Public Release Summary
on

Evaluation of the new active

Sulfuryl Fluoride

in the product

PROFUME GAS FUMIGANT

Australian Pesticides and Veterinary Medicines Authority

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FOREWORD

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

In undertaking this task, the APVMA works in close cooperation with advisory agencies, including the Department of Health and Ageing (Office of Chemical Safety), Department of the Environment Water and Resources, and State departments of agriculture and environment.

The APVMA has a policy of encouraging openness and transparency in its activities and of seeking community involvement in decision making. Part of that process is the publication of public release summaries for all products containing new active ingredients and for all proposed extensions of use for existing products.

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

This Public Release Summary is intended as a brief overview of the assessment that has been completed by the APVMA and its advisory agencies. It has been deliberately presented in a manner that is likely to be informative to the widest possible audience thereby encouraging public comment.

More detailed technical assessment reports on all aspects of the evaluation of this chemical can be obtained by completing the order form in the back of this publication and submitting with payment to the APVMA. Alternatively, the reports can be viewed at the APVMA Library, 18 Wormald st, Symonston, ACT.

The APVMA welcomes comment on the usefulness of this publication and suggestions for further improvement. Comments should be submitted to the Pesticides Program Division Manager, Australian Pesticides and Veterinary Medicines Authority, PO Box 6182, Kingston ACT 2604.

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LIST OF ABBREVIATIONS AND ACRONYMS

[This list should be modified to include all the acronyms and abbreviations that actually appear in the publication.]

ac	active constituent
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
BBA	Biologische Bundesanalstalt fur Land – und forstwirschaft
bw	bodyweight
d	day
DAT	Days After Treatment
DT_{50}	Time taken for 50% of the concentration to dissipate
EA	Environment Australia
E_bC_{50}	concentration at which the biomass of 50% of the test population is impacted
EC_{50}	concentration at which 50% of the test population are immobilised
EEC	Estimated Environmental Concentration
E_rC_{50}	concentration at which the rate of growth of 50% of the test population is impacted
EUP	End Use Product
Fo	original parent generation
g	gram
GAP	Good Agricultural Practice
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GVP	Good Veterinary Practice
h	hour
ha	hectare
Hct	Heamatocrit
Hg	Haemoglobin
HPLC	High Pressure Liquid Chromatography *or* High Performance Liquid Chromatography
id	intradermal
im	intramuscular
ip	intraperitoneal
IPM	Integrated Pest Management
iv	intravenous
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
kg	kilogram
K_{oc}	Organic carbon partitioning coefficient
L	Litre
LC_{50}	concentration that kills 50% of the test population of organisms
LD_{50}	dosage of chemical that kills 50% of the test population of organisms
LOD	Limit of Detection – level at which residues can be detected
LOQ	Limit of Quantitation – level at which residues can be dquantified
mg	milligram
mL	millilitre
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
NDPSC	National Drugs and Poisons Schedule Committee
ng	nanogram
NHMRC	National Health and Medical Research Council
NOEC/NOEL	No Observable Effect Concentration Level
OC	Organic Carbon
OM	Organic Matter

PPE	Personal Protective Equipment
ppm	parts per million
Q-value	Quotient-value
RBC	Red Blood Cell Count
s	second
sc	subcutaneous
SC	Suspension Concentrate
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
TGA	Therapeutic Goods Administration
TGAC	Technical grade active constituent
T-Value	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons
μg	microgram
vmd	volume median diameter
WG	Water Dispersible Granule
WHP	Withholding Period

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Introduction

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of *PROFUME GAS FUMIGANT,* which contains the new active ingredient, Sulfuryl fluoride. The product is proposed for the control of insects in buildings (commercial and residential), timber, construction materials, furnishings, shipping containers and vehicles (excluding aircraft) and for the control of stored product pests in commodity storage facilities and non-residential structures such as silos or warehouses, in fumigation chambers, food handling and processing facilities. Full details of the proposed use pattern are contained in the draft product label at the conclusion of this report.

Responses to this Public Release Summary will be considered prior to registration of the product. They 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.

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 (see order form on last page). They can also be viewed at the APVMA library located at the APVMA offices, 18 Wormald St, Symonston, ACT 2609.

Written comments should be received by the APVMA by 2nd October 2007. They should be addressed to:

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Applicant

Dow Agrosciences Australia Ltd

Product Details

It is proposed to register PROFUME GAS FUMIGANT, containing Sulfuryl fluoride at 998 g/kg as a Liquified gas formulation. PROFUME GAS FUMIGANT will be packaged in 56.7kg gas cylinder.

PROFUME GAS FUMIGANT is is proposed for the control of insects in buildings (commercial and residential), timber, construction materials, furnishings, shipping containers and vehicles (excluding aircraft) and for the control of stored product pests in commodity storage facilities and non-residential structures such as silos or warehouses, in fumigation chambers, food handling and processing facilities. Full details of the proposed use pattern are contained in the draft product label at the conclusion of this report.
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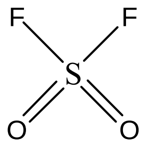
CHEMISTRY AND MANUFACTURE

ACTIVE CONSTITUENT

The active constituent sulfuryl fluoride is manufactured in the USA by Dow AgroSciences LLC at Dow Chemical USA, 901 Loveridge Road, Pittsburg CA 94565 and is pending approval by the APVMA (Approval Number: 60001). This active constituent will be approved simultaneously to the product Profume Gas Fumigant.

Chemical Characteristics of the Active Constituent

Common name:	Sulfuryl fluoride
Synonyms and Code Number:	None
Chemical name (IUPAC):	Sulfuryl fluoride
(CA):	Sulfuryl fluoride
Chemical Abstracts Service (CAS) Registry Number:	2699-79-8
Molecular formula:	F_2O_2S
Molecular weight:	102.1
Chemical structure:	



Physical and Chemical Properties of the Active Constituent

Colour/state	Gas/colourless
Odour	Not determined
Melting point	-136.7 °C
Boiling point	-54°C
Vapour pressure (20 °C)	1611467 Pa
Optical rotation	not optically active
Water solubility (20 °C)	1040 mg/L
Solvent solubility (20 °C)	n-heptane: 22 g/L xylene: 25 g/L 1,2-dichloroethane: 25 g/L methanol: 33 g/L acetone: 71 g/L ethyl acetate: 59 g/L
Partition coefficient	Log K_{ow}=0.14
Hydrolysis	DT_{50} @ 20°C
pH=4	281 days
pH=7	6.7 hours
pH=9	4.0 min (degrades to fluoride, fluorosulfate and sulfate ions)
Flammability	Not flammable
Auto-flammability	Non-flammable
Explosive properties	Not explosive
Surface tension	67.5 mN/m (90% saturated solution)

Oxidising properties	Not oxidising
Henry's Law Constant	158142 Pa m^3 mol^{-1} (calculated)
Storage stability	Sulfuryl fluoride is expected to be chemically stable for at least 2 years.
UV Spectrum	Purified water λ_{max} = 276 nm, absorbance = 0.340 λ_{max} = 290 nm, absorbance = 0.226 0.1 M HCl λ_{max} = 278 nm, absorbance = 0.554 λ_{max} = 290 nm, absorbance = 0.387
^{19}F-NMR Spectrum	δ 34.2 ppm
IR Spectrum	3060 cm^{-1} aromatic C-H stretching 1502 cm^{-1} SO_2 asymmetric stretching 1268 cm^{-1} SF_2 symmetric stretching 840-900 cm^{-1} SO_2 rock
Mass Spectrum	102 M^+, 83 M^+-F, 67 m/z 83 -O

PRODUCT

Distinguishing name:	Profume Gas Fumigant
Formulation type:	Liquified gas
Active constituent concentration:	Sulfuryl fluoride (998 g/kg)
Mode of Action	Glycolysis and citric acid cycle disruptor

Physical and Chemical Properties of the Product

The formulated product is the compressed gas of the technical active constituent and accordingly the physico-chemical properties of the product are as per the active constituent sulfuryl fluoride. The results of stability data showing that the assay of one batch of the substance when stored in the proposed packaging (compressed gas cylinder) demonstrated the active remained constant (99.8%) over a 28 month period when stored under normal conditions.

Recommendation

Based on a review of the chemistry and manufacturing details provided by the applicant, registration of Profume Gas Fumigant is supported.

TOXICOLOGICAL ASSESSMENT

The toxicological database for sulfuryl fluoride, 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 used to develop acceptable limits for dietary or other intakes (ADI and ARfD) at which no adverse health effects in humans would be expected.

All the toxicology studies submitted were performed on a formulated product 'Vikane Gas Fumigant' (synonyms-Profume Gas Fumigant), which contains approximately 99.8% sulfuryl fluoride, the active constituent.

Toxicokinetics and Metabolism Studies

Radiolabelled sulfuryl fluoride was rapidly absorbed via inhalation exposure at 30 or 300 ppm in rats, achieving maximum concentrations of ^{35}S-sulfuryl fluoride-derived radioactivity in both plasma and RBCs near the end of the 4-hr exposure period. Radioactivity was rapidly cleared from plasma and RBCs with initial half-lives of ~2.5 hr following a 30 ppm exposure and 1-2.5 hr following a 300 ppm exposure, but, the terminal half-life of radioactivity was ~2.5-fold longer in RBCs than plasma. Once absorbed, the ^{35}S was rapidly excreted, primarily via the urine (>80%), with a large proportion of the absorbed ^{35}S being excreted in the urine during the 4 h exposure period. Absorbed dose (radioactivity in urine, faeces and tissues) was estimated to be 14% at 30 ppm and 11% of the dose entering lungs at 300 ppm. There is no potential for sulfuryl fluoride to accumulate, as it gets rapidly hydrolysed to fluoride. Repeated exposure may lead to accumulation of fluoride, primarily in teeth or bones.

Acute Studies

Sulfuryl fluoride was found to be moderately acutely toxic by the oral route (LD_{50}~100 mg/kg bw in rat & guinea pig; sulfuryl fluoride bubbled into corn oil), however, this study was difficult to interpret due to the very high volume of corn oil administered (40 mL/kg bw). A standard dermal toxicity study could not be performed. The acute inhalational toxicity has been investigated in several studies and was found to be low in rats (4130-4675 mg/m^3) but moderate in mice (1668-2800 mg/m^3). Skin and eye irritation tests and a skin sensitisation study have not been conducted.

Short-term Studies

In a 66-day study with rats, animals were fed diets fumigated with sulfuryl fluoride. Growth was retarded in a dose-related manner in all but the lowest dose (19 ppm fluoride) group. There was no mortality reported. The NOEL was 2.5 mg total fluoride/kg bw/d, based on reduced body weight gain and evidence of fluorosis, but this study had limited level of detail in the report and investigated relatively few endpoints.

In a 14-day inhalation study in CD-1 mice, there was no effect in males and females at 30 ppm (125.10 mg/m^3) (approximately equivalent to 4.1 mg/kg bw/d systemic exposure). However, very slight vacuolation in the cerebrum of male and female mice was observed at 100 ppm (417 mg/m^3) (approximately equivalent to 13 mg/kg bw/d systemic exposure).

In a 14 day inhalational toxicity study in F344 rats, there was no effect at 100 ppm (417 mg/m^3) (approximately equivalent to 7.2 mg/kg bw/d systemic exposure). However, very slight or slight renal hyperplasia was observed in rats at 300 ppm (1251 mg/m^3) (approximately equivalent to 22 mg/kg bw/d systemic exposure).

In a 14-day inhalational toxicity study in rabbits, there was no effect at 100 ppm (417 mg/m^3) (approximately equivalent to 4.1 mg/kg bw/d systemic exposure). However, focal malacia (necrosis) and vacuolation in the cerebrum and inflammation of the respiratory tract was noted at 300 ppm (1251 mg/m^3) (approximately equivalent to 13 mg/kg bw/d systemic exposure).

In a 14-day exploratory inhalation study in beagle dogs, there was no effect at 100 ppm (417 mg/m^3) (approximately equivalent to 2.9 mg/kg bw/d systemic exposure). However, tremors and tetany were noted beginning with the 5th exposure at 300 ppm (1251 mg/m^3) (approximately equivalent to 8.7 mg/kg bw/d systemic exposure). No serum electrolyte or histologic central nervous system (CNS) changes were found to explain this effect. Also at 300 ppm (1251 mg/m^3), the upper respiratory tract showed histological signs of inflammatory changes.

Subchronic Studies

In a 13-week inhalation study in CD-1 mice, the NOEC was 30 ppm (125.10 mg/m^3) (approximately equivalent to 4.1 mg/kg bw/d systemic exposure), primarily based on reduced bodyweight (ca. 10%) and vacuolation in the brain at 100 ppm (417 mg/m^3) (approximately equivalent to 13 mg/kg bw/d systemic exposure). There was very slight to slight vacuolation in the cerebrum and thalamus/hypothalamus of males and females.

In a 13-week inhalation study in F344 rats, the NOEC was 30 ppm (125.10 mg/m^3) (approximately equivalent to 2.2 mg/kg bw/d systemic exposure), based on decreased brain weight in females at exposures levels of 100 ppm (417 mg/m^3) (approximately equivalent to 7.2 mg/kg bw per day).

In a 13-week inhalation study in New Zealand White rabbits, the NOEC was 30 ppm (125.10 mg/m^3) (approximately equivalent to 1.4 mg/kg bw/d systemic exposure), based on changes in the upper respiratory tract in one male animal and changes in the brain, comprising moderate vacuolation in the cerebrum, in one animal at 100 ppm (417 mg/m^3). At 300 ppm (partially 600 ppm), all rabbits had respiratory tract changes and most had brain changes.

In a 13-week inhalation study in beagle dogs, the NOEC was 100 ppm (417 mg/m^3)

(approximately equivalent to 2.9 mg/kg bw/d systemic exposure), based on slightly reduced body weights and histopathological changes in the brain at 200 ppm (834 mg/m^3). These comprised very slight, small, bilateral focal vacuolation and gliosis in the putamen region of two of eight dogs at 200 ppm (834 mg/m^3) (the male dog exhibited transient tremors and tetany some time after exposure ended on day 19 but appeared normal at all other times).

Chronic/Carcinogenicity Studies

CD-1 mice were exposed (inhalation-whole body exposure) to targeted concentrations of 0, 5, 20 or 80 ppm (0, 20.85 mg/m^3, 83.4 mg/m^3 or 333.60 mg/m^3) (0, 0.7, 3.0, 12 mg/kg bw/d) sulfuryl fluoride for 6 hours/day, 5 days/week for up to 18 months. The NOEC, for the 1-year study part of the main study, was 20 ppm (83.4 mg/m^3) (approximately equivalent to 3 mg/kg bw/d), based on reduced body weights and microscopic changes in the brain and thyroid at 80 ppm (333.60 mg/m^3) (approximately equivalent to 12 mg/kg bw/d). The NOEC, for the 18-month study, was 20 ppm (83.4 mg/m^3) (approximately equivalent to 3 mg/kg bw/d), based primarily on reduced body weights and microscopic changes in the brain, thyroid, liver and heart at 80 ppm (333.60 mg/m^3) (approximately equivalent to 12 mg/kg bw/d). There was no evidence of oncogenicity in either sex at any exposure concentration. The NOEC for carcinogenicity is 80 ppm (333.60 mg/m^3) (approximately equivalent to 12 mg/kg bw/d), the highest concentration tested. In addition to statistical analyses of the individual tumours, additional statistical procedures[1] were carried out to take account of the reduced survival at the highest dose. These did not identify any increases in tumour incidences.

Rats (Fischer 344) were exposed (inhalation-whole body exposure) to targeted concentrations of 0, 5, 20 or 80 ppm (0, 20.85 mg/m^3, 83.4 mg/m^3 or 333.60 mg/m^3) (0, 0.4, 1.4, 5.6 mg/kg bw/d) of sulfuryl fluoride for 6 hours/day, 5 days/week for up to 2 years. The NOEC was 20 ppm (83.4 mg/m^3) (approximately equivalent to 1.4 mg/kg bw/d), based on a variety of effects, including increased mortality, low body weights, very slight vacuolation in the brain, kidney pathology with associated clinical chemical effects and effects on other tissues, and pulmonary changes suggestive of irritation at 80 ppm (333.60 mg/m^3) (approximately equivalent to 5.6 mg/kg bw/d). There was no evidence for carcinogenicity in either sex at any exposure concentration up to 80 ppm (333.60 mg/m^3) (approximately equivalent to 5.6 mg/kg bw/d systemic exposure), the highest concentration tested.

Beagle dogs were exposed (inhalation-whole body exposure) to targeted concentrations of 0, 20, 80 or 200 ppm (0, 83.4 mg/m^3, 333.60 mg/m^3 or 834 mg/m^3) (0, 0.6, 2.3, 5.8 mg/kg bw/d) sulfuryl fluoride for 6 hrs/day, 5 days/week for one year. However, due to excessive morbidity and mortality by approximately 9 months, the 200 ppm (834 mg/m^3) exposed group of dogs was removed from the study and necropsied. The NOEC was 20 ppm (83.4 mg/m^3) (approximately 0.6 mg/kg bw/d systemic exposure), based on very slight inflammation and aggregates of macrophages in alveoli at 80 ppm (333.60 mg/m^3). The primary effects were respiratory in nature (e.g., severe inflammation) although other changes were evident, notably in the brain.

Reproduction Study

Male and female rats were exposed to targeted concentrations of 0, 5, 20 or 150 ppm (0, 20.85 mg/m^3, 83.4 mg/m^3 or 625.5 mg/m^3) (0, 0.4, 1.4, 10.8 mg/kg bw/d) sulfuryl fluoride via inhalation, 6 hours/day, 5 days/week prior to mating. Thereafter, males and females were exposed to these levels for 6 hrs/day, 7 days/week during mating, gestation and lactation (except gestation Day 21 to lactation Day 4, for animal welfare reasons) and through to

[1] *Peto, 1974; McConnell et al, 1996*

sacrifice. Sulfuryl fluoride had no effect on reproductive parameters when inhaled by rats at concentrations up to and including 150 ppm (625.5 mg/m^3) for 6 hours/day, 5-7 days for up to 20 consecutive weeks. General effects in parental animals were limited to an increased incidence of aggregates of alveolar macrophages in F0 and F1 males and females at 20 ppm (83.4 mg/m^3). At 150 ppm (625.5 mg/m^3), toxicity comprised reduced body weights, dental fluorosis alveolar macrophages and brain vacuolation. The NOEC for reproductive effects was 150 ppm (625.5 mg/m^3) (approximately equivalent to 10.8 mg/kg bw/d systemic exposure), the highest concentration tested. Parental toxicity was evident at 150 ppm (625.5 mg/m^3), toxicity comprised reduced bodyweights, overt dental fluorosis, alveolar macrophages and brain vacuolation. The parental NOEC was 5 ppm (20.85 mg/m^3) (approximately equivalent to 0.4 mg/kg bw/d systemic exposure), based on an increased incidence of aggregates of alveolar macrophages in adult F0 and F1 males and females at 20 ppm (83.4 mg/m^3). Reduced growth in F1 and F2 pups during the lactation period was noted at 150 ppm (625.5 mg/m^3) and was the only effect in offspring. The NOEC in offspring was 20 ppm (83.4 mg/m^3) (approximately equivalent to 1.4 mg/kg bw/d systemic exposure), based on reduced growth during lactation at 150 ppm (625.5 mg/m^3).

Developmental Studies

Mated Fischer 344 rats were exposed to 0, 25, 75 or 225 ppm (0, 104.25 mg/m^3, 312.75 mg/m^3 or 938.25 mg/m^3) (0, 1.8, 5.4, 16.2 mg/kg bw/d) of sulfuryl fluoride via inhalation, for 6 hrs/d on days 6 through 15 of gestation. There was no evidence of maternal toxicity, embryolethality, or fetotoxicity at exposure levels up to 225 ppm (938.25 mg/m^3) of sulfuryl fluoride. The incidences of major malformations, considered either individually or collectively at each exposure level, were not significantly increased in any treatment group when compared to control values. The incidence of resorptions was not significantly increased among rats in any exposure group indicating that sulfuryl fluoride was not embryolethal at exposure levels as high as 225 ppm (938.25 mg/m^3). The NOEC for maternal and fetotoxicity is 225 ppm (938.25 mg/m^3) (approximately equivalent to 16.2 mg/kg bw/d systemic exposure), the highest dose tested.

Inseminated NZW Rabbits were exposed to 0, 25, 75 or 225 ppm (0, 104.25 mg/m^3, 312.75 mg/m^3 or 938.25 mg/m^3) (0, 1.4, 4.3, 13 mg/kg bw/d) of sulfuryl fluoride via inhalation, for 6 hrs/day on days 6 through 18 of gestation. Maternal toxicity, as evidenced by a loss of body weight during gestation, was observed in the 225 ppm (938.25 mg/m^3) exposure group. Decreased foetal bodyweight, indicative of a fetotoxic effect, was also observed at 225 ppm (938.25 mg/m^3). No evidence of maternal toxicity or fetotoxicity was observed among rabbits exposed to 25 ppm (104.25 mg/m^3) or 75 ppm (312.75 mg/m^3) of sulfuryl fluoride. The incidence of resorptions was not significantly increased among rabbits in any exposure group indicating that sulfuryl fluoride was not embryolethal at exposure levels as high as 225 ppm (938.25 mg/m^3)**.** There was no evidence of teratogenicity. The NOEC for maternal and fetotoxicity was 75 ppm (312.75 mg/m^3) (approximately equivalent to 4.3 mg/kg bw/d systemic exposure).

Neurotoxicity Studies

Three studies specifically investigated the neurotoxicity of sulfuryl fluoride: an acute inhalation study in rats, a 13-week inhalation study in rats and a 1-year inhalation study in rats (a satellite group of the chronic / carcinogenicity study).

Fischer 344 rats were exposed to 0, 100 or 300 ppm (0, 417 mg/m^3 or 1251 mg/m^3) sulfuryl fluoride, 6 hrs/day on 2 consecutive days (this was considered to effectively represent an acute exposure of 12 hours in a 30-hour period). The study goals were to evaluate the effects of short-term inhalation exposure to high levels of sulfuryl fluoride on the CNS function of Fischer 344 rats. The study was conducted in female rats, as these were considered the most sensitive sex, based on flash evoked potential data, in a 13-week neurotoxicity study. This study focussed on investigating the most sensitive critical (neurological) end-point, visual, auditory and somatosensory evoked potential, when trying to establish an acute NOEC for sulfuryl fluoride. No adverse effects were produced at the highest tested concentration of 300 ppm (1251 mg/m^3) (approximately equivalent to 31 mg/kg bw/d systemic exposure).

Rats (Fischer 344) were exposed to 0, 30, 100 or 300 ppm (0, 125.1 mg/m^3, 417 mg/m^3 or 1251 mg/m^3) (0, 2.2, 7.2, 22 mg/kg bw per day) sulfuryl fluoride via inhalation for 6 hr/day, 5 days/week for 13 weeks. Exposure at 300 ppm (1251 mg/m^3) caused diminished weight gain, dental fluorosis, a slight decrease in grooming, slowing of visual, auditory and somatosensory-evoked potentials, mild pulmonary inflammation, and mild vacuolation in the brain (specifically, white fibre tracts of the caudate-putamen). Auditory brainstem responses (ABR's) and brain histopathology were also evaluated two months post-exposure in 2 male and 2 female rats. Both the ABR's and brain histopathology appeared normal at this time, indicating that these treatment effects were essentially reversible. Exposure to 100 ppm (417 mg/m^3) resulted in slight dental fluorosis and minor slowing of some evoked responses. All other measurements, including brain histopathology, were normal. The NOEC was 30 ppm (125.1 mg/m^3) (approximately equivalent to 2.2 mg/kg bw/d systemic exposure), based on alterations in evoked potentials at 100 ppm (417 mg/m^3) in females.

The chronic, 1-year, neurotoxicity study was conducted in concert with the 2-year rat inhalation study described earlier (Quast et al, 1993). In this study, rats (Fischer 344) were exposed to target concentrations of 0, 5, 20 or 80 ppm (0, 20.85 mg/m^3, 83.4 mg/m^3 or 333.6 mg/m^3) sulfuryl fluoride via inhalation for 6 hours/day, 5 days/week for approximately 12 months. Sulfuryl fluoride had no effect at any time on handheld and open field observations, grip performance or landing foot splay, and on any aspect of motor activity. Results of the gross and histopathologic evaluations of perfusion fixed tissues for neuropathologic assessment of rats exposed to sulfuryl fluoride for up to 12 months were found to be unaffected by exposure. The neurotoxicologic NOEC for this study was ≥ 80 ppm (333.6 mg/m^3) (approximately equivalent to 5.6 mg/kg bw/d systemic exposure), the highest concentration tested.

Genotoxicity Studies

Sulfuryl fluoride showed no genotoxic potential in *in vitro* tests for bacterial cell mutation or unscheduled DNA synthesis in mammalian cells. The *in vitro* tests for mutagenicity and clastogenicity in mammalian cells (mouse lymphoma $TK^{+/-}$ and rat lymphocytes) were positive, consistent with the database on fluoride ion genotoxicity. An *in vivo* micronucleus test with sulfuryl fluoride was negative. Exposures would be predominantly to fluoride ion as sulfuryl fluoride is a highly reactive compound. Furthermore, fluoride is considered not to represent an *in vivo* genotoxic risk to humans.

Other Studies

Incapacitation study

In order to estimate the rapidity with which sulfuryl fluoride might incapacitate an individual, rats were exposed via inhalation to 4,000, 10,000, 20,000 or 40,000 ppm (16680 mg/m^3, 41700 mg/m^3, 83400 mg/m^3 or 166800 mg/m^3) sulfuryl fluoride in a 14 litre cylindrical chamber that contained a motor-driven activity wheel. There was a clear dose-related decrease in the time the animals maintained the ability to walk as the concentration of sulfuryl fluoride increased. Animals from the 20,000 (83400 mg/m^3) and 40, 000 ppm (166800 mg/m^3) groups were unable to walk within 12 minutes and died less than 10 minutes later. The 10,000 ppm (41700 mg/m^3) group remained functional longer and lived for approximately 60 minutes after the exposure was discontinued. The rats exposed to 4,000 ppm (16680 mg/m^3) were able to walk considerably longer and lived for approximately 2.5 hours after the exposure was stopped. All rats had tonic convulsions prior to death. Necropsy revealed signs compatible with cardiovascular failure and acute death. Generally, there was a concentration-dependent increase in pulmonary congestion, oedema and haemorrhage.

Study on effect on physiological parameters

Experiments were conducted on rats exposed to 4000 ppm (16680 mg/m^3) or 20,000 ppm (83400 mg/m^3) sulfuryl fluoride via inhalation to investigate EEG, ECG, blood pressure, heart rate, body temperature (with and without water jacket) and respiration rate. The response to sulfuryl fluoride was similar between exposure levels and included a decrease in heart rate, a gradual increase in blood pressure (culminating in a rapid increase in systolic and pulse pressure just prior to death), decreased respiration, occasional spiking and high frequency loss in the EEG, and power loss in the EEG. Grossly, the rats exhibited paleness of the extremities and felt cold when removed from the exposure restraint. All physiological parameters ceased to function at about the same time the animals expired regardless of the dose level. No parameter was affected first and subsequently precipitated the death of the animal. Artificial maintenance of body temperature did not increase survival time; therefore, the loss of body temperature did not contribute significantly to the cause of death.

Study on ultrastructural assessment of the lungs of rats exposed to high concentrations of sulfuryl fluoride

An ultrastructural assessment of the lungs of rats exposed to high concentrations of sulfuryl fluoride via inhalation has also been conducted. Morphological changes in the lungs of rats exposed to 4000 ppm (16680 mg/m^3) sulfuryl fluoride were minimal and probably were not a significant factor in the death of the animals. On the other hand, extensive injury to the lungs of rats exposed to 20,000 ppm (83400 mg/m^3) sulfuryl fluoride probably compromised pulmonary function and contributed to the death of the animals. Factors other than pulmonary injury probably were involved in the death of animals at both concentrations.

Antidote study

A study was performed to investigate the protective and therapeutic effectiveness of calcium gluconate (the recommended antidote for fluoride toxicity), and three anticonvulsants (phenobarbital, diazepam or diphenylhydantoin) in animals exposed to lethal concentration of sulfuryl fluoride. This study showed calcium gluconate and phenobarbital, given before or after exposure to sulfuryl fluoride, appeared to ameliorate the acute toxic effects (seizures) and lethality in rats exposed to sulfuryl fluoride at 4,000 ppm (16680 mg/m^3) but not at 10,000 ppm (41700 mg/m^3). Treatment with diazepam followed by exposure to sulfuryl fluoride was relatively effective. However, treatment with diazepam after exposure to sulfuryl fluoride was not effective. Diphenylhydantoin is contra-indicated, inducing more severe seizures than seen in sulfuryl fluoride only animals.

Medical data

Sulfuryl fluoride has been used as a structural fumigant under the trade name ‘Vikane’ for over 40 years. Manufacturing plant health surveillance examinations revealed no significant sulfuryl fluoride-related health problems among employees. Since 1993, 335 reports of alleged human health effects associated with Vikane use have been reported to the U.S. EPA by Dow AgroSciences. There were 13 human deaths, primarily resulting from unauthorised entry into the tented fumigated structures, but the lethal concentration has not been determined. Over 300 incidents of non-lethal, adverse effects had symptoms of irritation of eyes and respiratory tract, headache, nausea, fever and diarrhoea; some of these might be due to exposure to chloropicrin used as a sensory marker.

Two epidemiological investigations of sulfuryl fluoride and methyl bromide fumigators have reported a small number of findings in the sulfuryl fluoride cohorts. Some of these findings appear to be related to physical activities associated with the fumigation process. Others present no clear pattern that can be attributed to the use of sulfuryl fluoride. In neither study, there was any biomonitoring to assess exposure.

PUBLIC HEALTH STANDARDS

Poisons Scheduling

The National Drugs and Poisons Schedule Committee (NDPSC) considered the toxicity of the product and its active ingredients and assessed the necessary controls to be implemented under States' poisons regulations to prevent the occurrence of poisoning.

At its 47th meeting, in June 2006, the NDPSC agreed that, based upon its moderate acute toxicity, low to moderate inhalation toxicity, be included in Schedule 6 of the SUSDP.

No-observed-Effect-Level (NOEL) and Acceptable Daily Intake (ADI)

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

The ADI for sulfuryl fluoride is 0.01 mg/kg bw/d. The ADI was established by applying a 100-fold safety factor to a NOEC of 20 ppm (approximately equivalent to 1.4 mg/kg bw/d systemic exposure) in a 24-month rat study.

Acute Reference Dose (ARfD)

The acute reference dose is the maximum quantity of an agricultural or veterinary chemical that can safely be consumed as a single, isolated, event.

The ARfD for sulfuryl fluoride is 0.3 mg/kg bw, based on a NOEC of 300 ppm (approximately equivalent to 31 mg/kg bw/d systemic exposure) in rats and applying a 100-fold safety factor.

Based on the above advice Profume Gas fumigant is supported on toxicological grounds.

RESIDUES ASSESSMENT

Metabolism

The metabolism of sulfuryl fluoride in plants is not well described. The studies provided did not meet contemporary requirements for plant metabolism studies. However as sulfuryl fluoride is a fumigant, conventional metabolism studies are not required.

Sulfuryl fluoride is converted to sulphate and fluoride ions upon contact with protein molecules:

$$SO_2F_2 + H_2O \rightarrow SO_4^{2-} + 2F^- + 4H^+$$

Sulphate ions are not considered to be of toxicological concern. The residues that are of concern as a result of fumigation are sulfuryl fluoride itself and fluoride ion (or inorganic fluoride), which forms after fumigation.

Analytical Methods

Methods for the determination of both sulfuryl fluoride residues and fluoride ion residues were provided for a number of commodities including whole cereal grains and processed fractions, corn and corn oil, dried fruit and nuts.

Fluoride ion was quantified using a fluoride selective electrode with a known double addition technique. The limits of quantitation ranged from 0.5 to 4 mg/kg in a range of commodities that were analysed.

Sulfuryl fluoride residues in fumigated commodities were determined by head-space determinations using GC/ECD. The limits of quantitation ranged from 4.2 to 8 μg/kg in a range of commodities.

Storage Stability

The stability of fluoride ion residues in stored fumigated commodities such as wheat grain, wheat flour, raisins, walnuts, corn grain and corn meal was investigated for up to 140 days in freezer conditions. The stability was demonstrated to be acceptable for all commodities with the exception of wheat flour, in which some degradation occurred up to 140 days.

The stability of sulfuryl fluoride residues in stored commodities was demonstrated by sorption of the fumigant in charcoal air sampling tubes and storage of the tubes in both ambient conditions for up to 46 days and under freezer storage conditions for up to 180 days. Under both sets of conditions, the residues of sulfuryl fluoride were demonstrated to be stable.

Residue Definition

The proposed residue definition for sulfuryl fluoride in fumigated commodities is *sulfuryl fluoride*. The terminal residue that forms as a result of sulfuryl fluoride fumigation is inorganic fluoride, which should also be considered as part of the residue for the purposes of monitoring and dietary exposure assessment. However as inorganic fluoride is naturally occurring and is present in the environment, it is not suitable for the purposes of monitoring for compliance.

Therefore, the residue definition for monitoring and compliance purposes is:

Sulfuryl fluoride *sulfuryl fluoride*

And, the residue definition for dietary intake purposes is:

Sulfuryl fluoride and inorganic fluoride ion (both determined separately)

As fluoride ion is already defined in Table 3 of the MRL Standard under ***Fluorine (inorganic salt)***, another entry is not required. The existing entry is:

Fluorine (inorganic salt) *Fluoride ion*

The same definition appears in the Australia New Zealand Food Standards Code.

The relevant entries recommended for inclusion in Table 3 of the APVMA MRL Std are therefore:

Sulfuryl fluoride *sulfuryl fluoride*
(***See also Fluorine (inorganic salt))***

The above definitions are the same as those proposed by the 2005 JMPR and ratified by the Codex Alimentarius Commission 2006.

Residue Trials

Cereal grains and processed commodities

Fumigation studies were conducted under laboratory conditions and in mills in the US and Europe, with CTPs ranging 200 to 2366 mg hr/L. Sulfuryl fluoride residues in grains and processed grain commodities following fumigation at CTPs corresponding to 1500 mg hr/L were considered as part of the MRL setting process. The fumigation experiments included single fumigations for a number of commodities, as well as repeat fumigations for wheat only.

Sulfuryl fluoride residues in varying types of wheat following fumigation (single and repeat fumigations) ranged <0.008 – 0.028 mg/kg. In rice grain (white, brown and polished), sulfuryl fluoride residues ranged <0.008 – 0.025 mg/kg. Sulfuryl fluoride residues in corn ranged <0.008 – 0.026 mg/kg. The range of sulfuryl fluoride concentrations for each of the whole grain commodities was similar, following fumigation for 24 hours and sampling at 1 day after fumigation. The concentrations of sulfuryl fluoride in wheat, following either a single or repeat fumigations, were also similar.

Combining the sulfuryl fluoride residues in various grains, the values are in rank order: <0.008, 0.008, 0.009 (3), 0.011, 0.016, 0.020, 0.021, 0.022, 0.023, 0.025, 0.026, 0.028 mg/kg; the estimated STMR is 0.018 mg/kg and the highest residue (HR) is 0.028 mg/kg. On the basis of the data generated for wheat, rice, barley, oats and corn, an MRL of 0.05 mg/kg sulfuryl fluoride is recommended for cereal grains.

Different types of Australian wheat sourced from NSW, Qld, SA and WA were fumigated at 1500 CTP. Fluoride ion residues ranged from 0.5 to 2.1 mg/kg in the fumigated wheat. The range of fluoride ion residues in the Australian wheat were within the range of concentrations found in wheat treated in overseas trials. The fluoride ion residues in Australian wheat are in rank order: <0.5, 0.56, 0.56, 0.59, 0.63, 0.80, 0.84, 0.86, 0.87, 0.88, 0.89, 0.91, 0.96, 1.1, 1.2, 1.2, 1.5, 1.9, 1.9, 2.0, 2.1 mg/kg. The STMR is 0.89 mg/kg and the HR is 2.1 mg/kg. The

Australian data are used in the chronic dietary estimates for fluoride, as the results are reflective of concentrations in grain to which Australian consumers are most likely to be exposed. In varying wheat varieties used in trials conducted in Europe and in the US, fluoride residues ranged 1.42 – 14.3 mg/kg.

The data for repeat fumigations vs single fumigations of wheat do not show any clear trends with respect to accumulation of fluoride ion residues, therefore the current MRL of 7 mg/kg for fluoride ion in cereal grains would remain appropriate for repeat fumigations, noting that median residues in the Australian trial were 0.89 mg/kg. In addition, a very large proportion of the cereal grains that are produced in Australia are consumed domestically and would not be fumigated more than once, therefore a higher level is not necessarily required for the proposed Australian GAP.

In relation to processed grain commodities, a processing study was conducted after fumigation of wheat and corn. Concentration of fluoride ion residues was observed in wheat shorts, bran and germ, with calculated processing factors of 1.2, 2.45 and 4.6, respectively. As wheat bran and wheat germ are traded commodities, it is appropriate to establish individual MRLs for these. The highest residues in Australian wheat were 2.1 mg/kg, therefore fluoride residues in wheat bran and wheat germ are 5.1 mg/kg and 9.66 mg/kg, respectively. MRLs of 7 and 10 mg/kg are recommended for wheat bran and wheat germ, respectively. As the existing MRL of 7 mg/kg for cereal grains remains appropriate, an MRL of 10 mg/kg is required for wheat germ only.

For chronic dietary exposure, using the STMR of 0.89 mg/kg from Australian trials and the processing factors of 2.45 for wheat bran and 4.6 for wheat germ, lead to STMR-Ps of 2.18 mg/kg for bran and 4.09 mg/kg for germ.

Dried Fruit and Nuts

Studies on the fumigation of dried fruits and nuts were conducted in the US. Studies included single as well as repeat fumigations (up to 5 successive fumigations) with sampling following each of the fumigations. As the proposed label directions do not preclude multiple fumigations, the data for repeat fumigations are considered as part of the MRL determination.

The data for walnuts were generated with a higher CTP than indicated on the proposed product label and higher than that used to generate data for other tree nuts. However the range of residues are within the values observed for pecans (which are similar to walnuts), which were treated at the proposed CTP. As use on peanuts is also proposed on the draft label, a separate MRL is required for peanut, which is classified as an oilseed in the Codex Classification. As peanuts are similar to walnuts and pecans in terms of oil content, the data may be extrapolated to peanuts in this case.

Sulfuryl fluoride residues in raisins, figs, dates and dried plums ranged <0.001 – 043 μg/kg. For the purposes of dietary intake assessment (acute and chronic), an HR of 0.043 mg/kg sulfuryl fluoride is recommended for dried fruit. For tree nuts, sulfuryl fluoride residues in walnuts, pistachios, pecans and almonds ranged 0.03 – 6.03 mg/kg. HRs of 4.8, 0.3, 6 and 0.13 mg/kg are recommended for walnuts, pistachios, pecans and almonds, respectively. Sulfuryl fluoride residues in tree nuts are in rank order: 0.033, 0.044, 0.045, 0.057, 0.063, 0.121, 0.277, 1.534, 2.407, 3.08, 4.79, 4.81, 4.91 and 4.95 mg/kg; the estimated STMR is 0.91 mg/kg.

Fluoride ion residues in dried fruit ranged <1.4 – 3.1 mg/kg and in nuts ranged 2.3 – 26 mg/kg.

On the basis of the data provided, the following MRLs are recommended:

Commodity	Sulfuryl fluoride	Fluoride ion
Dried fruit (raisins, figs, dates, dried plum)	0.07 mg/kg	5 mg/kg
Tree nuts (almonds, walnuts, pecans, pistachios)	7 mg/kg	30 mg/kg
Peanut	7 mg/kg	30 mg/kg

For chronic intake assessment, the fluoride ion concentrations in dried fruit are in rank order: <1.4 (7), <2.2 (3), <2.4 (4), 2.56, 2.74, 3.09 and 3.14 mg/kg. The estimated STMR is <2.2 mg/kg for dried fruit.

The fluoride ion concentrations in nuts are in rank order: 2.3, 2.91, 4.56, 5.96, 7, 7.2, 7.97, 9.59, 9.71, 12.35, 12.6, 17.9, 21.8 and 25.8 mg/kg. The estimated STMR is 8.79 mg/kg for nuts.

Animal Transfer Studies and Animal Commodity MRLs

Very little information on the transfer of sulfuryl fluoride from feed commodities to animal commodities such as meat, milk, eggs was provided by the Applicant. As sulfuryl fluoride is unlikely to be transferred to animal commodities such as milk, eggs, meat and offal, animal commodity MRLs for sulfuryl fluoride are not considered necessary. There may be transfer of fluoride ion into milk, meat and other commodities as a result of fumigated grain commodities being fed to livestock. However as inorganic fluoride ion is naturally present in milk and meat commodities, it would not be practical to establish inorganic fluoride MRLs for compliance or trade purposes.

The 2005 JMPR estimated the livestock dietary burden for inorganic fluoride, however determined that animal commodity MRLs could not be established, as livestock feeding studies were not provided. As there are no established MRLs for inorganic fluoride in animal commodities for trade purposes, in this case it is not considered necessary to establish such MRLs for compliance with domestic standards. There are no existing standards for animal commodities in the Food Standards Code.

Dietary Risk Assessment

Chronic Estimate of Dietary Exposure

The chronic dietary exposure to sulfuryl fluoride and fluoride ion is estimated by the National Estimated Daily Intake (NEDI) calculation encompassing all registered/temporary uses of the chemical and the mean daily dietary consumption data derived from the 1995 National Nutrition Survey of Australia. The NEDI calculation is made in accordance with WHO Guidelines[2] and is a conservative estimate of dietary exposure to chemical residues in food.

The NEDI for fluoride ion was estimated using Upper Levels of Intake[3] (UL) of fluoride as recommended by the Australian National Health and Medical Research Council (NHMRC)

2 Guidelines for predicting dietary intake of pesticide residues, WHO, 1997.

3 Upper Level of Intake is defined as the highest average daily nutrient intake likely to pose no adverse health effects to almost all individuals in the general population. Nutrient Reference Values for Australia and New Zealand, NHMRC Publication 2006.

and published in the Nutrient Reference Values for Australia and New Zealand[4] for different age groups.

For adults, the recommended Upper Level of Intake is 10 mg fluoride/day (for men and women of all age groups, ranging 19 years to >70 years). This is equivalent to 0.15 mg/kg bodyweight/day. As part of the chronic estimate, the exposure from fluoride in drinking water must also be included. The total intake of water (including water from foods as well as fluids) ranges 1.8L to 2.6L/day for adults[5]. A mean value of 2.2L/day is used to represent the mean intake of drinking water for the chronic dietary exposure assessment for fluoride ion. The concentration of fluoride in drinking water as recommended by the NHMRC is 1 mg/L[6].

For children, an Upper Level of 1.9 mg fluoride/day is used (equivalent to 0.1 mg/kg bw/day as calculated from reference bodyweights and reported UL values). The total intake of water (including water from foods as well as fluids) ranges 1L to 1.2L/day for children aged 1 to 8 years old [7]. A value of 1.2L/day is used to represent the mean intake of drinking water for the chronic dietary exposure assessment for fluoride ion.

Using all of the reference values and the calculated STMRs for cereal grains, dried fruits and nuts and STMR-Ps for wheat bran and wheat germ, lead to NEDI estimates equivalent to 71% of the UL for children and 25% of the UL for the general population (7 years and above). These estimates do not include the use of sulfuryl fluoride to fumigate processed commodities, as the resulting concentrations of fluoride ion in processed commodities are likely to exceed the UL, from exposure from all sources of food and water. Drinking water alone comprises 89% of the estimated fluoride exposure for children and 88% for the general population. The drinking water exposure approximates 63% of the UL for children and 22% of the UL for adults.

The NEDI for sulfuryl fluoride is equivalent to 2.4% of the ADI. This only includes use on cereal grains, dried fruit, peanuts and tree nuts.

It is concluded that the chronic dietary exposure of sulfuryl fluoride and fluoride ion is acceptable.

Short-term Estimate of Dietary Exposure

The short-term or acute dietary exposure is estimated by the National Estimated Short Term Intake (NESTI) calculation. The NESTI calculations are made in accordance with the deterministic method used by the JMPR[5] with 97.5th percentile food consumption data derived from the 1995 National Nutrition Survey of Australia. NESTI calculations are conservative estimates of acute exposure (24 hour period) to chemical residues in food.

The NESTIs for all relevant commodities are summarised in the following table. The highest acute dietary intake was estimated at 3% of the ARfD. It is concluded that the acute dietary exposure of sulfuryl fluoride is acceptable.

Commodity/Food	% ArfD (2 to 6 years)	% ArfD (general population)
Cereal grains and processed fractions	>0.2	>0.2

[4] Nutrient Reference Values for Australia and New Zealand, NH&MRC Publication 2006. Table 9: Minerals – Copper, Chromium, Manganese, Fluoride, Sodium and Potassium. 2006.
[5] Nutrient Reference Values for Australia and New Zealand, Table 4: Macronutrients and Water.
[6] NH&MRC 1991.
[7] Nutrient Reference Values for Australia and New Zealand, Table 4: Macronutrients and Water.

Dried fruit	>0.1	>0.1
Peanuts	4	>3
Tree nuts	3	3

Recommendations

MRL amendments

Upon granting of the application, the following amendments will be made to the MRL Standard. MRLs in Tables 1 and 3 will be recommended for inclusion in the Food Standards Code:

Table 1

Compound	Food		MRL (mg/kg)
ADD:			
Sulfuryl fluoride	GC 0800	Cereal grains	0.05
	DF 0167	Dried fruit	0.07
	SO 0697	Peanut	7
	TN 0085	Tree nuts	7

Table 1

Compound	Food		MRL (mg/kg)
Fluorine (inorganic salt)			
DELETE:		Fruits	7
		Vegetables	7
ADD:	DF 0167	Dried fruit	5
	SO 0697	Peanut	30
	TN 0085	Tree nuts	30
	CF 1210	Wheat germ	10

Table 3

Compound	Residue
ADD:	
Sulfuryl fluoride	Sulfuryl fluoride

Withholding Period: Allow a minimum of 24 hours following fumigation before consuming treated commodities.

ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

Commodities exported

The commodities that are considered as major export commodities in accordance with Part 5B of Ag MoRaG[8] are cereal grains and associated commodities and dried fruit.

[8] Part 5B of the Ag Manual of Requirements and Guidelines Series, Overseas Trade Aspects of Residues in Food Commodities, June 2006.

Destination and Value of Exports

The total exports of Australian cereal grains were estimated at 16,000 kt for 2005 – 2006 and 15, 779 kt for 2004 – 2005 for wheat; export of coarse grains were estimated at just over 6,000 kt for 2005 – 2006 and 5264 kt for 2004 – 2005.

The 8 largest export markets for Australian cereal grains (including wheat) by value are shown below (Australian Commodity Statistics 2005; ABARE Food Statistics 2006).

Destination	Value, $ million	
	2004 – 2005	2005 – 2006
Japan	617	425
China	943	342
Malaysia	198	168
Korea	323	270
Saudi Arabia	329	346
Thailand	111	130
Indonesia	545	588
UAE	94	159

In relation to export of dried fruit and nuts, the following statistics were available. Almonds and macadamias produced during 2004 – 2005 were valued at 77 and 119 million $AUS, respectively. This relates to 12 and 32 kt production, respectively. For dried vine fruit, 30 kt were produced during 2005 – 2006 and of that 7 kt was exported; the value of the exported fruit and market destinations was not available.

As sulfuryl fluoride is proposed as a methyl bromide replacement, not all shipments of Australian grain or domestic grain will be fumigated, while there is a quarantine and pre-shipment preference for methyl bromide. Also as grain is a bulked and blended commodity, it is likely that fumigated and non-fumigated lots may be bulked prior to processing.

As separate sulfuryl fluoride MRLs are not proposed for processed cereal grain commodities, as processed commodities themselves are not to be fumigated (in accordance with proposed directions for use), further consideration of trade of processed commodities is therefore not required.

Comparison of Australian MRLs with Codex and overseas MRLs.

The Codex Alimentarius Commission (Codex) is responsible for establishing Codex Maximum Residue Limits (CXLs) for pesticides. Codex CXLs are primarily intended to facilitate international trade, and accommodate differences in Good Agricultural Practice (GAP) employed by various countries. Some countries may accept Codex CXLs when importing foods. Sulfuryl fluoride was evaluated by the 2005 JMPR and CXLs were established by CAC in 2006. MRLs or tolerances established overseas are compared to the proposed Australian MRLs for sulfuryl fluoride in the table below.

Commodity	Sulfuryl Fluoride MRLs/Tolerances (mg/kg)				
	Australia	Japan*	US	Codex	Germany**
Cereal grains	0.05	0.1	–	0.05	0.05
Corn grain	–	0.05	0.05	–	–
Rice	–	0.04	0.04	–	–
Rice polished	–	–	0.01	–	–
Barley, millet, oats, sorghum, triticale, wheat	–	–	0.1	–	–

Barley bran, wheat bran	–	–	0.05	–	–
Cereal brans	–	–		0.1	–
Rice bran	–	–	0.01	–	–
Wheat germ	–	–	0.02	0.1	–
Tree nuts	7	3	3	3	10
Peanuts	7	0.5	0.5	–	–
Dried fruit	0.07	1	0.05	0.06	0.05

* Japanese provisional list updated February 2007; MRLs were not listed for processed fractions.
** EU MRLs have not been established for sulfuryl fluoride.

There is a noticeable difference in the value established for tree nuts both in Australia and Germany, compared to the Codex value. It is noted that animal commodity MRLs have been established for sulfuryl fluoride in the USA, where specific commodities are fumigated in accordance with US GAP. The commodities and MRLs are: dried egg 1 mg/kg; cheese 2 mg/kg; hog meat 0.02 mg/kg; cattle meat, dried 0.01 mg/kg.

Potential risk to trade

Export of treated produce containing detectable residues of sulfuryl fluoride may pose a risk to Australian trade in situations where (i) no residue tolerance (import tolerance) is established in the importing country or (ii) where residues in Australian produce are likely to exceed a residue tolerance (import tolerance) established in the importing country.

For grains, nuts and dried fruits, as MRLs have been established by Codex, USA and some EU countries, there is likely to be general acceptance of fumigated commodities by a number of importing markets. For cereal grains, Japan as a large market has established MRLs through its provisional MRL system and other countries may accept Codex MRLs. Industry comment is required however on the discrepancy between the proposed Australian MRL for tree nuts and peanuts and the Codex MRL for tree nuts and lack of a Codex MRL for peanuts.

The overall risk to export trade in animal commodities is considered to be negligible, as fumigation of animal commodities is not proposed in the directions for use of the product.

The relevant industry groups should be given the opportunity to comment on the perceived level of risk and whether any industry-initiated strategies are required to manage the risk. The opportunity to comment will be facilitated through the public consultation process, by response to this Public Release Summary.

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

Formulation, packaging, transport, storage and retailing

Profume Gas Fumigant will be manufactured overseas and will be imported into Australia fully labelled and ready for distribution. Profume Gas Fumigant is packaged as a compressed liquid gas in high pressure steel cylinders (1.2 m long x 25 cm diameter).

Use pattern

Profume Gas Fumigant is a pressurised gas formulation and is intended for the control of insects in a variety of different use situations. The product will only be used by professional fumigators. For all fumigations, the maximum recommended use rate is 1500 gh/m^3 CTP with a target maximum concentration of 128 g/m^3 (approximately 30 700 ppm). The required amount of Profume Gas Fumigant needed for specific situation is calculated by the use of Profume Fumiguide, a PC-based computer program. Chloropicrin, a stenching agent, may also be introduced into the structure during fumigation. The label also provides the operation details required for fumigation.

Exposure during use

The product will only be used by licensed fumigators trained under the Dow AgroSciences Precision Fumigation Program. In occupational situations, exposure to sulfuryl fluoride gas is expected to occur mainly via inhalation. An analysis of activities during fumigation revealed that workers might be exposed to sulfuryl fluoride during fumigation, aeration, and during re-entry. There are no exposure models available to estimate worker exposure during the use of Profume Gas Fumigant.

The applicant has submitted exposure studies, where the potential exposure to fumigators and aerators resulting from the fumigation of mills with sulfuryl fluoride, was determined. All the parameters used in these studies are comparable to the draft label for Profume Gas Fumigant and were considered adequate for this assessment. Based on the exposure data obtained from these studies, MOE values were calculated using a NOEC of 20 ppm. Since the NOEC is derived from animal toxicity testing, MOE of 100 or above are usually considered to be acceptable.

During fumigation, the MOE ranged from 5 to 500 and 6 of 9 operations had a MOE that was considered to be unacceptable. During aeration, the MOE ranged from 8 to 111 and 5 of 6 operations were considered to be unacceptable. These results showed that workers are likely to be at risk of inhalation toxicity during fumigation and aeration. Furthermore, sulfuryl fluoride is a colourless and odourless gas and procedures (discussed further below) are required to protect workers from possible exposure without being aware of it.

Exposure during re-entry

Post-application exposure may include re-entry by workers to the treated structures to clear the treated structures for re-occupation, and to remove the equipment associated with fumigation. The applicant has submitted re-entry exposure studies, as part of worker exposure studies, to determine the potential exposure of re-entry workers resulting from the fumigation of mills with sulfuryl fluoride.

Based on a NOEC of 300 ppm and an acceptable MOE of 100, an upper exposure level of equal to or less than 3 ppm was calculated for re-entry purposes. In the exposure studies submitted, analysis of the air monitoring samples collected post-clearance in the mills revealed that the highest 8-hr TWA value was 4.85 ppm during the first 8 hr of monitoring and 2.75 ppm during the second 8 hr of monitoring in one mill (one out of five). All other values (4 hr and 8 hr TWA) were less than 1.30 ppm. Therefore, workers are not expected to be at risk following the use of Profume Gas Fumigant provided that the sulfuryl fluoride concentration in air is no more than 3 ppm at the time of re-entry. A re-entry statement in this context has been recommended for Profume Gas Fumigant.

Recommendations for safe use

The proposed label will include adequate information on procedures and safety equipment relating to the use of Profume Gas Fumigant, for all stages of pre, during and post application. This includes requirements and procedural advice on;

- thorough walk-through inspections prior to fumigation with all entrances being locked upon leaving,
- notification of owners and employees at the facility being fumigated,
- sign posting of fumigated areas,
- monitoring of gas levels with an appropriate detection device of sufficient sensitivity (<1ppm) for occupational exposure during fumigation and for re-entry purposes post-fumigation,
- requirements for the use of positive pressure self contained breathing apparatus (SCBA) or combination air supplied/SCBA respirator,
- leaking or damaged cylinders and transport

Users should also follow the instructions and Safety Directions on the product label.

The following re-entry statement is appropriate for Profume Gas Fumigant:

“Do not allow entry into the treated structures until the concentration of Profume Gas Fumigant is confirmed to be less than 3 ppm, measured with an approved detection device. If prior entry is required, wear an approved positive pressure self-contained breathing apparatus (SCBA) or combination air supplied/SCBA respirator

Conclusions

Profume Gas Fumigant can be used safely if handled in accordance with the instructions and Safety Directions on the product label and in accordance with relevant OHS and public health standards and regulations.

ENVIRONMENTAL ASSESSMENT

Environmental exposure

The primary source of sulfuryl fluoride in the environment is from its use as a fumigant. Sulfuryl fluoride is a gas under essentially all environmental conditions and is expected to disperse in the atmosphere, with only very small amounts (0.007%) estimated to partition from the air to the water phase. Sulfuryl fluoride is expected to dissipate from the atmosphere with a half-life of about 3 years.

Sulfuryl fluoride is rapidly hydrolysed to fluorosulfate and fluoride in water. The estimated half-lives at pH 5.9, 7.0 and 9.0 are 3.1 days, 4.6 hours and 2.8 minutes, respectively. The estimated half-life in the ocean (17^{o}C, pH 8.1) is 41 minutes. Note that sulfuryl fluoride was more persistent in the aquatic toxicity studies described below. Exposure of soils to sulfuryl fluoride is expected to be minimal.

The fate of sulfuryl fluoride in the atmosphere is unclear. Its atmospheric lifetime has been estimated as less than 4.5 years (half-life less than 3.2 years) based on the detection limit for its analysis in air. The concentration of sulfuryl fluoride in the troposphere is less than 0.5 ppt. Significant sinks are likely to include hydrolysis in ocean waters and stratospheric dissociation. Reaction with hydroxyl radicals and uptake and degradation by soils and vegetation are possible sinks. The estimated global warming potential of sulfuryl fluoride is less than 378 based on a 100 year time horizon. The carbon dioxide equivalent emissions of sulfuryl fluoride represent less than 0.004% of the total current and future emissions of radiatively active gases.

Sulfuryl fluoride will not contribute to stratospheric ozone depletion as it contains no chlorine or bromine atoms and is considered a methyl bromide replacement. Emissions of sulfur from sulfuryl fluoride are negligible relative to current anthropogenic sulfur emissions.

Environmental effects

No studies were conducted on the toxicity of gaseous sulfuryl fluoride to terrestrial organisms as there are no standard ecotoxicological test methods for such exposures. The most sensitive result from inhalation testing in mice was 400 ppm.

Static renewal testing was conducted in zebra fish, and static testing in Daphnia magna and green algae, in order to allow classification and labelling of sulfuryl fluoride. The 96 hour LC50 in zebra fish was 0.89 mg/L based on mean time-weighted average concentrations. Measured concentrations declined by about half in the 24 hours between renewals, which suggests greater hydrolytic stability than described above (the pH of the dilution water was 7.7). The 48 hour EC50 in Daphnia magna was 0.62 mg/L. Measured concentrations were 26-47% of nominal at the end of the exposure period. The 96 hour EC50s in *Selenastrum capricornutum* were 0.8 mg/L based on biomass and 6.36 mg/L based on growth rate. Final concentrations were 8-46% of nominal, with greater losses at the lower concentrations because of elevated pH in the replicates where algal growth was more vigorous. These results indicate that sulfuryl fluoride is highly toxic to aquatic life.

Environmental risk assessment

Environmental release and exposure to sulfuryl fluoride is expected to be limited to leaks during fumigation and atmospheric release following fumigation. Sulfuryl fluoride is expected to disperse in the atmosphere following release from fumigation. Although degradation pathways are undefined, sulfuryl fluoride is expected to dissipate from the atmosphere with a half-life of 3.2 years. The submission indicates that the concentration of sulfuryl fluoride in air when the fumigant is released after fumigation is likely to remain below 2.5 ppm, based on atmospheric monitoring in the UK.

The risk of sulfuryl fluoride to terrestrial organisms is expected to be low because atmospheric concentrations are unlikely to exceed 2.5 ppm (less than 1% of the most sensitive inhalational endpoint in mice) and will decline rapidly as the fumigant disperses in the atmosphere.

For aquatic exposure, the applicant has estimated a concentration of 175 ng/L, based on an import volume of 100 tonnes used in a small area (100 km^2) where 1% is covered by surface water. The risk of such exposures to aquatic life is assessed as minimal.

The APVMA is satisfied that the proposed use of the new active constituent sulfuryl fluoride in the product ProFume Gas Fumigant for the control of insect and rodent pests in enclosed situations, such as structures, vehicles and containers, is not likely to have an unintended effect that is harmful to animals, plants or things, or to the environment.

EFFICACY AND SAFETY ASSESSMENT

Evaluation of efficacy of Profume gas fumigant

Results from ten efficacy trials in combination with 24 published papers were assessed to demonstrate efficacy of the proposed product as a fumigant to control a range of stored insect pests in various situations including buildings (residential and non-residential), shipping containers, vehicles, and warehouses and various insect pests in dwellings. The trial data included a variety of laboratory and field experiments, which comprehensively tested for optimal fumigation procedures (i.e. temperature required during fumigation), and to establish lethal doses for pests at all life stages.

The trials were conducted using standard methodology including adequate controls, replication and appropriate statistical analysis, and were conducted using application methods consistent with the product label. The trials covered a wide range of insect pests such as stored insect pests and termites, and were conducted in the US, Australia and the UK. Given this product is used in enclosed environments (buildings, shipping containers etc) overseas data was considered relevant and appropriate.

The product is to be used up to a maximum use rate of 1500 g-h/m^3 CTP not exceeding a maximum concentration of 128 g/m^3. Application rate and exposure time are determined via the ProFume Fumiguide, a PC based computer program used to calculate the required dosage and exposure required specific to the situation.

Stored product pests

All trials were conducted at temperatures ranging from 15°C to 30°C. A range of rates, temperatures and concentration-time were conducted. The pests were treated at all life stages ranging from eggs, to adults. Published data submitted and reviewed confirmed the efficacy of sulfuryl fluoride against the proposed pests. The data demonstrated 100% mortality for all stages of *S. grenarius*, *T. confusem* and *T.molitor*. Whilst some adults of *S. paniceum* and *T. versicolor* survived under some conditions, no reproduction occurred. The maximum rate was required to kill all eggs of *E. kuehniella.*

A number of trials demonstrated that the tolerance of insect eggs was greater than that for other stages, and that control of eggs was also dependent on the age of the egg. One trial tested the toxicity of sulfuryl fluoride to different age groups of eggs of *Ephestia kuehniella*. Results showed eggs aged 1-2 days were more tolerant to fumigation than other age groups, followed by eggs 2-3 days old, 0-14 days old and lastly 3-4 days old.

A trial on *Plodia interpunctella* tested the concentration-time relationship for fumigant efficacy of sulfuryl fluoride on eggs at 25°C and 30°C. This trial demonstrated that at higher temperatures less time was required to gain control. A second trial tested the concentration-time relationship for eggs of *Ephestia kuehniella* and *Tribolium castaneum* at 25°C and 30°C. Experimental design was acceptable and application of the product was consistent with label recommendations.

These trials demonstrated that the use of Profume gas fumigant was effective on the above mentioned pests at all life stages when used in accordance with label directions and in conjunction with the ProFume Fumiguide.

A trial was conducted to test cross-resistance of phosphine resistant strains of *Tribolium* *castaneum* using sulfuryl fluoride and methyl bromide. All samples were examined for surviving or emerging larvae weekly after fumigation until all survivors had emerged. Experimental design was acceptable and application of the product was consistent with label recommendations.

Results showed no evidence of cross-resistance between phosphine and sulfuryl fluoride. Treatment of eggs also showed no evidence of cross-resistance, and the phosphine resistant strain was nearly twice as susceptible to sulfuryl fluoride as the reference strain.

Trials on *Anthrenus flavipes*, *Attagenus megatoma*, *Lasioderma serricorne* and *Dermestes maculates* tested efficacy at all life stages. The data demonstrated that it took 2-8 days to kill adults and larvae. Eggs required higher rates (7-30 times more sulfuryl fluoride than adult and larval stages). Data reviewed supports the efficacy of sulfuryl fluoride against the above-mentioned pests.

Termites

Research investigating the mode of action of poisoning termites using sulfuryl fluoride concluded that disturbances in intermediary metabolism by inorganic fluoride were the main toxic mechanism. In addition to published literature, laboratory trials were submitted and reviewed using 10 termite species, which supported the proposed use pattern. The provided information and data demonstrated the product would be effective for the proposed use against termites.

Sealing of food in buildings before fumigation

A trial was conducted testing the ability of tarpaulins for use as containment barriers and a trial to test the permeability of double and single layered polyethylene film reduced SF levels in bagged food exposed during fumigation. The double-layered polyethylene film reduced the residual sulfuryl fluoride levels by more than 96% and the single layered reduced levels by 79%. However, it is nylon bagging which is recommended on the label and nylon bags were tested in two trials. No sulfuryl fluoride residues were detected by nylon enclosures at the intermediate and low sulfuryl fluoride concentrations. This data is considered adequate to demonstrate that nylon bagging is appropriate including that double bagging is recommended on the label, as supported by both the above-mentioned trials.

Trials also compared tape seals and tarp seal when fumigating an empty food processing and storage warehouse. The tape seal involved applying a 3 layered tape around doors, to PVC frame installed and attached with duct tape to roller doors, to 6mL polyethylene sheeting attached to frame and covering door and wrapped around each roof vent and ventilation stack and sealed to the roof with duct tape. Tarp seals were trialled, by draping over roof vents, roofs, walls and closed doors to the ground, with seams rolled and clipped and ground sealed with sand snakes. The following pests were present in trials; *Trogoderma variabile* (adults, larvae and pupae), *Plodia interpuctella* (1-3 day old eggs), and *Tribolium confusum* (eggs).

Application rate, replication and appropriateness of experimental conditions were consistent with proposed directions for use. Results demonstrated gas retention was improved eight fold in the tarp seal trial compared to the tape seal trial. The tarp seal reduced the amount of sulfuryl fluoride used and increased the concentration-time dosage. The concentration-time of 816 gh/m^3 achieved during the tape seal trial resulted in 100% mortality of Indian meal moth eggs and 99.99% mortality of all stages of warehouse beetle. A concentration-time of 1364 gh/m^3 achieved during the tarp seal trial resulted in 100% mortality of all insects.

This trial was considered to adequately demonstrate the efficacy in controlling *Trogoderma* *variabile*, *Plodia interpuctella* and *Tribolium confusum*. It also supports the use of tarps (preferred) and the use of tape for trapping the gas, both of which are recommended on the label.

The data and information provided as reviewed support all label claims.

PRODUCT LABEL

POISON

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

Dow AgroSciences

ProFume* Gas Fumigant

ACTIVE CONSTITUENT: 998 g/kg SULFURYL FLUORIDE

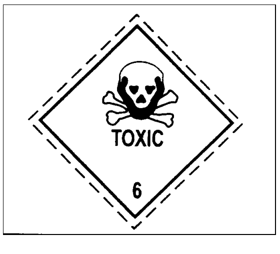
For the control of insects in buildings (commercial and residential), timber, construction materials, furnishings, shipping containers and vehicles (excluding aircraft) and for the control of stored product pests in storage facilities such as silos or warehouses, in fumigation chambers, food handling and commodity processing facilities as specified in the Directions for Use table.

For use only by licensed fumigators trained under Dow AgroSciences' *PRECISION FUMIGATION Program**

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

Contents: 56.7 kg



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DIAL 000
FOR POLICE OR FIRE BRIGADE

UN 2191 SULFURYL FLUORIDE

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DIRECTIONS FOR USE (ALL STATES)

RESTRAINTS:

DO NOT apply when the temperature within the commodity or at the site of pest activity to be fumigated is below 5°C.
DO NOT connect cylinders to introduction equipment until all fumigation warning signs have been posted and the space to be fumigated is cleared of people, non-target animals and secured.
DO NOT fumigate processed cereal commodities.
DO NOT use on any commodity, empty containers, railcars or other transportation vehicles that are in transit or likely to be in transit during exposure or ventilation.

<table>
<tr><td colspan="2">Rate of Use: For all fumigations, the maximum use rate is 1500 g-h/m^3 CTP. Do not exceed a maximum concentration of 128 g/m^3.</td></tr>
<tr><th>Situations</th><th>Pests</th></tr>
<tr><td>Dwellings (including mobile homes)
Buildings
Construction materials, timber and logs
Furnishings (household effects)
Shipping containers (including those containing pallets, machinery and non-food items)
Vehicles (including cars, buses, surface ships, rail cars and recreational vehicles but <u>excluding</u> aircraft).</td><td>Existing infestations of insects such as borers, bedbugs, cockroaches, clothes moths, carpet beetles and drywood termites.</td></tr>
<tr><td>Commodity storage and non-residential structures <u>NOT</u> containing food commodities including food handling and processing facilities, pet food facilities, mills, warehouses, silos, stationary transportation vehicles (railcars, trucks etc., <u>excluding</u> aircraft and passenger railcars), temporary and permanent fumigation chambers.</td><td rowspan="3">All life stages of stored product pests including;
Indian meal moth (Plodia interpunctella),
Mediterranean flour moth (Ephestia kuehniella),
Confused flour beetle (Tribolium confusum),
Rust red flour beetle (Tribolium castaneum),
Warehouse beetle (Trogoderma variabile),
Saw-toothed grain beetle (Oryzaephilus surinamensis),
Dried fruit moth (Ephestia cautella),
Drugstore beetle (Stegobium paniceum),
Tobacco beetle (Lasioderma serricorne),
Hide beetle (Dermestes maculatus),
Grain weevil (Sitophilius granarius),
Rice weevil (Sitophilius oryzae),
Rust red grain beetle (Cryptolestes ferrugineus) and
Lesser grain borer (Rhyzopertha dominica)

Note: Not all seed varieties have been tested for viability following fumigation. Refer to Dow AgroSciences for specific advice (1-800-700-096).</td></tr>
<tr><td>Commodity storage structures (as listed above) containing the following food commodities only:
Cereal grains eg. barley, corn or maize, millet, oat, popcorn, rice, sorghum, spelt, triticale, wheat, wild rice and polished rice.
Dried fruits eg. apricots, dates, figs, prunes, raisins and sultanas.
Nuts eg. almonds, beech nuts, brazil nuts, cashews, chestnuts, hazel nuts, hickory nuts, macadamias, peanuts, pecans, pine nuts, pistachios and walnuts.
Baled hay for animal feed and pet food.</td></tr>
<tr><td>Seed storage facilities holding seeds of additional plant varieties stored for propagation purposes only (i.e. NOT intended for human consumption).</td></tr>
<tr><td colspan="2">CRITICAL COMMENTS: The ProFume Applicator’s Manual and the ProFume Fumiguide contain important information for the safe and effective use of this product. They must be used <u>and</u> must be in the user’s possession during fumigation. Most fumigation can be achieved at much lower rates than the maximum. The ProFume Fumiguide*, a PC-based computer program, should be used to calculate the required dosage and the amount of ProFume needed specific to the situation. You must be trained under the Dow AgroSciences’ Precision Fumigation™ program in order to access the ProFume Fumiguide*. If the ProFume Applicator’s Manual is lost or access to the Fumiguide program has expired, contact your ProFume distributor or Dow AgroSciences’ representative to obtain a replacement copy.</td></tr>
</table>

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

WITHHOLDING PERIOD: Allow a minimum of 24 hours following fumigation before consuming treated commodities.

GENERAL INFORMATION

ProFume is a hazardous material and should be used only by licensed fumigators trained under the Dow AgroSciences' Precision Fumigation™ training program.

The release of high pressure fumigant can be forceful and there is potential for personal injury. Care must be exercised when fumigating, especially tarped commodities, so that the fumigant is not released too rapidly and "balloons" the tarp off the restraining sand or water snakes. A fog-out can also occur if the fumigant is released too rapidly, cooling the air temperature below the dew point. The rapid discharge of ProFume through introduction equipment will result in cooling parts of the equipment and the cylinders. Contact with the cooled equipment can cause frostbite. When used for fumigation of enclosed spaces, such as houses and other structures, warehouses, vaults, chambers, trucks, vans, boxcars, ships and other transport vehicles, 2 persons trained in the use of this product, one of whom is licensed by the competent state authority, must be present during introduction of the fumigant, re-entry prior to aeration, and during the initiation of the initial aeration procedure. **Two persons need not be present if monitoring is conducted remotely (*i.e.* outside the area being fumigated).**

Use of warning agent: **Chloropicrin** is a warning agent that can be introduced into a structure during fumigation only where relevant to avoid direct exposure to ProFume. Chloropicrin may be released into a building at least 5 to 10 minutes prior to introduction of ProFume in situations where there is a high risk of persons inadvertently remaining in, or entering into, a fumigated building. To introduce the warning agent, place a handful of wicking agent (*e.g.* cotton) in a shallow chloropicrin evaporation container (eg. dish). Do not use containers or application equipment made of magnesium, aluminium or their alloys, as chloropicrin may be severely corrosive to such metals. To enhance the distribution of chloropicrin throughout the structure, place the container in the air stream of a fan. Pour chloropicrin over the wicking agent. Dispense no more than 30 ml for 425 m^3 of space to be fumigated. Establish at least one chloropicrin introduction site for every 1275 m^3 of space to be fumigated.

Chloropicrin need not be used when fumigating rail cars; however a walk-through inspection must be preformed of each railcar with doors being immediately locked upon leaving each car, and a guard must be posted during fumigation introduction, exposure period and aeration.

Chloropicrin is a warning agent that causes smarting of the eyes, tears and discomfort, and has a very disagreeable pungent odour at very low concentrations. Chloropicrin must be used by a person certified to apply ProFume, or under their supervision. Fumigators must observe the precautionary statements and safety recommendations appearing on the label of this product.

PRECAUTIONS

Do not apply fumigant directly onto any surface.

Do not use this product without the Fumiguide® Program for ProFume. The ProFume Fumiguide is a computer program available to calculate safe and effective levels of ProFume for fumigating structures and commodities. Carefully read the label and the ProFume® Applicator's Manual before using this product. Extinguish all flames including pilot lights of furnaces, hot water heaters, dryers, gas refrigerators, ranges, ovens, broilers, and open flames. Turn off or unplug all electrical heating elements such as those in heaters, dryers, *etc*. Shut off automatic switch controls for appliances and lighting systems that will be included in the space to be fumigated. Contact your local gas company to determine what procedures should be followed in your area for shutting off natural gas or propane service. Gas service should be shut off at the main service valve. ProFume Gas Fumigant can also react with strong bases such as some photo developing solutions.

Never allow untrained individuals to use ProFume.

Walk through of areas to be fumigated & securing structure entrances

A thorough walk-through inspection of areas to be treated must be performed immediately prior to the introduction of the fumigant with all entrances being locked upon leaving. To secure the structure against unauthorised entry during fumigation use a locking device or barricade on all exterior doors or doorways. A locking device or barricade must be demonstratively effective in preventing an exterior door or doorway from being opened using normal opening or entering processes by anyone other than the certified applicator in charge of the fumigation or persons under their direct supervision.

Notify appropriate owners, employees, and/or operators at the facility where the fumigation will occur. All entrances and all sides of the fumigated structure or fumigated space must have warning signs (see below):

Posting (Signage) of Fumigated Areas

The applicator must post all entrances to the fumigated areas with signs showing:

1. The SKULL and CROSSBONES symbol.
2. The statement, "**Area under fumigation, DO NOT ENTER**".
3. The date of fumigation.
4. Name of Fumigant used.
5. Name, address and telephone number of the applicator.

Only a licensed fumigator may authorize removal of placards and the structure must remain posted for fumigation until clear for re-entry when the concentration of ProFume in the treated site is 3 ppm or less. The concentrations of ProFume Gas Fumigant must also be monitored in breathing zones outside the structure as appropriate.

No one should be in treated areas if the level of ProFume Gas Fumigant is above 3 ppm unless provided with an approved, positive pressure self contained breathing apparatus (SCBA) or combination air supplied/SCBA respirator. Since the approved clearance devices give immediate readings, respiratory protection is not required when clearing with these instruments after having completed the initial aeration procedure. However, if a reading indicates levels in excess of 3 ppm, leave the affected area immediately.

Re-entry

Do not allow entry into the treated structures until the concentration of ProFume Gas Fumigant is confirmed to be less than 3 ppm, measured with an approved detection device.

If required to enter into the fumigated area during the aeration procedure, approved respiratory protection must be worn until concentration of ProFume is confirmed not to exceed 3 ppm with an approved detection device. No one shall be in fumigated areas if the level of ProFume is above 3 ppm unless wearing an approved positive pressure self-contained breathing apparatus (SCBA) or combination air supplied/SCBA respirator. However once the initial aeration procedure has been undertaken, use of an approved full facepiece respirator with combined dust and gas cartridge may be used if in the treatment area for short periods. Once the concentration is confirmed to be less than 3 ppm, the structure is cleared for immediate re-entry.

Note 1: Only an approved detection device of sufficient sensitivity (LOD <1 ppm) can be used to confirm a concentration of ProFume of 3 ppm or less. Such devices must be calibrated according to manufacturer recommendations. Refer to the ProFume Applicator's Manual for further guidance on detection devices.

Note 2: Before using any make or brand of SCBA, learn how to use it correctly. Determine that it is in good working order, has an adequate air supply for the job at hand, fits properly, and provides an adequate seal around the face.

Leak Procedures
Evacuate immediate area of leak. Use an approved positive pressure self-contained breathing apparatus (SCBA) or combination air-supplied/SCBA respirator for entry into affected areas to correct problem.

Move leaking or damaged cylinder outdoors or to an isolated location, observing strict safety precautions. Work upwind if possible. Do not permit entry into leakage area by unprotected persons until concentration of fumigant is determined to be 3 ppm or less, as determined by an approved detection device with sufficient sensitivity.

Additional Precautions and Safety Information
Do not wear gloves or rubber boots. Do not reuse clothing or shoes that have become contaminated with liquid ProFume until thoroughly aerated. Wear loose fitting or well-ventilated long-sleeve shirt, long pants, shoes and socks.

In all cases of overexposure, when symptoms such as nausea, difficulty in breathing, abdominal pain, slowing of movements and speech, or numbness in extremities are exhibited, get medical attention immediately. Take person to a doctor or emergency treatment facility.

Transportation of Cylinders
Do not transport cylinders in closed vehicles where the same common airspace is occupied by personnel. On public roads transport only when secured in an upright position.
Do not use rope slings, hooks, tongs, or similar devices to unload cylinders.
Do not remove valve protection bonnet and safety cap until immediately before use.
When cylinder is empty, close valve, screw safety cap onto valve outlet, and replace protection bonnet before returning to supplier.
ProFume cylinders must never be transported by aircraft under any circumstances.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT
ProFume Gas Fumigant is a highly toxic gas. Do not expose non-target organisms. This pesticide is toxic to fish and wildlife.

STORAGE AND DISPOSAL
Storage:
Store in a dry, cool, well-ventilated, secured and locked area. Storing indoors in occupied areas in buildings is **not** recommended.
ProFume cylinders are under pressure and must not be stored near heat or open flame. Exposures to temperatures above 70°C will cause a fusible plug to melt and the contents will be released. Store cylinders upright; secured to a rack or wall to prevent tipping. Cylinders should not be subjected to rough handling or mechanical shock such as dropping, bumping, dragging, or sliding. Do not store near food, feedstuffs, fertilisers or seed.
Disposal:
Empty cylinders **MUST** be returned to your supplier. **DO NOT** use cylinders for any other purpose. Follow proper cylinder handling directions above.

SAFETY DIRECTIONS
Direct contact with liquid may cause irreversible eye damage and/or freeze burns on exposed skin. Wear splash resistant goggles or full face shield when handling the liquid product during introduction of fumigant or when working around any lines containing fumigant under pressure. Harmful if inhaled. Do not inhale vapour. If required to enter into a fumigated area, an approved positive pressure self-contained breathing apparatus (SCBA) or combination air-supplied/SCBA respirator must be worn until concentration of ProFume is confirmed not to exceed 3 ppm with an approved detection device.

FIRST AID
If poisoning occurs, contact a doctor or Poisons Information Centre. Phone 131126 (Australia).

MATERIAL SAFETY DATA SHEET

Additional information is listed on the Material Safety Data Sheet for **PROFUME GAS FUMIGANT** which is available from Dow AgroSciences on request. Call Customer Service Toll Free on 1 800 700 096 or visit www.dowagrosciences.com.au

Barcode for stock identification

APVMA Approval No.: 59952/1/0907

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.
Chronic	Of long duration.
Codex MRL	Internationally published standard maximum residue limit.
Desorption	Removal of an absorbed material from a surface.
Efficacy	Production of the desired effect.
Formulation	A combination of both active and inactive constituents to form the end use product.
Genotoxicity	The ability to damage genetic material
Leaching	Removal of a compound by use of a solvent.
Metabolism	The conversion of food into energy
Toxicokinetics	The study of the movement of toxins through the body.
Toxicology	The study of the nature and effects of poisons.

APVMA PUBLICATIONS ORDER FORM

To receive a copy of the full technical report for the evaluation of [active constituent] in the product [product name], please fill in this form and send it, along with payment of $30 to:

[name]
[section]
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
Kingston ACT 2604

Alternatively, fax this form, along with your credit card details, to:
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