar beet is: <0.01 (15), 0.01 (9), 0.02 (3), and 0.03 (3) mg/kg. An MRL of 0.05 mg/kg is therefore recommended for sulfoxaflor in root and tuber vegetables [except potato].

The processing study showed that residues of sulfoxaflor (parent compound) concentrates slightly in peel (1.8X), potato flakes (2.5X), potato chips (2.1X), dried potatoes (3.6X), and French fries (1.6X).

STMR-P and HR-P values for sulfoxaflor in peel, potato flakes, potato chips (crisps), dried potatoes and French fries are 0.018, 0.025, 0.021, 0.036, and 0.016 mg/kg.

Brassica vegetables

The proposed GAP in brassica vegetables is a maximum of four applications, at rates up to 100 g ai/ha, and a harvest withholding period of days. A sizeable global residue data package for brassica vegetables is available for sulfoxaflor, including 15 trials in broccoli (two in Australia, seven in Europe and six in the USA), 14 trials in cabbage (two in Australia and six each in Europe and the USA), ten trials in cauliflower (two in Australia and eight in Europe), and two Australian trials in Brussels sprouts.

The combined data set for broccoli and cabbage, at a 3-day withholding period after 4 × 100 g ai/ha applications is: <0.01 (2), 0.01, 0.02 (2), 0.03 (2), 0.04 (2), 0.06 (2), 0.07 (3), 0.08 (3), 0.09, 0.10, 0.11, 0.12 (2), 0.17, 0.24, 0.28, 0.32, 0.40, 0.41, and 1.6 mg/kg (STMR = 0.08 mg/kg).

Residues of sulfoxaflor in cauliflower at 3-day harvest interval were: <0.01 (3), 0.01 (2), 0.02 (3), 0.03, and 0.07 mg/kg (STMR = 0.015 mg/kg).

An MRL 3 mg/kg is proposed for sulfoxaflor in brassica vegetables [except cauliflower]. An MRL of 0.1 mg/kg is proposed for sulfoxaflor in cauliflower.

Grapes

The proposed GAP in table grapes is a maximum of four applications per season, at a dilute spray concentration of 10 g ai/100 L, in a spray volume of 1000 L/ha, with a maximum per-hectare application rate of 100 g ai/ha, and a harvest withholding period of 7 days.

The proposed GAP in wine grapes is a maximum of two applications per season no later than 80% capfall (BBCH growth stage 68), at a dilute spray concentration of 7.5 g ai/100 L, in a spray volume of 1000 L/ha, with a maximum per-hectare application rate of 75 g ai/ha, and a harvest withholding period not being required when the product is used as directed.

A substantial global residue data package for grapes was presented with the application, using treatment regimes matching the proposed GAPs for both table and wine grapes. Trials matching the table grapes GAP (4 × 100 g ai/ha, at a target re-treatment interval of 7 days with a harvest interval of 7 days) were conducted in both table and wine grapes in the USA (nine trials), Australia (nine trials), New Zealand (three trials) and Europe (twelve trials). Trials matching the proposed wine grapes GAP for Australia (2 × 75 g ai/ha applications approximately 14 days apart, with all applications on or before 80% capfall, were conducted (four trials in Australia and two trials in New Zealand).

Residues of sulfoxaflor in table and wine grapes 7 days after the last of four applications in accordance with the proposed GAP for table grapes were: 0.01, 0.03, 0.05 (2), 0.06, 0.10 (2), 0.11 (3), 0.12 (2), 0.13 (2), 0.16 (4), 0.17, 0.18, 0.24, 0.27, 0.28, 0.31, 0.36, 0.37, 0.40, 0.50, 0.56, 0.59, 1.1 (2), and 1.9 mg/kg (STMR = 0.16 mg/kg).

An MRL of 3 mg/kg is proposed for grapes [excluding wine grapes].

Residues of sulfoxaflor in wine grapes collected at harvest after two applications of 75 g ai/ha (equivalent to a dilute spray concentration of 7.5 g ai/100 L in a volume of 1000 L/ha) at or before BBCH 68 were: ND (6). The LOQ and LOD were 0.01 and 0.005 mg/kg respectively.

An MRL of *0.01 mg/kg is proposed for sulfoxaflor in wine grapes.

The processing study shows that sulfoxaflor (parent compound) concentrates in raisins (3.5X). Residues in wet pomace were at the same level as those in raw grapes (processing factor = 1.0X). According to the OECD Feed Tables, wet pomace typically contains 15% dry matter, giving a processing factor for dry grape pomace of 6.7X.

The calculated HR-P and STMR-P values for raisins (using the raw table grape HR and STMR values) are 6.7 and 0.56 mg/kg respectively. An MRL of 10 mg/kg is therefore proposed for sulfoxaflor in dried grapes.

The calculated HR-P and STMR-P values for dry pomace (using the raw table grape HR and STMR values, as pomace could originate from juice manufacture from table grapes, as well as from wine making) are 13 and 1.1 mg/kg respectively. A Table 4 entry MRL of 20 mg/kg is therefore proposed for sulfoxaflor in dry grape pomace.

Citrus fruit

The proposed GAP in citrus fruit is a maximum of two applications per season at a dilute spray concentration of 10 g ai/100 L, in a spray volume of 2000 L/ha, with a maximum per-hectare application rate of 200 g ai/ha, and a harvest withholding period of 1 day.

A sizeable global residue data package for sulfoxaflor in citrus fruit has been generated, including trials in oranges (six trials in Australia, four trials in Brazil and twelve trials in the USA), mandarins (four trials in Australia), lemons (six trials in the USA), and grapefruit (eight trials in the USA).

The combined data set for sulfoxaflor in citrus fruit at 1 day after the last of two applications at 200 g ai/ha (corresponding to a dilute spray concentration of 10 g ai/100 L applied in a spray volume of 2000 L/ha) is: <0.01, 0.01 (3), 0.02, 0.03, 0.04 (2), 0.05, 0.06 (2), 0.07, 0.08, 0.09 (2), 0.10 (3), 0.12, 0.13 (2), 0.14 (2), 0.15, 0.16 (3), 0.17, 0.18, 0.19, 0.24, 0.25, 0.29, 0.32 (2), 0.36 (2), 0.45 (2), and 0.46 mg/kg (STMR = 0.13 mg/kg).

An MRL of 0.7 mg/kg is recommended for sulfoxaflor in citrus fruit, in conjunction with a 1-day harvest withholding period.

The orange processing studies show that residues of sulfoxaflor concentrate significantly in dry pulp (processing factor of 8.3X) and peel (maximum processing factor of 9.1X).

The calculated HR-P values for dry pulp and peel are 3.8 and 4.2 mg/kg. The calculated STMR-P values for dry pomace and peel are 1.1 and 1.2 mg/kg respectively.

A Table 4 entry of 5 mg/kg is recommended for citrus pulp, dry.

Pome fruit

The proposed GAP in pome fruit is a maximum of two applications per season a dilute spray concentration of 10 g ai/100 L, in a spray volume of 2000 L/ha, with a maximum per-hectare application rate of 200 g ai/ha, and a harvest withholding period of 7 days.

A large global residue data package in pome fruit was presented, including residue trials in apples (two in Australia, four in New Zealand, four in Europe and twelve in the USA) and pears (two trials in Australia and six each in the USA and Europe).

The apple and pear residue datasets for trials conducted at GAP were combined for the purpose of determining an MRL for pome fruit: 0.01, 0.04 (2), 0.05 (2), 0.06 (3), 0.07 (2), 0.08 (4), 0.09 (2), 0.10 (2), 0.11, 0.12 (3), 0.13, 0.14 (2), 0.15, 0.16, 0.18, 0.21 (2), 0.22, 0.24, 0.25, 0.27 and 0.30 mg/kg (STMR = 0.105 mg/kg).

An MRL of 0.5 mg/kg is recommended for sulfoxaflor in pome fruit, in accordance with a harvest withholding period of 7 days.

The processing study showed that residues of sulfoxaflor (parent compound) concentrate slightly in wet pomace (1.1X) and more significantly in dry pomace (4.2X).

The HR-P values for wet apple pomace and dry apple pomace are 0.33 and 1.3 mg/kg respectively. The STMR-P values for wet apple pomace and dry apple pomace are 0.09 and 0.34 mg/kg. A Table 4 entry of 2 mg/kg is recommended for sulfoxaflor in apple pomace, dry.

Stone fruit

The proposed GAP in stone fruit is a maximum of two applications at a dilute spray concentration of 7.5 g ai/100 L, or four applications at a dilute spray concentration of 2.5 g ai/100 L. The maximum specified spray volume is 2000 L/ha, giving maximum per-hectare application rates of 150 and 50 g ai/ha respectively. The proposed harvest withholding period is 7 days.

A substantial global package of residue data for stone fruit was presented, including residue trial data in peaches (seven trials in Australia, one trial in New Zealand, and six trials each in Europe and the USA), nectarines (four trials in Australia and one trial in New Zealand), plums (one trial in Australia and six trials in the USA), apricots (one trial each in Australia and New Zealand), and cherries (one trial each in Australia and New Zealand, and six trials each in the USA and Europe). Trials were carried out at 1.33X the proposed global stone fruit GAP (2 × 200 g ai/ha applications made in a dilute spray application, at a target interval of 7 days, with a target harvest interval of 7 days for the magnitude of residue trials).

The residue data for cherries were significantly different from the data set for the other stone fruits.

Residues of sulfoxaflor in cherries at 7 days after the last of two applications at 200 g ai/ha (or four applications at 100 g ai/ha where side-by-side plots were treated and this regime gave the higher residue) were: 0.40, 0.56, 0.58, 0.75, 0.79, 0.89, 0.93, 0.95, 1.0, 1.1, 1.3, 1.4, and 1.6 (2) mg/kg (STMR = 0.94 mg/kg). An MRL of 3 mg/kg is recommended for sulfoxaflor in cherries, in association with a 7-day harvest withholding period.

The combined data set for stone fruit except cherries is: 0.02 (2), 0.03, 0.04, 0.05, 0.06, 0.07, 0.10 (3), 0.11, 0.12 (3), 0.13, 0.14, 0.16 (2), 0.17, 0.18, 0.19 (2), 0.20, 0.22, 0.24, 0.25 (2), 0.30 (2), 0.34, 0.36, 0.37, 0.45, and 0.63 mg/kg (STMR = 0.16 mg/kg). An MRL of 1 mg/kg is recommended for sulfoxaflor in stone fruit [except cherries], in conjunction with a 7-day harvest withholding period.

The cherry processing study showed that residues of sulfoxaflor (parent compound) concentrate slightly (1.1X) in jam and significantly in dried cherries (5.2X).

Using the HR and STMR values for raw cherries as the worst case for stone fruit processing (1.6 and 0.94 mg/kg respectively), HR-P and STMR-P values were calculated.

The HR-P values were 1.8 and 8.3 for jam and dried fruit respectively. The STMR-P values were 1.0 and 4.9 mg/kg for jam and dried fruit respectively.

Animal feeds

Evaluation of the field trials and processing studies showed that finite sulfoxaflor residues could be found in a large number of animal feeds (see discussion above). The following entries in Table 4 of the MRL Standard were recommended: apple pomace, dry: 2 mg/kg; canola fodder (dry): 3 mg/kg; canola forage (green): 3 mg/kg; citrus pulp, dry: 5 mg/kg; cottonseed meal and hulls: 0.5 mg/kg; forage of cereal grains (green): 2

mg/kg; grape pomace, dry: 20 mg/kg; soya bean fodder: 5 mg/kg; soya bean forage (green): 5 mg/kg; soya bean hulls: 0.5 mg/kg; straw and fodder of cereal grains, dry: 1 mg/kg; and tomato pomace, dry: 20 mg/kg.

4.3 Crop rotation

In the field crop rotation study conducted in the USA, sulfoxaflor was applied to spinach, carrot or lettuce as four foliar applications at 100 g ai/ha, with the primary crops being harvested 3 days after the last application, and rotational crops (sorghum, grass, mustard greens and radish) being planted at target intervals of 30, 90, 180 and 270-365 days after treatment. Other than one detection at 0.02 mg/kg in radish tops at a 124-day plant back interval, sulfoxaflor parent compound was not found above the LOQ of 0.01 mg/kg in any of the samples from crops planted in rotation (radish roots and tops, mustard greens, sorghum forage, stover and grains, and grass forage and hay). No additional sulfoxaflor MRLs are proposed in relation to rotational cropping.

4.4 Animal commodity MRLs

Mammalian livestock

The calculated maximum dietary burden of sulfoxaflor is 3 and 2.1 ppm for beef and dairy cattle respectively.

A lactating cattle feeding study was conducted, with cattle being dosed 0.45, 2.37, 6.75, and 35.2 ppm dry weight in feed daily for 29-30 days. A very strong linear relationship between milk and tissue residues and feeding level was observed for all matrices. The linear regression equations were therefore used to calculate the expected maximum and mean residues in cattle matrices.

An MRL of 0.1 mg/kg is recommended for sulfoxaflor in milk (HR = 0.079 mg/kg, STMR = 0.035 mg/kg). An MRL of 0.2 mg/kg is recommended for sulfoxaflor in meat (mammalian); the HR for muscle is 0.13 mg/kg, while that for fat is 0.052 mg/kg. The STMR is 0.043 and 0.015 mg/kg for muscle and fat. An MRL of 0.5 mg/kg is recommended for sulfoxaflor in edible offal (mammalian); the HR for liver is 0.33 mg/kg, while the HR for kidney is 0.21 mg/kg. The STMR for liver is 0.12 mg/kg, while that for kidney is 0.041 mg/kg.

Residues of sulfoxaflor parent compound were lower in cattle fat than in cattle muscle at all feeding levels. The same pattern was observed for poultry fat and muscle. Similarly, residues of sulfoxaflor in cream were slightly lower than those in skim milk at all feeding levels. Finally, the $\log K_{OW}$ value for sulfoxaflor is ~0.8 at 20 °C at pH 5, 7 and 9, well below the threshold of 3 for considering a compound as fat soluble. Sulfoxaflor residues therefore are not fat soluble.

The depuration data from the cattle feeding study showed that residues of sulfoxaflor decline fairly rapidly in cattle matrices after withdrawal of treated feed. A period of five days is sufficient for residues of sulfoxaflor in milk to decline below the limit of quantitation, while a period of nine days is needed for sulfoxaflor residues in tissues to drop below the limit of quantitation.

Poultry

The calculated maximum dietary burden for sulfoxaflor in poultry is 0.012 ppm (dry weight basis).

In the laying hen feeding study, the lowest dose level was 0.145 ppm sulfoxaflor in feed (dry weight). At this dose, the maximum residues of sulfoxaflor (parent compound) in eggs, muscle, liver and fat were <0.01 mg/kg, <0.01 mg/kg, 0.028 mg/kg, and <0.01 mg/kg respectively. The expected maximum dietary burden for sulfoxaflor in both broiler and laying hens is less than 10% of the lowest feeding level of 0.145 ppm. The scaled residues of sulfoxaflor in eggs, muscle, liver and fat are <0.01 mg/kg, <0.01 mg/kg, 0.0028 mg/kg (<0.01 mg/kg), and <0.01 mg/kg. MRLs of *0.01 mg/kg are recommended for sulfoxaflor in poultry meat, edible offal and eggs.

Based upon the metabolism study, livestock dietary burden calculation, and the stockfeed residues data, the following animal commodity MRLs are recommended: edible offal (mammalian) (0.7 mg/kg); eggs (*0.01 mg/kg); meat (mammalian) (0.3 mg/kg); milks (0.2 mg/kg); poultry, edible offal of (*0.01 mg/kg); and poultry meat (*0.01 mg/kg).

4.5 Spray drift

A first tier spray drift model calculation shows that buffer zones are necessary to ensure that residues in the milk, meat and offal of grazing animals downwind of the application area are below the limit of quantitation. However, it is noted that Codex MRLs are shortly expected to be established for milk and mammalian meat and offal at higher levels than corresponding limits proposed for Australia (see table below). Further, an application has been made for establishment of import tolerances (including for animal commodities) in the European Union, and applications are expected to be made shortly for similar tolerances in Korea, Japan and Taiwan. Sulfoxaflor residues in pasture forage dissipate relatively quickly (mean half life of 4.1 days in grass and broadleaf pasture). Likewise, residues in the milk and tissues of grazing livestock are short lived (half lives of sulfoxaflor residues in lactating cattle milk and tissues range from 1.2-2.8 days). Given the inherent conservative nature of the spray drift modelling calculations, and given that buffer zones are not required to ensure compliance with domestic MRLs, it is not proposed to establish buffer zones for sulfoxaflor.

4.6 Bioaccumulation potential

The octanol-water partition coefficient ($\log_{10}K_{OW}$) of sulfoxaflor was measured at pH values of 5, 7 and 9, and varied between 0.799 and 0.806 at 20 °C. The $\log_{10}K_{OW}$ value for the major plant metabolite of sulfoxaflor (X11719474) is <0.3 at pH 5, 7 and 9. This indicates a low potential for bioaccumulation. Residues of sulfoxaflor are not designated as fat soluble.

4.7 Risk Assessment Conclusions

Estimated dietary intake

The chronic dietary intake risk for sulfoxaflor has been assessed. The ADI for sulfoxaflor is 0.04 mg/kg bw/day, based upon a NOEL of 4.24 mg/kg bw/day and a 100-fold safety factor. The NEDI calculation is made in accordance with WHO Guidelines2 and is a conservative estimate of dietary exposure to chemical residues in food. The NEDI for sulfoxaflor, is equivalent to <5% of the ADI. DIAMOND Modelling3 of chronic dietary exposure is also performed on new chemicals. The DIAMOND model estimated the chronic dietary exposure of sulfoxaflor as <5% of the ADI for the general population.

The acute reference dose (ARfD) for sulfoxaflor is 0.25 mg/kg bw, based on a NOEL of 25 mg/kg bw, and a safety factor of 100. The NESTI calculations are made in accordance with the deterministic method used by the JMPR5 with 97.5th percentile food consumption data derived from the 1995 National Nutrition Survey of Australia. NESTI calculations are conservative estimates of short-term exposure (24 hour period) to chemical residues in food. The highest NESTI calculated was 26% of the ARfD. It is concluded that the acute dietary exposure is acceptable.

It is concluded that the dietary exposure to sulfoxaflor is low and the risk from residues in food is acceptable when Transform Insecticide is used according to label directions.

Recommendations

The following amendments to the MRL Standard are recommended in relation to the proposed use of Transform Insecticide:

TABLE 1

Compound	Food		MRL (mg/kg)
ADD: Sulfoxaflor	VB 0040	Brassica vegetables [except cauliflower]	3
	VB 0404	Cauliflower	0.1
	GC 0080	Cereal grains	*0.01
	FS 0013	Cherries	3
	FC 0001	Citrus fruits	0.7
	SO 0691	Cottonseed	0.3

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.

Compound	Food		MRL (mg/kg)
	DF 0269	Dried grapes (=Currants, Raisins, Sultanas)	10
	MO 0105	Edible offal (mammalian)	0.5
	PE 0112	Eggs	*0.01
	VC 0045	Fruiting vegetables, cucurbits	0.5
	VC 0050	Fruiting vegetables (other than cucurbits)	1
	FB 0269	Grapes [excluding wine grapes]	3
	VL 0053	Leafy vegetables [except lettuce, head]	5
	VL 0482	Lettuce, Head	1
	MM 0095	Meat (mammalian)	0.2
	ML 0106	Milks	0.1
	FP 0009	Pome fruit	0.5
	VR 0589	Potato	0.01
	PM 0111	Poultry, edible offal of	*0.01
	PM 0110	Poultry meat	*0.01
	SO 0495	Rape seed [canola]	*0.01
	VR 0075	Root and tuber vegetables [except potato]	0.05
	VD 0541	Soya bean (dry)	0.3
	FS 0012	Stone fruit [except cherries]	1
	FB 1236	Wine grapes	*0.01

*MRL set at the limit of quantitation.

TABLE 3

Compound	Residue definition
ADD: Sulfoxaflor	Sulfoxaflor

TABLE 4

Compound	Animal feed commodity		MRL (mg/kg)
ADD: Sulfoxaflor	AB 0226	Apple pomace, dry	2
		Canola fodder (dry)	3
		Canola forage (green)	3

Compound	Animal feed commodity		MRL (mg/kg)
	AB 0001	Citrus pulp, dry	5
		Cottonseed meal and hulls	0.5
	AF 0081	Forage of cereal grains (green)	2
	AB 0269	Grape pomace, dry	20
	AL 0541	Soya bean fodder	5
	AL 1265	Soya bean forage (green)	5
		Soya bean hulls	0.5
	AS 0081	Straw and fodder of cereal grains (dry)	1
		Tomato pomace, dry	20

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

HARVEST WITHHOLDING PERIODS:

Canola, wheat, barley, and wine grapes	Not required when used as directed
Citrus fruit, cucurbits and fruiting vegetables	Do not harvest for 1 day after the last application.
Brassica vegetables, leafy vegetables	Do not harvest for 3 days after the last application.
Pome fruit, stone fruit and table grapes, root vegetables	Do not harvest for 7 days after the last application.
Cotton and soybeans	Do not harvest for 14 days after the last application.

GRAZING AND STOCKFEED WITHHOLDING PERIODS:

Soybeans	Do not graze or cut for stock food for 7 days after the last application.
Canola, wheat and barley	Do not graze or cut for stock food for 14 days after the last application.

5 ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

5.1 Commodities exported and main destinations

Commodities connected with the application that have a potential for finite residues of sulfoxaflor and are also major export commodities, are pome, citrus and stone fruit, table grapes, soybeans, cottonseed, dairy products, and mammalian meat.

The total exports of Australian apricots in 2010/2011 were worth US$1.468 million (Australian Bureau of Statistics). The largest markets were the United Arab Emirates, Hong Kong and France.

Total cherry exports in 2010/2011 were worth A$12.995 million, with the largest markets being Taiwan ($3.138 million), Hong Kong ($3.060 million), and Thailand ($1.852 million).

Total peach and nectarine exports in 2010/2011 were worth A$12.656 million, with the largest markets being Hong Kong ($5.167 million), the United Arab Emirates ($2.653 million), and Singapore ($1.598 million).

Plum exports in 2010/2011 were A$9.213 million, with the largest markets being Hong Kong ($5.471 million), Singapore ($1.565 million) and the UK ($0.876 million).

Apple exports in 2010/2011 were worth US$5.924 million, with the largest markets being Indonesia ($2.346 million), Papua New Guinea ($1.393 million), and the UK ($0.978 million).

Pear and quince exports in 2010/2011 were worth A$7.465 million, with the largest markets being Canada ($2.468 million), New Zealand ($2.046 million), and New Caledonia ($0.529 million).

Orange exports in 2010/2011 were worth A$95.3 million, with the largest markets being Japan ($34.3 million), Hong Kong ($12.8 million), the USA ($17.4 million), Singapore ($5.16 million), and Canada ($4.1 million).

Mandarin exports in 2010/2011 were worth A$39.0 million, with significant markets including Hong Kong ($5.81 million), Indonesia ($5.19 million), the USA ($4.76 million), New Zealand ($4.61 million), Taiwan ($3.61 million), Japan ($1.94 million), and Russia ($1.11 million).

Table grape exports in 2010/2011 were worth A$79.5 million, with significant markets including Hong Kong ($27.1 million), Indonesia ($12.6 million), Thailand ($9.87 million), Vietnam ($7.12 million), Singapore ($6.05 million), Russia ($1.78 million), and Taiwan ($1.24 million).

In 2010/2011, 268 kilotonnes of cottonseed were exported, with the largest individual markets being Japan and Korea.

In 2010/2011, 2.09 kilotonnes of soybeans were exported, along with 0.97 kilotonnes of oil, and 3.51 kilotonnes of soybean meal.

The significant export markets for animal commodities are listed in Part 5B of APVMA MORAG.4 Total exports of dairy products in 2011/12 were worth $2.216 billion, with key export destinations including Japan, Singapore, China, the Philippines, Korea, Malaysia, Indonesia, Thailand and the USA. Total exports of beef and veal were worth $4.466 billion in 2011/12, with the major destinations including Japan, the USA, Korea, Indonesia, Russia and Taiwan. Total exports of lamb and mutton were worth $1.423 billion in 2011/12, with the key destinations including the USA, the European Union, Japan, China, and the Middle East. Overseas MRLs are established or proposed in only some overseas markets.

5.2 Overseas registration status

The residues aspects of sulfoxaflor have been considered by the Joint Meeting on Pesticide Residues (JMPR), and MRLs advanced by the Codex Committee on Pesticide Residues (CCPR) for consideration by the Codex Alimentarius Commission. Establishment of a range of Codex MRLs is expected by July 2013. An application has been made to the European Union for establishment of import tolerances in animal commodities, and the full range of crops covered by the global data package. Similar applications for establishment of import tolerances are planned for Japan, Korea and Taiwan.

Sulfoxaflor products are registered in Canada, Indonesia, Korea, Panama and Vietnam.

The following relevant Australian and overseas MRLs have been established or proposed:

Sulfoxaflor plant commodity MRLs

COUNTRY	COMMODITY	TOLERANCE, mg/kg
Australia	Cereal grains	*0.01
	Cherries	3
	Citrus fruits	0.7
	Cottonseed	0.3
	Dried grapes (= Currants, Raisins, Sultanas)	10
	Grapes [excluding wine grapes]	3
	Pome fruit	0.5
	Soya bean (dry)	0.3
	Stone fruit [except cherries]	1

[4] http://www.apvma.gov.au/morag_ag/vol_3/part_05b_trade.php

COUNTRY	COMMODITY	TOLERANCE, mg/kg
	Wine grapes	*0.01
USA	Barley	0.4
	Beans (dry)	0.2
	Citrus fruit	0.7
	Climbing vine fruit	2
	Cottonseed	0.2
	Pome fruit	0.5
	Raisins	6
	Rapeseed [canola]	0.4
	Soya bean	0.2
	Stone fruit	3
	Wheat	0.08
Canada	Barley	0.4
	Beans (dry)	0.2
	Citrus fruits	0.7
	Cottonseed	0.2
	Pome fruit	0.5
	Raisins	6
	Rapeseed [canola]	0.4
	Small climbing vine fruits (includes grapes)	2
	Soya bean	0.2
	Stone fruit	3
	Wheat	0.08
Korea	Apple	0.4
	Citrus fruit	1
	Pear	0.4
Codex (advanced to	Barley	0.6

COUNTRY	COMMODITY	TOLERANCE, mg/kg
Step 5/8 at CCPR 45, 6-11 May 2013)	Cottonseed	0.4
	Dried grapes	6
	Grapes	2
	Rape seed	0.15
	Soya bean (dry)	0.3
	Wheat	0.2

The residue definition for sulfoxaflor in plant commodities is parent only for Codex, the USA and Canada.

The following Australian and overseas animal commodity MRLs/tolerances have been proposed:

Sulfoxaflor animal commodity MRLs

COUNTRY	COMMODITY	TOLERANCE, mg/kg
Australia	Edible offal (mammalian)	0.5
	Eggs	*0.01
	Meat (mammalian)	0.2
	Milks	0.1
	Poultry, edible offal of	*0.01
	Poultry meat	*0.01
USA	Cattle, goat, horse and sheep, fat	0.1
	Cattle, goat, horse and sheep, meat	0.15
	Cattle, goat, horse and sheep, meat by-products	0.4
	Milk	0.15
	Pig fat	0.01
	Pig meat	0.01
	Pig meat byproducts	0.01
	Poultry fat	0.01
	Poultry meat	0.01
	Poultry meat byproducts	0.01

	Eggs	0.01
Canada	Meat byproducts of cattle, goats, horses and sheep	0.05
	Meat of cattle, goats, horses and sheep	0.02
	Fat of cattle, goats, horses and sheep	0.01
	Meat and fat of poultry	0.02
	Meat byproducts of poultry	0.02
	Meat and fat of pigs	0.01
	Meat byproducts of pigs	0.01
	Eggs	0.01
	Milk	0.06
Codex (advanced to Step 5/8 at CCPR 45, 6-11 May 2013)	Edible offal (mammalian)	0.6
	Eggs	0.1
	Meat (mammalian)	0.3
	Milk	0.2
	Poultry meat	0.1
	Poultry, Edible offal of	0.3

The animal commodity residue definition in the USA and Canada, and for Codex, is the same as proposed for Australia, parent compound only.

5.3 Potential Risk to Trade

Finite MRLs are proposed for citrus, pome and stone fruit, grapes, dried grapes, soya bean, cottonseed, milk, and mammalian meat and offal.

Some export destinations for soya bean, cottonseed, table grapes, dried grapes, citrus fruit, pome fruit, stone fruit, milk and mammalian meat and offal do not currently have MRLs for sulfoxaflor. Exports of these commodities are therefore at possible risk as a result of the proposed uses of sulfoxaflor in Australia.

Finite residues of sulfoxaflor are not expected to be found in canola seed, cereal grains, wine grapes and poultry commodities, and MRLs are proposed at the limit of quantitation.

Pome fruit: The available residues trial data show that pome fruit from orchards treated with sulfoxaflor may contain residues when harvested (range of residues from supervised Australian, European, American and Canadian apple and pear residues trials (n = 35) was 0.01-0.30 mg/kg; STMR = 0.10 mg/kg).

The proposed pome fruit MRL is the same as the MRLs established for the USA and Canada, while being higher than the Korean limits for apple and pear.

The residue dataset included eight trials in which 2 × 100 g ai/ha applications were made prior to the end of flowering. In these, residues of sulfoxaflor in pome fruit were <0.01 (8) mg/kg. This represents an alternative use pattern for growers producing pome fruit for export to countries without suitable tolerances in place for sulfoxaflor.

Residues of sulfoxaflor may have an impact on the export of Australian pome fruit to the major importing countries. The APVMA welcomes comment on the industry's ability to manage the risk, and on whether sulfoxaflor residues will unduly prejudice Australian trade in pome fruit.

Stone fruit: The available residues trial data show that stone fruit from orchards treated with sulfoxaflor may contain residues when harvested (range of residues from supervised Australian, New Zealand, American and European peach, nectarine, apricot, and plum residue trials (n = 34) was 0.02-0.63 mg/kg; STMR = 0.16 mg/kg; from the cherry trials (n = 14) the range was 0.40-1.6 mg/kg; STMR = 0.94 mg/kg).

The proposed MRL for stone fruit except cherries is lower than those established for the USA and Canada, while the proposed cherry MRL is the same as the stone fruit group MRL proposed for the USA and Canada.

The residue trial program included an application regime of 2 × 100 g ai/ha applications prior to BBCH stage 69 (end of flowering): two trials each in apricots and cherries and four trials each in peaches and nectarines. This corresponds to a dilute spray concentration of 5 g ai/100 L at the maximum spray volume specified on the label (2000 L/ha). Residues at harvest were ND (10), <0.01 and 0.06 mg/kg.

Residues of sulfoxaflor may have an impact on the export of Australian stone fruit to the major importing countries. The APVMA welcomes comment on the industry's ability to manage the risk, and on whether sulfoxaflor residues will unduly prejudice Australian trade in stone fruit.

Citrus fruit: The available residues trial data show that citrus fruit from orchards treated with sulfoxaflor may contain residues when harvested (range of residues from supervised Australian, Brazilian, and American orange, mandarin, grapefruit and lemon residue trials (n = 40) was <0.01-0.46 mg/kg; STMR = 0.13 mg/kg).

The proposed citrus fruit MRL is the same as those for the USA and Canada, and lower than the Korean limit.

Residues of sulfoxaflor may have an impact on the export of Australian citrus fruit to the major importing countries. The APVMA welcomes comment on the industry's ability to manage the risk, and on whether sulfoxaflor residues will unduly prejudice Australian trade in citrus fruit.

Table grapes: The available residues trial data show that table grapes from vineyards treated with sulfoxaflor may contain residues when harvested (range of residues from supervised Australian, New Zealand, and European grape residue trials (n = 33) was 0.01-1.9 mg/kg; STMR = 0.16 mg/kg).

The proposed MRL for sulfoxaflor in grapes [excluding wine grapes] is higher than the limits proposed by Codex and established in the USA and Canada. However, based on the trial data, residues of sulfoxaflor are expected to comply with the US, Canadian and Codex limits.

If use in table grapes is restricted to 2 × 75 g ai/ha applications (equivalent to a spray concentration of 7.5 g ai/100 L and a spray volume of 1000 L/ha), i.e. the use pattern proposed for wine grapes, residues in fruit will be <LOQ. This represents an alternative use pattern for growers producing table grapes for export to countries without suitable tolerances in place for sulfoxaflor.

Residues of sulfoxaflor may have an impact on the export of Australian table grapes to the major importing countries. The APVMA welcomes comment on the industry's ability to manage the risk, and on whether sulfoxaflor residues will unduly prejudice Australian trade in table grapes.

Dried grapes: The available residues trial and processing data show that dried grapes from vineyards treated with sulfoxaflor may contain residues when harvested (the calculated HR-P value from supervised Australian, New Zealand, and European grape residue trials and the processing study is 6.7 mg/kg, while the STMR-P is 0.56 mg/kg).

The proposed MRL for sulfoxaflor in dried grapes is higher than the limits proposed by Codex and established in the USA and Canada. Residues of sulfoxaflor in dried grapes are may exceed the US, Canadian and Codex limits.

If use in grapes for dried fruit production is restricted to 2 × 75 g ai/ha applications (equivalent to a spray concentration of 7.5 g ai/100 L and a spray volume of 1000 L/ha), i.e. the use pattern proposed for wine grapes, residues in fresh fruit and dried fruit will be <LOD. This represents an alternative use pattern for growers producing dried grapes for export to countries without suitable tolerances in place for sulfoxaflor.

Residues of sulfoxaflor may have an impact on the export of Australian dried grapes to the major importing countries. The APVMA welcomes comment on the industry's ability to manage the risk, and on whether sulfoxaflor residues will unduly prejudice Australian trade in dried grapes.

Cereal fodder (oaten hay): The available residues trial data show that hay from crops treated with sulfoxaflor may contain residues when cut (range of residues from supervised Australian, New Zealand and European cereal residue trials (n = 18) was <0.01-0.68 mg/kg; STMR = 0.07 mg/kg).

There are no limits for sulfoxaflor currently listed in the Japanese stockfeed standards.

Residues of sulfoxaflor may have an impact on the export of Australian oaten hay to the major importing countries. The APVMA welcomes comment on the industry's ability to manage the risk, and on whether sulfoxaflor residues will unduly prejudice Australian trade in oaten hay.

Soya bean: The available residues trial data show that soya beans from crops treated with sulfoxaflor may contain residues when harvested (range of residues from supervised Brazilian and American soya bean residue trials (n = 19) was <0.01-0.21 mg/kg; STMR = 0.07 mg/kg).

The proposed MRL for soya bean is higher than the Canadian and US MRLs, and is the same as the proposed Codex limit. Based on the trial data, residues of sulfoxaflor in soya bean are expected to be at or below the US and Canadian limits.

Residues of sulfoxaflor may have an impact on the export of Australian soya bean to the major importing countries. The APVMA welcomes comment on the industry's ability to manage the risk, and on whether sulfoxaflor residues will unduly prejudice Australian trade in soya bean.

Cottonseed: The available residues trial data show that cottonseed from crops treated with sulfoxaflor may contain residues when harvested (range of residues from supervised Australian, European, Brazilian and American cotton residue trials (n = 22) was <0.01-0.18 mg/kg; STMR = 0.03 mg/kg).

The proposed cottonseed MRL is higher than the Canadian and US MRLs, and is lower than the proposed Codex limit. Based on the trial data, residues of sulfoxaflor in cottonseed are expected to be below the US and Canadian limits.

Residues of sulfoxaflor may have an impact on the export of Australian cottonseed to the major importing countries. The APVMA welcomes comment on the industry's ability to manage the risk, and on whether sulfoxaflor residues will unduly prejudice Australian trade in cottonseed.

Dairy products: Based on a lactating cattle feeding study, and the calculated dietary burden for sulfoxaflor in dairy cattle, an MRL of 0.1 mg/kg is proposed for milk. The major contributor to the dietary burden for meat producing animals is soya bean forage, followed by canola forage and dried citrus pulp. The calculated highest residue and STMR values are 0.079 and 0.035 mg/kg respectively.

The proposed milk MRL is higher than the Canadian limit, and is lower than the US and Codex limits. Residues of sulfoxaflor in milk may exceed the Canadian MRL.

It is noted that consumption of fruit processing byproducts such as grape pomace and dried citrus pulp at generally accepted proportions of the diet (20% and 30% of the diet respectively) may result in residues of sulfoxaflor in milk at low levels (up to 0.02 mg/kg). Consumption of cereal forages and hays may result in sulfoxaflor residues of up to 0.033 mg/kg in milk using the HR residue values from the trials, and <0.01 mg/kg in milk using the STMR values. Consumption of canola forages and fodders may result in sulfoxaflor residues of up to 0.03 mg/kg in milk using the HR values, and <0.01 mg/kg using the STMR values. Consumption of soya bean forages and fodders may result in sulfoxaflor residues of up to 0.047 mg/kg using the HR values and <0.01 mg/kg using the STMR values.

To mitigate the risk of finite residues in animal commodities, particularly dairy products, the following additional label restraint is proposed: Do not use on canola grown as a forage crop and do not use on dual-use canola prior to grazing. Dual use on canola refers to the practice of grazing canola during the vegetative stage, then later harvesting the same crop for seed. Similar additional statements in relation to cereal and soya bean crops could be included on the label if required.

Residues of sulfoxaflor may have an impact on the export of Australian dairy products to the major importing countries. The APVMA welcomes comment on the industry's ability to manage the risk, and on whether sulfoxaflor residues will unduly prejudice Australian trade in dairy products.

Meat (mammalian): Based on a lactating cattle feeding study, and the calculated dietary burden for sulfoxaflor, an MRL of 0.2 mg/kg is proposed for meat (mammalian), and an MRL of 0.5 mg/kg is proposed for mammalian edible offal. The major contributor to the dietary burden for meat producing animals is soya bean forage, followed by canola forage and dried citrus pulp. The calculated HR values are 0.128, 0.052,

0.33 and 0.21 mg/kg for muscle, fat, liver and kidney respectively. The calculated STMR values are 0.043, 0.015, 0.12 and 0.041 mg/kg for muscle, fat, liver and kidney respectively.

The proposed meat MRL is lower than the proposed Codex limit, and higher than the USA and Canadian limits for meat and fat. Residues of sulfoxaflor in meat and fat may exceed the Canadian MRLs, and the US MRLs for pig meat and fat, while residues are expected to comply with the US MRLs for sheep, horse, cattle and goat meat and fat.

The proposed mammalian edible offal MRL is lower than the proposed Codex limit. It is higher the US and Canadian limits. Residues of sulfoxaflor in mammalian offal may exceed the Canadian MRLs and the US MRLs for pig offal, while the residues are expected to comply with the US limits for sheep, horse, cattle and goat offal.

The depuration phase of the cattle feeding study shows that a period of 9 days is sufficient to ensure that residues of sulfoxaflor in the meat and offal of cattle decline to <LOQ. An Export Slaughter Interval (ESI) of 14 days is proposed to mitigate the risks to meat exports of the proposed uses of sulfoxaflor.

Residues of sulfoxaflor may have an impact on the export of Australian meat to the major importing countries. With the implementation of the proposed 14-day ESI, the APVMA considers the risk to be low and acceptable. The APVMA welcomes comment on the industry's ability to manage the risk, and on whether sulfoxaflor residues will unduly prejudice Australian trade in meat.

6 OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

Sulfoxaflor (CAS: 946578-00-3) is not listed in Safe Work Australia's (SWA) Hazardous Substances Information System (HSIS) Database (SWA, 2013). Based on the available data, OCS classified sulfoxaflor as a non-hazardous substance according to the NOHSC Approved Criteria for Classifying Hazardous Substances (NOHSC, 2004). No human health risk phrases will be required for this new active constituent.

Based on the product toxicology information and concentrations of sulfoxaflor in the product (24%), Transform Insecticide is not classified as a hazardous substance in accordance with the NOHSC Approved Criteria for Classifying Hazardous Substances (NOHSC, 2004). Thus, no human health risk phrases have been assigned.

Formulation, packaging, transport, storage and retailing

The active constituent sulfoxaflor will be manufactured overseas. The product Transform Insecticide will be manufactured overseas and imported into Australia in 1L, 5L, 10L and 20L high density polyethylene (HDPE) containers.

Use pattern

Transform Insecticide is intended to be used as an insecticide and will be applied to a variety of broadacre (i.e. canola, cereals, cotton, forage brassicas and soybeans), vegetable (i.e. cucurbits, fruiting vegetables, green peas and beans, leafy vegetables, root and tuber vegetables and vegetable brassicas), trees and wine crops (i.e. citrus, grapes, pome and stone fruits) for the control of aphids, plant bugs, whiteflies, planthoppers, mealybugs and scales.

Transform Insecticide will be applied by aerial application to all crops except tree and vine crops by professionals, by groundboom application to all crops, by handheld (vehicle mounted tank (VMT) and backpack) spray application to vegetable crops, trees and vine crops and by airblast to fruit trees and vines by professionals or by farmers with private on-farm equipment. The proposed application rate for this product is between 10 mL to 800 mL of Transform Insecticide/hectare (2.4 - 192 g a.i./ha). The product will be applied at a maximum dilution rate of 1:75 for aerial application and 1:250 for groundboom, airblast and handheld spray application.

Maximum use rates for broadacre and vegetable crops are for treatment of Greenhouse whitefly and maximum use rates for tree and vine crops are indicated for treatment of fruit crops. Target sprays against insect populations should be performed at 7- 21 day intervals. However, the application rate should not exceed 4 times per crop in any one season, except where otherwise indicated.

Exposure during use

Commercial providers and farmers with their employees will be the main users of Transform Insecticide. Workers may be exposed to the product when opening containers, mixing/loading, application, and cleaning up spills and equipment. The main route of exposure to the product will be dermal with inhalation, although ocular exposure is also possible. No suitable worker exposure studies were submitted. Consequently, in the absence of suitable exposure data for the proposed mode of application, the Pesticide Handler Exposure

Database (PHED) Surrogate Exposure Guide (1998) was used to estimate exposure. The toxic endpoint of concern and identified NOAEL is derived from repeat dose study in animals, and in this instance a margin of exposure (MOE) of 100 or above is acceptable. The MOE takes into account both interspecies extrapolation, intraspecies variability and the seriousness of the critical health effect of concern.

For workers conducting aerial mixing and loading and groundboom mixing, loading and application, an acceptable level of exposure (MOE ≥ 100) was obtained when wearing cotton overalls buttoned to the neck and wrist (or equivalent clothing) and elbow length chemical resistant gloves. Additionally, for backpack spray application, levels of exposure to workers were estimated to be acceptable only when wearing an additional layer of clothing over normal clothing and elbow length chemical resistant gloves.

Application of Transform Insecticide by aerial spray or groundboom methods may lead to unintended bystander exposure via chemical spray drift, though it is expected that good agricultural practices will be followed.

Exposure during re-entry

Based on the risk assessment for workers conducting high or very high exposure activities (such as thinning, harvesting, bagging, tying mature plants and irrigation), the margins of exposure are considered to be acceptable (i.e. MOE >100) for re-entry into all crops types. Therefore no re-entry statement is required.

Recommendations for safe use

Users should follow the First Aid Instruction, Safety Directions and Precautionary Statements on the product label.

Transform Insecticide 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

Dow AgroSciences has applied for approval of the new active constituent sulfoxaflor in conjunction with registration of the end use product Transform™ Insecticide containing that active constituent. This is the first time approval for sulfoxaflor has been sought in Australia. Transform™ Insecticide is an aqueous suspension concentrate (SC) formulation containing 240 g ac/L. The product will be marketed for the control of a range of insect pests in canola, cereal crops, cotton, forage brassicas, soybeans, vegetable crops, and tree and vine crops. It will be applied at up to 800 mL/ha (192 g ac/ha) up to twice per year or up to 400 mL/ha (96 g ac/ha) up to 4 times per year with minimum intervals between treatment of 14 and 7 days, respectively.

7.2 Environmental Fate

Hydrolysis

Sulfoxaflor is stable to hydrolysis under acidic, neutral and alkaline conditions. No major or minor transformation products were detected.

Photolysis

Sulfoxaflor has limited absorption of UV/VIS light in the environmentally significant wavelength range of 290-800 nm. In standard aqueous photolysis studies only slight degradation was shown. In a standard soil photolysis study, sulfoxaflor degraded more rapidly in the dark controls. Photolysis is only expected to be a minor degradation pathway for sulfoxaflor.

Sulfoxaflor is unlikely to remain stable in the atmosphere, due to reactions with photo-chemically produced hydroxyl radicals with an estimated half-life of 0.647 days.

Biodegradation

Aerobic

The metabolism of sulfoxaflor in aerobic soil was investigated in four US soils and four European soils under laboratory conditions at temperatures between 10 and 25°C. Sulfoxaflor is readily degradable with half-lives between 0.05 and 0.6 days. Degradation was slower under sterile conditions.

The main metabolite X11719474 was formed rapidly, reaching peak values of 98 to 100% of applied radioactivity by day 1 to 31. Biotransformation of the main metabolite was more pronounced in the European soils, producing the minor metabolites X11579457 and X11579540 which were not observed in the US soils. The primary aerobic degradation pathway for sulfoxaflor is the biological oxidation of the cyano-carbon bond producing X11719474. In the European soils, the main metabolite was further degraded through loss of the urea side-chain, forming the two minor metabolites. The major metabolite was present at the end of the study period at between 35 and 90% of the applied radioactivity, and was slightly degradable with half-lives ranging from 85 to greater than 1,000 days. The half-lives for the minor metabolites X11579457 and X11519540 ranged from 96 to 670 days and from 71 to greater than 1000 days, respectively.

Under field conditions in several North American locations, sulfoxaflor generally dissipated slightly less rapidly than under laboratory conditions. Sulfoxaflor dissipated from the top 15 cm of soil with half-lives between 0.33 and 8.1 days for bare soil and between 0.13 and 1.9 days for cropped soil. The major metabolite at all sites was X11719474 which dissipated with half-lives ranging from 27 to 248 days in bare soil and from 40 to 109 days in cropped plots. The annual carryover for X11719474 was observed at up to 46%. Biotransformation was the major route of dissipation with leaching significant only for the major metabolite.

In aerobic aquatic conditions (two pond water sediment systems comprising either a sand or a silt loam) sulfoxaflor dissipates by a combination of partitioning to the sediment from the water phase and also degradation in water and sediment. Sulfoxaflor is more persistent in sediment and is considered slightly degradable in the whole system with half-lives ranging from 11 to 65 days in water, 46 to 102 days in sediment and 37 to 88 days in the total system. X11719474 was the major transformation product in the water and sediment layers of both systems. The concentration of this metabolite steadily increased in both water and sediment reaching maximum concentrations before gradually declining. In the silt loam sediment system, non-extractable residues increased to 26%.

Anaerobic

Sulfoxaflor is readily degradable based on an anaerobic study on one US and one European soil with half-lives of 0.17 and 2.5 days, respectively. The major metabolite X11719474 formed throughout the aerobic and anaerobic phases, peaking to 95 and 98% of the applied radioactivity at days 4 and 20 days. At the end of the study, the X11719474 was present at 49-75% of the applied radioactivity, while non-extractable residues had increased to 20-25% of the applied radioactivity. X11719474 is very slightly degradable with half-lives of 320 to 532 days.

In anaerobic aquatic conditions (two pond water sediment systems comprising either a sand or a sandy clay loam), the degradation of sulfoxaflor is considerably less pronounced by comparison to aerobic conditions. The half-lives of sulfoxaflor were 84 to 261 days water, 103-382 days in the whole system and undetectable degradation in sediment. Sulfoxaflor was mainly bound as non-extractable residues in the sandy clay loam system, comprising 37% of the material balance. No major transformation products were formed, but X11719474 was detected towards the end of the study in both the water and sediment layers but did not exceed 8.4% in the total system. The anaerobic biotransformation of X11719474 was studied seperately in the same two pond water sediment systems. This metabolite did gradually move to sediment in both systems but no significant degradation occurred (half life greater than 1,000 days).

Mobility

Sulfoxaflor has high to very high mobility in soil with K_d values ranging from 0.19 to 1.29 (K_{oc} of 12 to 72). No strong relationship between K_d and the soil parameters pH, organic carbon, % clay or cation exchange capacity were observed. The Freundlich exponent generally ranged from 0.9 and 1.1, indicating a linear relationship between adsorption and sulfoxaflor concentration. The desorption constants values for the Freundlich single-point desorption isotherms were slightly higher than the corresponding adsorption Kf constants for the same soil sample, ranging from 1.75 to 6.62 (K_{foc} of 53 to 585), while for the Freundlich consecutive desorption isotherms were in the same range, ranging from 0.18 to 0.89 (K_{foc} of 6 to 61). The results indicate that binding is not irreversible and some parent is expected to desorb from the soil.

The metabolite X11719474 also has high to very high mobility in soil with adsorption K_d values ranging from 0.18 to 1.24 (K_{oc} of 7 to 80). For the metabolites X11579457 and X11519540, the 1/n values for two of the soils indicated non-linear adsorption behaviour and for these, the Freundlich values are more appropriate. Both X11579457 and X11519540 have very high molbility with K_f values ranging from 0.13 to 0.79 (K_{foc} of 2 to 44) and 0.01-0.39 (K_{foc} of 1 to 25), respectively.

Uptake, translocation and metabolism in plants

The uptake, translocation and metabolism of sulfoxaflor were investigated on 2-3 leaf cabbage, pepper and cotton plants and also on 5 leaf pepper plants. Sulfoxaflor was taken up by treated leaves from less than 5 to 90%, but minimal amounts (less than 0.2% of the applied radioactivity) moved out of the treated leaves, suggesting that sulfoxaflor is not transported through the phloem. In addition, phosphor images showed that sulfoxaflor applied to the leaf moved to the leaf edge with no visible movement back to the leaf petiole and that sulfoxaflor applied to the stem moved to the foliage above the application point and concentrated at the leaf tips. It was concluded that sulfoxaflor moves through the plant exclusively via the xylem. In plants, sulfoxaflor is oxidatively cleaved to X11721061 which is conjugated to X11889781, glucose malonate.

7.3 Environmental Effects

Avian

Sulfoxaflor is at most moderately toxic to birds by acute oral exposure with an LD_{50} of 676 mg ac/kg bw for bobwhite quail. Based on the lowest LC_{50} value of >5650 mg ac/kg feed, sulfoxaflor is practically non-toxic to birds in short term dietary exposures. However, reduced body weight gain was a notable dose-dependent sublethal effect in both test species (NOEC values of <165 mg ac/kg bw for bobwhite quail and 215 mg ac/kg bw for mallard duck). The major metabolite X11719474 is considered to be practically non-toxic to birds on an acute oral basis. In longer-term tests, no subchronic or reproductive effects were observed at the limit dose for either bobwhite quail (NOAEC 81 mg ac/kg bw/day) or mallard duck (NOEC = 26 mg ac/kg bw/day).

Fish

The saltwater species, the sheepshead minnow, was most species with an LC_{50} value of 288 mg ac/L, exhibiting mortality at the highest test concentration and dose-dependent sub-lethal effects. No mortality or sublethal effects were observed in an acute limit test with the metabolite X11719474. Based on these results, sulfoxaflor and X11719474 are practically non-toxic to fish on an acute basis. In the early life stage tests, hatching and survival were apparently unaffected but significant and dose dependent reductions in mean fry weight and mean fry length were observed in the Fathead minnow and Sheepshead minnow, respectively. Based on the most sensitive NOEC of 0.63 mg ac/L, sulfoxaflor is at most slightly toxic to the early life stages of fish.

Aquatic invertebrates

In the acute toxicity testing, Sulfoxaflor and the metabolite X11719474 are categorised as practically non-toxic to daphnids. Sulfoxaflor is slightly toxic on an acute basis to the Eastern Oyster based on a dose-dependent inhibition of shell growth. However, the Mysid shrimp is considerably more sensitive and based on mortality effects has the most sensitive acute EC_{50} value of 0.67 mg ac/L, which categorises sulfoxaflor as highly acutely toxic to aquatic invertebrates. The Mysid shrimp is also the most sensitive to longer term exposure, with a NOEC of 0.13 mg ac/L based on significantly reduced mean days to first F_0 brood. This classifies sulfoxaflor as slightly toxic to aquatic invertebrates on a chronic basis.

Algae and aquatic plants

Green algae and the Marine diatom were not sensitive to sulfoxaflor in limit tests conducted at 95.6 mg ac/L. Significant and clearly dose dependent inhibition of growth rate, yield or biomass was measured in bluegreen algae and the Freshwater diatom. However, the ER_{50} is greater than 95.6 g ac/L for all species which categorises sulfoxaflor as, at worst, slightly acutely toxic to algae. Based on the lowest chronic endpoint of 3.54 mg ac/L, sulfoxaflor is very slightly toxic to algae on a chronic basis. Duckweed showed no sensitivity to sulfoxaflor, which is considered to be practically non-toxic to this species.

Sediment dwelling organisms

In an acute sediment spiked test with chironomids, a dose-dependent reduction in survival resulted in an LC_{50} of 0.161 mg Total radioactive residues (TRR)/kg dry sediment. Growth (dry weight) of surviving chironomids was significantly inhibited in a dose-dependent pattern, resulting in a NOEC of 0.0488 mg TRR/kg dry sediment. In the water spiked chronic test, no treatment-related effects on development rate were observed, but a significant reduction in emergence at the highest test concentration resulted in a NOEC value of 0.0455 mg TRR/L.

Mammals

The acute oral LD_{50}s for mice and rats were determined to be 750 mg ac/kg bw and 1000 mg ac/kg bw. Temporary treatment related signs of toxicity were observed in mice at 560 mg ac/kg bw and included labored respiration, muscle convulsions, decreased activity, and decreased resistance to removal. Based on the lowest acute LD_{50} value of 750 mg ac/kg bw, sulfoxaflor is slightly toxic to mammals on an acute basis. In the chronic test with rats, reproductive effects (neonatal survival and associated lower percentage of live pups) were observed at the highest test concentration (24.6 mg ac/kg/day) resulting in a NOEL value of 6.1 mg/kg/day.

Bees

Sulfoxaflor is toxic to honeybees on both an acute oral (LD_{50} value of 0.146 µg ac/bee) and on an acute contact (LD_{50} value of 0.379 µg ac/bee) basis. Honeybees were more sensitive to the formulation GF-2032 SC. This formulation is highly toxic to honeybees on an oral basis (LD_{50} of 0.0515 µg ac/bee) and toxic on a contact basis (0.130 µg ac/bee). Honeybee larvae were sensitive to sulfoxaflor in single and multiple dose feeding studies. The day 7 LC_{50} values for the single and multiple dose studies were 2.65 µg ac/bee larvae and 0.247 µg ac/bee larvae, respectively. Sulfoxaflor is at most toxic to honeybee larvae.

Several tunnel tests and residue studies were provided. A laboratory foliage residue toxicity test indicated bees were not harmed by exposure to dried residues on foliage. Residue studies indicate that sulfoxaflor can be systemically translocated to flower pollen and nectar and subsequently found in worker bee stomachs. Tunnel tests indicated that sulfoxaflor had short term impacts on worker bee mortality and flight intensity. The tunnel and laboratory studies indicate that there may be acute mortality to larval bees, but no other developmental effects on brood.

Terrestrial Invertebrates

In Tier 1 testing with sulfoxaflor, parasitic wasps were the most sensitive species with an LR_{50} value of 0.019 g ac/ha, but with no apparent effects on reproduction. A Tier 2 extended laboratory test resulted in a higher LR_{50} value of 1.28 g ac/ha and again without effects on reproduction. When wasps were exposed over a period of 48 hours to fresh-dried or aged (3, 7 or 14 days) residues, mortality was no longer considered unacceptable (defined as <30% corrected mortality relative to the control) by three days after treatment at application rates up to 45 g ac/ha.

Earthworms

Sulfoxaflor is highly acutely toxic to eathworms with an LC_{50} of 0.885 mg ac/kg dry soil. Chronic exposure had no significant impact on fresh weight of surviving adults, but increased mortality and a reduction in the number of juveniles at the highest treatment level resulting in a NOEC of 0.64 mg ac/kg soil.

Soil microbial activity

Sulfoxaflor did not affect the short-term respiration and nitrogen turnover in a soil treated up to 0.161 mg ac/kg dry soil. However, the long-term influence on nitrogen turnover and soil respiration is unclear based on the relatively low application rates compared to the proposed maximum application rate in Australia.

Terrestrial plants

The effects of the formulation GF-2032 SC on the vegetative vigour and seedling emergence of terrestrial non-target plants were determined in Tier 1 and 2 tests. In Tier 2 testing, inhibition did not exceed 25% for any parameter. The ER_{25} values were >400 g ac/ha for seedling emergence and >200 g ac/ha for vegetative vigour.

7.4 Risk Assessment

At the proposed rate the resulting predicted environmental concentration (PEC) of sulfoxaflor and its formulations showed an acceptable risk to birds and earthworms, and no down-wind no-spray zones are required for the protection of aquatic species or terrestrial plants. The risk to soil microflora at the proposed rates in Australia is unclear. The insecticidal action of sulfoxaflor is exhibited on honeybees and non-target beneficial insects, including parasitic wasps.

The risk to honeybees from sulfoxaflor applied at the maximum proposed application rate was determined to be unacceptable, with application not suitable for use in areas where bees are foraging. The proposed label includes directions which will reduce the impact on honey bees. The APVMA welcomes comment on the risk to the honey bee industry and the impact that the use of the proposed product may have on that industry. In addition, the unacceptable risk to beneficial insects indicated an incompatibility with IPM practices; these hazards are reflected on the product label.

8 EFFICACY AND SAFETY ASSESSMENT

Data were presented from 101 field and 2 laboratory efficacy and/or crop safety trials conducted in Australia and several other countries between 2006 and 2010 which demonstrate that Transform Insecticide (Transform SC) can be used to control certain sap sucking insect pests in various broadacre, vegetable and fruit crops without causing damage to those crops.

There is sufficient consistency in the results from common pests, crops, rates of applied active and formulations to accept the data from overseas trials will be applicable to the claims for Transform SL in Australia.

The majority of the trials (93 of the 103) use sulfoxaflor as the 240g/L SC formulation proposed for registration as Transform SC. Seven of these trials also included sulfoxaflor as the 500g/kg WG formulation. In addition, various other sulfoxaflor formulations are included in the trials. The efficacy and crop safety demonstrated in all of these trials is similar regardless of formulation and it is accepted that, in terms of efficacy and crop safety, the formulations used in the trials are bioequivalent.

Ninety nine trials tested the efficacy of sulfoxaflor formulations against 22 of the 26 pests claimed on the Transform SC label, either alone or with crop safety. Each of these trials demonstrated >90% control or statically significant reduction in pest numbers and comparable performance with current industry standard insecticides. The trial data was drawn from trials across a number of years and geographically diverse areas, using application techniques and rates equivalent to the label claims and instructions. The results were sufficient to demonstrate efficacy against of all the following pests claimed on the Transform SC label: Aphids including Green peach, Cabbage, Oat, Rose-grain, Cotton/melon, Brown sowthistle, Soybean, Woolly apple, Turnip, Corn, Cowpea, Cherry, Black peach and grain aphid, Green mirid, Greenhouse whitefly, Citrophilus mealybug, Citrus mealybug, Longtailed mealybug, Tuber mealybug, Citricola scale, Pink wax scale, Red scale, Citrus snow (white louse) scale, Kelly's citrus thrip and Apple dimpling bug.

Crop safety was considered in ninety eight trials, either alone or in conjunction with efficacy. No evidence of phytotoxicity or crop effects was reported in any of these trials. The trials were carried out in a wide range of crops and varieties representing the majority of the crops claimed on the proposed Transform SC label. Thirty of the trials were carried out using sulfoxaflor at rates above the maximum (1.5x – 6x), 56 of the trials are carried out at the maximum rate and 12 were carried out at the minimum rate proposed for particular crops. These trials demonstrated crop safety in the following: Broad acre crops (canola, cereals, cotton, forage brassicas and soybeans), Vegetable Crops (cucurbits, fruiting vegetables, leafy vegetables, root and tuber vegetables and vegetable brassicas) and Tree and Vine Crops (citrus, table and wine grapes, pome fruit and stone fruit. The data adequately establish the crop safety claimed for the use situations proposed on the Transform SC label.

All trials were conducted using suitable methodology and, with the exception of the two laboratory trials, were conducted in situations equivalent to commercial practice. Ninety five of the 101 trials were conducted as fully randomised with Complete Block design, 3-4 replicates, industry standard comparison treatments and untreated controls. The remaining 6 trials were non-randomised with 1-2 replicates but the results are sufficiently to provide secondary support to the proposed label claims. The formulations tested and rates used are consistent with or comparable to, those proposed for registration.

The label claims and instructions proposed in the Claims for Use statement, the Directions for Use table and the various recommendations and statements on the labels for Transform SC is consistent with the results of the trials and other information presented.

9 LABELLING REQUIREMENTS

CAUTION

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

Dow AgroSciences

Transform™

Insecticide

ACTIVE CONSTITUENT: **240 g/L SULFOXAFLOR**

GROUP 4C INSECTICIDE

For the control of aphids and other insect pests in canola, cereals, cotton, soybeans and various fruit and vegetable crops as specified in the Directions for Use.

IMPORTANT: READ THE ATTACHED BOOKLET BEFORE USE.

Contents: 1, 5, 10 & 20 L

Dow AgroSciences Australia Limited
A.B.N. 24 003 771 659
20 Rodborough Road
FRENCHS FOREST NSW 2086
www.dowagrosciences.com.au
CUSTOMER SERVICE TOLL FREE **1-800 700 096**

DIRECTIONS FOR USE:

Broadacre, Vegetable and Fruit Crops (refer to individual Tables 1 to 3 below for specific directions. Please note SPRAY DRIFT RESTRAINTS below that apply to all uses.

SPRAY DRIFT RESTRAINTS:

DO NOT apply by air or ground applicators with spray droplets smaller than a MEDIUM spray droplet size category according to nozzle manufacturer specifications that refer to the ASABE S-572 Standard or the BCPC Guideline.**DO NOT** apply when wind speed is less than 3 or more than 20 kilometres per hour as measured at the application site.

DO NOT apply during surface temperature inversion conditions at the application site.

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

DO NOT apply if there are aquatic and wetland areas including aquacultural ponds, surface streams and rivers downwind from the application area and within the mandatory no-spray zones below:

Aerial application: 20 metres (for all crops except tree and vine crops – see Table 3)
Ground application: 5 metres (all crops).

TABLE 1 BROADACRE CROPS
Canola, Cereals, Cotton and Soybeans
DIRECTIONS FOR USE:
Restraints (specific to Broadacre Crops):
DO NOT apply more than 4 times to any of these crops in any one season, except where otherwise indicated.
DO NOT use rotary atomisers when applying aerially
Note: Monitor crops for pest species by regular field scouting. Target sprays against insect populations when they exceed threshold levels. Repeated applications at 14-21 day intervals as new infestations occur unless otherwise directed in the **CRITICAL COMMENTS**.
CAUTION: this product is highly toxic to bees: read the PROTECTION OF LIVESTOCK section in this booklet before use.

Table 1 cont.

CROP	PEST	RATE (mL/ha)	CRITICAL COMMENTS
Canola	If honeybees are present in the target area during flowering see the **Protection of Livestock** directions.		
	Aphids (including cabbage aphid, green peach aphid and turnip aphid)	100 + wetting agent **	The 1st application can be made anytime up to full flowering (50% flowers open on the main raceme) and, if required, a 2nd application can be made no later than 14 days after full flowering. **DO NOT** make more than 2 applications per crop. **DO NOT** use on canola grown as a forage crop and **DO NOT** use on dual-use canola prior to grazing.
Cereals (including wheat and barley) ONLY up to flag leaf stage	Aphids (including Oat aphid and Corn Aphid as vectors of Barley Yellow Dwarf Virus), Grain aphid, Rose grain aphid and Green peach aphid	50-100	**Do not** make more than 2 applications per crop. Do not apply to crop later than the flag leaf stage. Use higher rate under heavy aphid infestations and/or when water volume is reduced, such as with aerial application*. Some species of aphids tend to infest cereal plants at the base of the plant, often inside the leaf sheath and below the soil surface. These entrenched aphids at the base of the plant may not be adequately controlled by Transform

TABLE 1 cont.

CROP	PEST	RATE (mL/ha)	CRITICAL COMMENTS
Cotton	If honeybees are present in the target area during flowering see the **Protection of Livestock** directions		
	Aphids (including green peach aphid, cotton aphid and cowpea aphid)	200-300	Use higher rate under heavy aphid infestations and/or when water volume is reduced, such as with aerial application*.
	Green mirid	200 – 300	Use the lower rate when infestation is predominately nymphs. Use higher rate when control of adults and/or residual control is desired.
	Greenhouse whitefly	400	Ensure accurate species identification
Soybeans	Soybean aphid	100 - 200	Use higher rate when canopy closure may adversely affect application coverage.
	Greenhouse whitefly	400	Ensure accurate species identification
*Apply by air using a minimum water volume of 30 L/ha			
** Addition of a wetting agent may improve control under less than ideal application conditions. Use the wetter according to its label directions. See Wetting Agent Section below for recommended products.			

TABLE 2 VEGETABLE CROPS

Cucurbits, Fruiting vegetables, Green peas and beans, Leafy vegetables, Root and tuber vegetables and Vegetable brassicas.

DIRECTIONS FOR USE:

RESTRAINTS (specific to Vegetable Crops):

DO NOT apply more than 4 times to any of these crops in any one season, except where otherwise indicated.

DO NOT use rotary atomisers when applying aerially

Note: Monitor crops for pest species by regular field scouting. Target sprays against insect populations when they exceed threshold levels. Make repeated applications at 7 day intervals as new infestations occur unless otherwise directed in the **CRITICAL COMMENTS**.

CAUTION: this product is highly toxic to bees: read the PROTECTION OF LIVESTOCK section in this booklet before use.

CROPS	PEST	RATE (mL/ha)	CRITICAL COMMENTS
Cucurbits, field-grown, including pumpkin, squash, melons, cucumbers	If honeybees are present in the target area during flowering see the **Protection of Livestock** directions.		
	Green peach aphid, Melon (cotton) aphid	200 – 300	Use higher rate under heavy aphid infestations or if longer residual control (>7 days) is required.
	Greenhouse whitefly	400	Ensure accurate species identification.
Fruiting vegetables, including chilli, capsicum, eggplant, okra and tomatoes [excluding sweet corn and mushrooms]	Green peach aphid	200 – 300	Use higher rate under heavy aphid infestations or if longer residual control (>7 days) is required.
	Greenhouse whitefly	400	Ensure accurate species identification.
Leafy vegetables, including lettuce (all varieties), Asian greens, silver beet and spinach	Green peach aphid, Brown sowthistle aphid	200–300	Use higher rate under heavy aphid infestations or if longer residual control (>7 days) is required.
	Greenhouse whitefly	400	Ensure accurate species identification.

Table 2 cont.

CROPS	PEST	RATE (mL/ha)	CRITICAL COMMENTS
Root and tuber vegetables, including potatoes, carrots and turnips	Green peach aphid	200–300	Use higher rate under heavy aphid infestations or if longer residual control (>7 days) is required.
Vegetable brassicas, including Asian greens, broccoli, Brussels sprouts, cabbage and cauliflower	Aphids, including cabbage aphid, green peach aphid and turnip aphid	200–300 (+ wetting agent)*	Use higher rate under heavy aphid infestations or if longer residual control (>7 days) is required
	Greenhouse whitefly	400 (+ wetting agent)*	Ensure accurate species identification
* Addition of a wetting agent may improve control under less than ideal application conditions. Use the wetter according to its label directions. See Wetting Agent Section below for recommended products.			

TABLE 3 TREE and VINE CROPS

Citrus, Grapes, Pome and Stone Fruit

DIRECTIONS FOR USE:

RESTRAINTS (specific to Tree and Vine Crops):

DO NOT apply with aircraft.

DO NOT apply more than twice per crop per season for all situations except for use on table grapes and for aphid control on stone fruit, which can have up to 4 applications in any one season.

Carefully monitor crops for pest species by regular field scouting. Repeat applications at a 14 day interval if a new infestation occurs unless otherwise directed in the **CRITICAL COMMENTS.**

CAUTION: this product is highly toxic to bees: read the PROTECTION OF LIVESTOCK section in this booklet before use.

SPRAYING TREE and VINE CROPS: In the following table, all rates are given for dilute spraying where spray volumes may vary in order to obtain good coverage to the point of run-off. For concentrate spraying refer to the "**CONCENTRATE SPRAYING**" section on this label.

CROPS	PEST	RATE (mL/100L)	CRITICAL COMMENTS
Citrus, including oranges, lemons, grapefruit, limes, mandarins and tangerines	If honeybees are present in the target area during flowering see the **Protection of Livestock** directions.		
	Citrophilous mealybug Citrus mealybug Longtailed mealybug	40	Use the 40 mL/100 L rate in up to 2000 litres/ha water. If using higher application volumes, dilute accordingly. Do not exceed a total use of 800 mL of product per ha in a single application.
	Citricola scale, Pink wax scale Citrus snow (white louse) scale and red scale	40	
	Kelly's citrus thrip	40	
Grapes (table grapes)	Longtailed mealybug	30-40	Use the 40 mL/100L rate in up to 1000 litres/ha. If using higher application volumes, dilute accordingly. Do not exceed a total use of 400 mL of product per ha in a single application. Use the higher rate for mid-late season application to ensure adequate coverage

Table 3 cont.

CROPS	PEST	RATE (mL/100L)	CRITICAL COMMENTS
Grapes (wine grapes)	Longtailed mealybug	30	Do not apply later than 80% capfall. Use the 30 mL/100 L rate in up to 1000 litres of water. If using higher application volumes, dilute accordingly. Do not exceed a total use of 300 mL of product per ha in a single application.
Pome fruit, including apples, pears and nashi	If honeybees are present in the target area during flowering see the **Protection of Livestock** directions.		
	Apple dimpling bug	30	Apply the rate in up to 2000 litres of water. Do not exceed 800 mL of product per ha in a single application.
	Longtailed mealybug and tuber mealybug	40	
	Woolly (apple) aphid	40	
Stone fruit, including apricots, cherries, nectarines , peaches and plums	If honeybees are present in the target area during flowering see the **Protection of Livestock** directions		
	Apple dimpling bug	30	Apply this rate in up to 2000 litres of water per hectare. Do not exceed 600 mL of product per ha in a single application.
	Cherry aphid, Green peach aphid, Black peach aphid	10	Apply this rate in up to 2000 litres of water per hectare. Do not exceed 200 mL of product per ha in a single application.
PEST NAMES: Apple dimpling bug (*Campylomma liebknechti*), Black peach aphid (*Brachycaudus persica*), Brown sowthistle aphid (*Uroleucon sonchi)*, Cabbage aphid (*Brevicoryne brassicae*), Cereal aphids (*Rhopalosiphum* spp. – vectors of Barley Yellow Dwarf Virus), Cherry aphid (*Myzus cerasi*), Citricola scale (*Coccus pseudomagnoliarum*), Citrophilous mealybug (*Pseudococcus calceolariae*), Citrus mealybug (*Planococcus citri*), Citrus snow (white louse) scale (*Unaspis citri*) Corn aphid (*Rhopalosiphum maidis*), Cotton aphid (*Aphis gossypii*), Cowpea aphid (*Aphis craccivora*), Grain aphid (*Sitobion miscanthi*), Green mirid (*Creontiades dilutus*), Green peach aphid (*Myzus persicae*), Greenhouse whitefly (*Trialeurodes vaporariorum*), Kelly's citrus thrips (*Pezothrips kellyanus*), Longtailed mealybug (*Pseudococcus longispinus*), Melon aphid (*Aphis gossypii*), Oat aphid (*Rhopalosiphum padi*), Pink wax scale (*Ceroplastes rubens*), Red scale (*Aonidiella aurantii*), Rose-grain aphid (Metopolophium dirhodum), Soybean aphid (*Aphis glycines),* Tuber mealybug (*Pseudococcus viburni*), Turnip aphid (*Lipaphis pseudobrassicae*) and Woolly (apple) aphid (*Eriosoma lanigerum*).			

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

HARVEST WITHHOLDING PERIODS (WHP)

Canola, cereals:
NOT REQUIRED WHEN USED AS DIRECTED.

Citrus fruit, cucurbits and fruiting vegetables (except sweet corn):
DO NOT HARVEST FOR 1 DAY AFTER APPLICATION.

Brassica vegetables, leafy vegetables:
DO NOT HARVEST FOR 3 DAYS AFTER APPLICATION.

Pome fruit, root and tuber vegetables, stone fruit and table and wine grapes:
DO NOT HARVEST FOR 7 DAYS AFTER APPLICATION.

Cotton and soybeans:
DO NOT HARVEST FOR 14 DAYS AFTER APPLICATION.

GRAZING AND STOCKFOOD WITHHOLDING PERIODS (WHP):

Canola forage (failed crop), straw and stubble:
DO NOT GRAZE OR CUT FOR STOCKFEED FOR 14 DAYS AFTER APPLICATION.

Cereals:
DO NOT GRAZE OR CUT FOR STOCKFEED FOR 14 DAYS AFTER APPLICATION.

Cotton:
DO NOT FEED COTTON TRASH TO LIVESTOCK

Soybeans:
DO NOT GRAZE OR CUT FOR STOCKFEED FOR 7 DAYS AFTER APPLICATION.

LIVESTOCK DESTINED FOR EXPORT MARKETS

The grazing withholding period only applies to stock slaughtered for the domestic market. Some export markets apply different standards. To meet these standards, ensure that in addition to complying with the grazing withholding period, that the Export Slaughter Interval, is observed before stock are sold or slaughtered.

EXPORT SLAUGHTER INTERVAL (ESI) – 14 days:

After observing the grazing withholding period, livestock that has been grazed on or fed treated crops should be placed on clean feed for 14 days prior to slaughter.

CROPS FOR EXPORT: **Some crops for export to particular destinations outside of Australia may require a longer interval before harvest to comply with residue standards of importing countries. Please check with your exporter.**

GENERAL INSTRUCTIONS
Insecticide Resistance Warning

GROUP	4C	INSECTICIDE

For insecticide resistance management, Transform Insecticide is a Group 4C insecticide. Some naturally occurring insect biotypes resistant to Transform Insecticide and other Group 4C insecticides may exist through normal genetic variability in any insect population. The resistant individuals can eventually dominate the insect population if Transform Insecticide and other Group 4C insecticides are used repeatedly. The effectiveness of Transform Insecticide on resistant individuals could be significantly reduced. Since occurrence of resistant individuals is difficult to detect prior to use, Dow AgroSciences Australia Limited accepts no liability for any losses that may result from the failure of Transform Insecticide to control resistant insects. Transform Insecticide may be subject to specific resistance management strategies. For further information contact your local supplier, Dow AgroSciences representative or local agricultural department agronomist.

MIXING
- Agitate or shake the container immediately prior to use.
- Half fill the spray tank with water, add the appropriate amount of accurately measured Transform Insecticide, then complete filling the tank.
- Ensure thorough agitation by mechanical or hydraulic action at all times during mixing and application.
- Use only clean water within the range pH 5-9 to dilute Transform Insecticide.

COMPATABILITY
If intendending to tank mix Transform with other agricultural chemicals or plant nutrients consult Dow AgroSciences.

WETTING AGENTS
Not all surfactants or crop oils are of eaqual quality. Dow AgroSciences does not support the use of alternative products other than those listed below.
Agral® Spray Adjuvant, Nufarm Chemwet 1000 and Spreadwet 1000 Wetting Agent. If intending to use other wetting agents consult Dow AgroSciences.

Agral® Trademark of a Syngenta Group Company

STORAGE OF DILUTED SPRAY MIX
Whenever possible the spray mix should be used immediately after it is prepared. However, if weather conditions or mechanical breakdown prevent immediate use, the spray mix may be stored for up to 72 hours without loss of activity. The spray mix should be agitated thoroughly by mechanical or hydraulic action at regular intervals during storage to prevent sedimentation. Ensure that the stored spray mix is thoroughly agitated at least once every 8 hours. The spray mix must be stored out of direct sunlight.

APPLICATION
Thorough coverage of the crop is essential. Ensure this by increasing water volume with plant growth stage. Do not apply when conditions are unsuitable for water-based spray applications. Avoid high temperature, strong winds, inversion conditions, imminent rain or any conditions that may reduce the quality of spray coverage or result in drift from the target area. Techniques to

minimise drift should be employed at all times when aerially applying sprays to, or near, sensitive areas (see RESTRAINTS).

For optimum results follow the application specifications listed below:
Ground Spraying (Broadacre crops): Apply in a minimum of 50 L/ha of water with spray droplets no smaller than medium category according to nozzle manufactuer specifications that refer to the ASABE S-572 Standard of the BCPC Guideline.
Increase spray volumes as the crop grows.

Ground Spraying (Vegetable crops): Apply in a minimum of 250 L/ha of water with spray droplets no smaller than medium category according to nozzle manufactuer specifications that refer to the ASABE S-572 Standard of the BCPC Guideline.. Increase spray volumes as the crop grows.

Aerial Spraying (Broadacre arable and vegetable crops only): Apply in a minimum of 30 L/ha of water with spray droplets no smaller than a medium category according to nozzle manufacturer specifications that refer to the ASABE S-572 Standard or the BCPC Guideline.

PRECAUTION: (Aerial Application)
DO NOT use human flaggers/markers unless they are protected by engineering controls such as enclosed cabs.

DILUTE SPRAYING

- Use a sprayer designed to apply high volumes of water up to the point of run-off and match to the crop being sprayed.
- Set up and operate the sprayer to achieve even coverage throughout the crop canopy. Apply sufficient water to cover the crop to the point of first run-off. Avoid excessive run-off.
- The required water volume may be determined by applying different test volumes, using different settings on the sprayer, from industry guidelines or expert advice.
- Add the amount of product specified in the DIRECTIONS FOR USE table for each 100 L of water. Spray to the point of runoff. If volume to be applied is <1000L/ha then use the low volume (concentrate) application method for calculation of chemical rate. For volumes > 1000 L/ha use dilute spray rate.

CONCENTRATE SPRAYING
Use a sprayer designed and set up for concentrate spraying (that is a sprayer which applies water volumes less than those required to reach the point of run-off) and matched to the crop being sprayed. Set up and operate the sprayer to achieve even coverage throughout the crop canopy using your chosen water volume.
Determine an appropriate dilute spray volume (see **DILUTE SPRAYING** above) for the crop canopy. Consult your local advisor, agronomist or Department of Primary Industries to determine this volume. This is needed to calculate the concentrate mixing rate. The mixing rate for concentrate spraying can then be calculated in the following way:

CONCENTRATE SPRAYING EXAMPLE

1. Dilute spray volume as determined above: e.g. 1000 L/ha
2. Your chosen concentrate spray volume: e.g. 500 L/ha
3. The concentration factor is 2X (1000 / 500)

4. If the dilute label rate is 40 mL/100 L, then the concentrate rate becomes 2 X 40, i.e. 80 mL/100 L of concentrate spray

The chosen spray volume, amount of product per 100 L of water and the sprayer set up and operation may need to be changed as the crop grows. For further information on concentrate spraying, users are advised to consult relevant industry guidelines, undertake appropriate competency training. Always follow Industry Best Practices.

RAINFASTNESS

Rain can wash Transform Insecticide from treated plant surfaces and result in reduced insect control. Avoid making spray applications if rain is expected before the spray can dry completely.

CLEANING SPRAY EQUIPMENT

After using Transform Insecticide empty the tank and completely drain the system. Rinse the tank, pumps, lines, hoses, filters and nozzles by circulating clean water through the system. Drain and repeat the rinsing procedure twice.

PROTECTION OF LIVESTOCK

Highly toxic to bees. Will kill bees foraging in the crop to be treated or in hives which are over-sprayed or reached by spray drift.

Apply in the morning or late in the evening when bees are not active. This product may be toxic to bees for up to 3 hours following application. Toxicity is reduced when spray has dried. For treatments made to crops in flower or upwind of plants that are likely to be visited by bees, avoid spraying within 3 hours of likely bee activity (during the daytime if temperatures are expected to exceed 12 °C). It is recommended that orchard floors containing flowering plants be mown just prior to spraying. In top fruit crops the risk to bees from spraying during flowering applies from pink/white bud until after petal fall.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT

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

PROTECTION OF NON-TARGET INSECTS

Sulfoxaflor may have adverse effects on parasitic wasps particularly where IPM is practiced.

STORAGE AND DISPOSAL

Store in the closed, original container in a cool well-ventilated area. DO NOT store for prolonged periods in direct sunlight. DO NOT store near food, feedstuffs, fertilisers or seed.

Disposal: 1 L label only

Rinse container before disposal. Add rinsings to the spray tank. Do not dispose of undiluted chemicals on site. Dispose of at 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 or Territory government regulations. Empty containers and product should not be burnt.

Disposal: 5 L, 10 L, 20 L, label only

This container can be recycled if it is clean, dry, free of visible residues and has the drumMUSTER logo visible. Triple or pressure rinse container for disposal. Dispose of rinsate by adding to the spray tank. Do not dispose of undiluted chemicals on site. Wash outside of the container and the

cap. Store cleaned container in a sheltered place with cap removed. It will then be acceptable for recycling at any drumMUSTER collection or similar container management site. The cap should not be replaced but may be taken separately.
If not recycling, break, crush, or puncture and deliver empty packaging for appropriate disposal to an approved waste management facility. If an approved waste management facility is not available bury the empty packaging 500 mm below the surface in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots, in compliance with relevant Local, State or Territory government regulations. DO NOT burn empty containers or product

SAFETY DIRECTIONS
May irritate the eyes. Avoid contact with the eyes. When opening the container and preparing the product for use and using the product by (groundboom and aerial application), wear cotton overalls buttoned to the neck and wrist (or equivalent clothing), and elbow length chemical resistant gloves. If applying by spraying equipment carried on the back of the user, wear cotton overalls, over normal clothing, buttoned to the neck and wrist, and elbow length chemical resistant gloves. Wash hands after each use. After each day's use wash gloves and contaminated clothing.

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

PRECAUTIONS

DO NOT use this product in domestic situations or areas where the public gathers

SPILL AND LEAK MANAGEMENT
Do not touch or walk through spilled material. Wear a face shield or goggles, overalls buttoned to neck and wrist, chemical resistant gloves and footwear. Stop leak when safe to do so. Dam area and prevent entry into waterways, and drains.

Small spills/leaks: Contain and absorb small spills with a proprietary absorbent suitable for chemical spills or inert materials such as sand, soil or sawdust. Collect spilled product and place in sealable container for disposal. Spill residues may be cleaned using water and detergent. Contain and absorb wash water for disposal. Absorb and collect washings and place in the same sealable container for disposal. Dam the area of large spills and report them to Dow AgroSciences Emergency Services at 1-800 033 882.

MATERIAL SAFETY DATA SHEET
Additional information is listed on the Material Safety Data Sheet for **Transform™ Insecticide** which is available from Dow AgroSciences on request. Call Customer Service Toll Free on 1-800 700 096 or visit www.dowagrosciences.com.au

EMERGENCY RESPONSE
(All Hours)
RING FROM ANYWHERE IN AUSTRALIA
1-800 033 882
(LOCAL CALL FEE ONLY)

IN A TRANSPORT EMERGENCY ONLY
DIAL 000
FOR POLICE OR FIRE BRIGADE

Barcode
for stock
identification

APVMA Approval No. :64101/xxxxx

DOM/BatchNo:

10 ABBREVIATIONS

AC/ac	active constituent
ACCS	Advisory Committee on Chemicals Scheduling
ADI	Acceptable Daily Intake (for humans)
ai	active ingredient
APVMA	Australian Pesticides and Veterinary Medicines Authority
ARfD	Acute reference dose
BBCH	Scale used to identify phenological developmental stages of plants (Biologische Bundesanstalt, Bundessortenamt and CHemical industry)
bw	bodyweight
d	day
DSEWPaC	Department of Sustainability, Environment, Water, Population and Communities
°C	Degrees Centigrade
CHO	Chinese Hamster Ovary
CIPAC	Collaborative International Pesticides Analytical Council
cm	centimetre
d	Day
DAT	Days After Treatment
DSEWPaC	Department of Sustainability, Environment, Water, Populations and Communities
DT_{50}	Time taken for 50% of the concentration to dissipate
EC_{50}	concentration at which 50% of the test population are adversely impacted
$ER_{25/50}$	the rate that results in an undesirable change or alteration of 25%(or 50%) in the test endpoint being measured relative to the control
EU	European Union
EUP	End Use Product
F_1	First generation
g	gram
GAP	Good Agricultural Practice
GI	Gastro Intestinal

GJR	Global Joint Review
h	hour
ha	hectare
HDPE	High Density Polyethylene
HPLC	High Performance Liquid Chromatography
HR	highest residue
HR-P	Calculated highest residue - processed commodity
HSIS	Hazardous Substance Information System
IPM	Integrated Pest Management
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
JMPR	Joint FAO/WHO Meetings on Pesticide Residues
K_d	distribution coefficient for adsorption
K_f	Freundlich desorption coefficient
kg	kilogram
K_{oc}/ K_{foc}	Organic carbon adsorption coefficient
K_{ow}	Octanol-Water Partition Coefficient
L	Litre
LC_{50}	concentration that kills 50% of the test population of organisms
LC/MS/MS	liquid chromatography-tandem mass spectrometer
LCT	Leydig Cell Tumours
LD_{50}	dosage of chemical that kills 50% of the test population of organisms
LH	Lutenising Hormone
LLNA	Local Lymph Node Assay
LOD	Limit of Detection – level at which residues can be detected
LOAEL	Lowest Observable Adverse Effect Level
LOQ	Limit of Quantitation – level at which residues can be quantified

LR_{50}	Application rate that kills 50% of the test population of organisms
m	metre
mg	milligram
mL	millilitre
MMAD	Mass Median Aerodynamic Diameter
MoA	Mode of Action
MOE	Margin Of Exposure
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
nAChR	nicotinic acetylcholine receptor
ND	Not Detectable
NDPSC	National Drugs and Poisons Schedule Committee
NEDI	National Estimated Daily Intake
NESTI	National Estimated Short Term Intake
nm	nanometres
NOHSC	National Occupational Health and Safety Commission
NOEC	No Observable Effect Concentration
NOAEL	No Observable Adverse Effect Level
/NOEL	No Observable Effect Level
OC	Organic Carbon
OCS	Office of Chemical Safety (Department of Health and Ageing)
OECD	Organisation for Economic Cooperation and Development
OM	Organic Matter
Pa	Pascals
PEC	predicted environmental concentration
PHED	Pesticide Handler Exposure Database
PMRA	Pest Management Regulatory Agency (Canada)

P_{ow}	octanol/water partition coefficient
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
RBC	Red Blood Cell
RSD	Relative Standard Deviation
s	second
SC	Suspension Concentrate
STMR	Supervised Trials Median Residue
STMR-P	STMR corrected for processing
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons
SWA	Safe Work Australia
$T_{1/2}$	Elimination Half-Life
TGAC	Technical grade active constituent
T_{max}	Time to achieve maximum concentration
TRR	Total Radioactive Residue
µg	microgram
US EPA	U.S. Environmental Protection Agency
UV/VIS	Ultra Violet/Visible Light
VMT	Vehicle Mounted Tank
WG	Water Dispersible Granule
WHP	Withholding Period

GLOSSARY

Active constituent	The substance that is primarily responsible for the effect produced by a chemical product
Acute	Having rapid onset and of short duration.
Carcinogenicity	The ability to cause cancer
Chronic	Of long duration
Codex MRL	Internationally published standard maximum residue limit
Desorption	Removal of a material from or through a surface
Efficacy	Production of the desired effect
Formulation	A combination of both active and inactive constituents to form the end use product
Genotoxicity	The ability to damage genetic material
Hydrophobic	repels water
Leaching	Removal of a compound by use of a solvent
Log P_{ow}	Log to base 10 of octanol water partitioning co-efficient, synonym K_{OW}
Metabolism	The chemical processes that maintain living organisms
Photodegradation	Breakdown of chemicals due to the action of light
Photolysis	Breakdown of chemicals due to the action of light
Subcutaneous	Under the skin
Toxicokinetics	The study of the movement of toxins through the body
Toxicology	The study of the nature and effects of poisons

REFERENCES

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