File No: NA/949

September 2001

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

Solkane 365mfc

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Director Chemicals Notification and Assessment

FULL PUBLIC REPORT

Solkane 365mfc

1. APPLICANT

A-Gas (Australia) Pty Ltd of 9-11 Oxford Road, LAVERTON NORTH VIC 3026 has submitted a standard notification statement in support of their application for an assessment certificate for Solkane 365mfc.

2. IDENTITY OF THE CHEMICAL

The chemical name, CAS number, molecular and structural formulae, molecular weight, spectral data and formulation details have been exempted from publication in the Full Public Report and the Summary Report.

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C & 101.3 kPa: Volatile colourless liquid

Boiling Point: 40.1°C

(Solvay Pharmaceuticals 1999)

Density: 1.27 g/cm^3

Vapour Pressure: 43.3 kPa at 20°C

Water Solubility: 1.70 g/L at 21.2°C

Partition Co-efficient $\log P_{ow} = 1.61$ (see comments below) (n-octanol/water): (Solvay Pharmaceuticals 1999)

Hydrolysis as a Function of pH: Not determined (see comments below)

Adsorption/Desorption: Log $K_{oc} = 4-9$ (see comments below)

(Solvay Pharmaceuticals 1999)

Henry's Law Constant: $\log H = 3.53$ (see comments below)

Dissociation Constant: Not determined. The notified chemical does not contain

any dissociable groups

Flash Point: Flammable. Flash point could not be determined in test

(see comments below)

Flammability Limits: Upper Explosive Limit = 13.3% v/v in air

Lower Explosive Limit = 3.8% v/v in air.

Autoignition Temperature: 580°C

(Solvay Pharmaceuticals 1998)

Explosive Properties: Not explosive; does not contain any chemically

unstable or highly energetic groups. (Solvay Pharmaceuticals 1998)

Reactivity/Stability: No oxidising properties

(Solvay Pharmaceuticals 1998)

The tropospheric lifetime of the notified chemical is estimated to be 10.8 years (see environmental fate

section below).

Conversion Factor (vapour): 1 ppm $v/v = 6.07 \text{ mg/m}^3 (25^{\circ}\text{C})$

3.1 Comments on Physico-Chemical Properties

The boiling point of the notified chemical was determined using OECD TG 103 (Solvay Pharmaceuticals 1999f).

The vapour pressure of the notified chemical was determined using a capacitance manometer according to Method A4 of Commission Directive 92/69/EEC (Solvay Pharmaceuticals 1998a). A total of 35 measurements were made between 18.44 and 23.43°C and the vapour pressure was determined from the resulting vapour pressure curve. The vapour pressure is 43.3 kPa at 20°C which indicates the notified chemical is highly volatile (Mensink, 1995).

The water solubility was determined using a modified flask method (Solvay Pharmaceuticals 1999a). The notified chemical (\sim 1 mL) was added to HPLC grade water (250 mL) in a glass brown flask without headspace, with the solution stirred for the period of the test. The solution was sampled at 1, 2 and 4 h and 1, 2, 5 days. Prior to sampling, the solutions were allowed to stand for up to 45 min. After equilibration, a 100 \square L sample was taken in triplicate, diluted 100 times with purified water and analysed by gas chromatography. This method indicated that the solubility of the notified chemical is 1.70 g/L.

The Henry's Law Constant was calculated from the measured vapour pressure (VP), water solubility (S) and molecular weight (MW) through the relation H = VP X MW/S. The relatively high value of H indicates the compound to be appreciably volatile from water (Mensink 1995).

The rate of hydrolysis of the notified chemical was determined in a sealed vessel using OECD TG 111 (Solvay Pharmaceuticals 1999b) over a 5 day period in buffers of pH 4, 7 and 9 at 50 °C and at with initial concentrations of the test compound in each buffer around 1, 10, 1000 mg/L. The preliminary study indicated the notified chemical was not hydrolysed at neutral pH. More detailed studies suggested the notified chemical exhibited some hydrolytic instability at pH 4, 7, and 9, however, given the volatility of the chemical, this may be attributed loss of test material rather than hydrolytic degradation. Furthermore, the C-F bond is the strongest single bond

commonly encountered in organic compounds (bond strength around 480 kJ/mole) and the stability of fluorocarbons to attack by acids and bases is well known (Greenwood and Earnshaw, 1989).

The n-octanol/water partition coefficient was determined using OECD TG 107 (Solvay Pharmaceuticals 1999c). An aliquot (2.5-10 mL) a stock solution of the notified chemical (98 mg/L) was added to water saturated with n-octanol in capped vials. The vials were vertically rotated for 18 h and then equilibrated. After this time samples of the two phases were removed and analysed by gas chromatography. The log partition coefficient for the notified chemical is 1.61. This equates to a P value of 40.1 which indicates that the notified chemical may be considered to be hydrophilic and has a low affinity for organic matter in the soil.

This is confirmed by the low log K_{oc}. The K_{oc} was determined using OECD TG 106 (Solvay Pharmaceuticals 1999d) and was determined for 3 soil types.

Soil	pН	% Organic Carbon	Koc
alkaline loamy soil	7.5	3.2	9
sandy soil	6.0	4.1	3
acid loamy soil	6.1	2.0	4

As such, the notified chemical is classified as being very hydrophilic and mobile in soil.

The compound contains no acidic or basic functional groups so dissociation constant data are not relevant.

Flash point was determined using a Pensky-Martens closed cup flash-point apparatus according to EEC test method A.9. No flash point could be determined under the conditions of the test. The vapour near the surface of the liquid test substance could not be ignited. A flame near the ignition source was observed during testing, but this was not regarded as a flash-point according to the test guideline (Krips H.J, 1999).

4. PURITY OF THE CHEMICAL

Degree of Purity: >99.5%

Hazardous Impurities: None

Non-hazardous Impurities None

(> 1% by weight):

Additives/Adjuvants: None

5. USE, VOLUME AND FORMULATION

Use

The notified chemical will be used as a primary blowing agent in polyurethane foam systems. The foam will be used as an insulating material in manufactured goods such as refrigerators, eskies and cool rooms panels. The notified chemical is a replacement for the current blowing

agent, HCFC 141b.

The notified chemical will not be manufactured in Australia. It will be imported in standard UN approved 205L steel drums, transported by road to the storage and distribution facility, and then distributed to customers for blending.

Volume

In year one the import volume for the notified chemical is anticipated to be 10 000 kg. This volume is expected to rise to 20 000 kg by year five.

Formulation

Two processes are involved in the formulation of polyurethane foam - blending and foaming production.

During the blending process, the notified chemical will be pumped from closed top drums directly into a closed 1000 L stainless steel blending vessel, where it will be firstly mixed with Heptafluoropropane. The blended product, which contains 93% concentration of the notified chemical, will then be blended with polyols to produce the polyol blend which is then decanted from the blending vessel into 205 L closed top steel drums. The area immediately above the drum will be ventilated with an extractor. The drums will be transported by road to the final users.

During the foaming process, an air pump will be used to transfer the polyol blend containing the notified chemical from the drums to a closed 1000 L foaming machine via a 1.5 m length of pipe. The foaming machine will combine the blend with isocyanide resin in controlled portions. The foam, which contains between 1% and 7.5% of the notified chemical, results from the chemical reactions that take place, trapping the notified chemical in the foam (closed cell). The viscous foam is then discharged at low pressure through a pouring tube into a mould, where it will be left to partially cure and solidify for 30 minutes, and then put out onto a pallet for 3 days to complete the curing process. A horizontal slicer and bansaw will be used to cut the foam to size.

Both the blending and foaming operations will be undertaken within closed loop systems in the presence of local and general ventilation.

6. OCCUPATIONAL EXPOSURE

There is potential for the exposure of workers involved in the transport and the storage of the notified chemical, workers involved in the blending and foaming operations and staff involved in quality control and research & development.

Nature of Activity &	Maximum Potential Exposure Duration & Personal Protective
Number of Workers	Equipment
Transport and Storage, 6-9	2-3 hours/day; 10-15 days/year.

Blending Operations, 9-12

8 hours/day; 50 days/year. Overalls, aprons/boots of butyl rubber if there is a risk of splashing, neoprene chemical gloves.

Foaming Operators, 15-20

8 hours/day; 100 days/year.

Overalls, aprons/boots of butyl rubber if there is a risk of splashing, neoprene chemical gloves, protective goggles and respirators or dust masks (for workers sizing the foam blocks).

Laboratory QC and R&D Staff, 9-12

2 hours/day; 50 days/year. Laboratory coats, chemical gloves, safety spectacles or goggles

Dockside and transport

Occupational exposure is not expected except in the event of an accident.

Formulation of Polyol Blend

Manufacture of the polyol blend is largely an enclosed process and loss of Solkane 365mfc to the atmosphere is not anticipated. However dermal and inhalation exposure to the notified chemical is possible when connecting and disconnecting pump lines and during maintenance. Exposure for process workers is limited by pumping from and into closed drums and by operating at ambient (not elevated) temperatures.

Laboratory quality assurance and research and development staff could be exposed to the notified chemical when taking samples and preparing small batches for testing. Exposure of these staff is limited by having small sample sizes. Exposure will also be limited by maintaining temperature control of the materials and the environment, and by using laboratory fume hood extraction.

Skin and inhalation exposure may also occur when cleaning blending vessels and if drips and spills occur during the blending operation. Spill buckets and trays are placed under points of charge and discharge on the blending vessel. These will be collected into drums before being disposed of by a licensed disposal contractor. Exposure to vapours and drips and spills may be possible during this collection process.

Foam production and application

In foam production, the process is largely enclosed, however, dermal and inhalation exposure to the notified chemical is possible when connecting and disconnecting the transfer lines to the foam machine. During blending with the isocyanate resin, the notified chemical is vapourised and inhalation exposure may occur if there are leaks in the system.

Skin and inhalation exposure to the notified chemical may also occur during discharge of the viscous foam through a pouring tube into the mould, particularly if splashing occurs. However, splashing is minimised by discharging the foam at a low pressure. In addition, the notified chemical will be largely trapped within the foam matrix, especially as it cures, thereby reducing the risk of inhalation exposure. Exposure to small amounts of the notified chemical may occur when the moulded foam is cut to size, due to release of the chemical from the closed cell nature of the foam.

Similar exposure may occur if the foam is transferred directly into an appliance such as a

refrigerator door.

Storage and transport

Occupational exposure is not expected except in the event of an accident.

Control Measures and Worker Education and Training

The notifier states that all operators will be trained in the handling of dangerous goods, and that material safety data sheets (MSDS) will be available to all personnel.

7. PUBLIC EXPOSURE

Polyurethane foam insulating material containing 1-7.5% of the notified chemical will be used in domestic refrigerant products eg. fridges and eskies, which are sealed. Consequently, there will be no public contact with the notified chemical during normal use of these products.

8. ENVIRONMENTAL EXPOSURE

8.1 Release

When used as a blowing agent for production of polymer foam the notified chemical will be released into the environment in two ways: (1) into the atmosphere by diffusion, and (2) minor releases into water through equipment cleaning, housekeeping and vessel maintenance.

Release into the Atmosphere

Almost all of the notified chemical will eventually be released into the atmosphere. The notifier estimates that up to 200 kg per annum of the notified chemical may be released during formulation of the blowing agent. The notifier further estimates that up to 200 kg per annum of the notified chemical will remain in the empty import drums and up to 200 kg per annum will be released to the environment from the foam manufacturing process. The foam moulding machines will be cleaned with dichloromethane. The organic solvent will be allowed to evaporate and the resulting solid will be disposed of in landfill. As a result of trimming and reshaping processes, approximately 20% of the foam produced will be incinerated.

The remainder of the notified chemical will remain incorporated within foam. The notifier indicates that, over time, loss via diffusion throughout the service lifetime of the foam products is expected, though they claim this will be slower than for other blowing agents due to the lower diffusion constant and good ageing behaviour of the foam.

Advice solicited and obtained from the Australian Greenhouse Office indicated that most of the blowing agent is expected to escape from the foam over 20 years, which is roughly equivalent to the service life of most domestic appliances.

At the end of the foam's lifecycle, products into which the foam has been incorporated will be disposed of in landfill or incinerated. During subsequent degradation of the polymer matrix, all of the notified chemical will be released into the atmosphere. In the case of incineration, the notifier claims that the blowing agent is destroyed prior to atmospheric release, although the high thermodynamic stability of hydrofluorocarbons indicates that this may not be the case and most would be liberated to the atmosphere. Although it may take some time for full emissions to be realised, as a worst case scenario, it must be assumed that 100% of the imported chemical will be released into the atmosphere.

8.2 Fate

Atmosphere

The notified chemical is a highly fluorinated low molecular weight alkane most of which is expected to enter the atmosphere and is also expected to persist in this environment. The initial degradation of the notified chemical in the atmosphere is expected to occur through hydrogen abstraction by hydroxy radicals resulting in the production of fluorohydrocarbon radicals. Following production of this radical after hydrogen abstraction, the species subsequently reacts with oxygen, nitrogen oxide and chlorine atoms to give the corresponding alkoxy and haloalkyl radicals. These would in turn decompose to COF₂, HF, CO₂ and HCl through further reactions with oxygen and water vapour. In this study, no other long-lived organic intermediates were detected during the degradation process. The HF would eventually be precipitated to the surface in rainwater. The atmospheric half-life of the chemical in the troposphere was estimated to be 10.8 years.

The rate constant for degradation through hydrogen abstraction may also be estimated using published data from an OECD monograph (OECD, 1992), and using the appropriate procedures described in this document, the rate constant for hydrogen abstraction from the notified chemical is estimated as $k_{abs} = 2.06 \times 10^{-14}$ cm³ molecule/sec. The atmospheric half life may then be estimated through the relation $t_{1/2} = Log(2)/([OH\bullet] \times k_{abs})$ where $[OH\bullet]$ is the average concentration of atmospheric hydroxy radicals which is given as 5×10^5 radicals/cm³ by Calamari (1993). Using these data and relationships, the value of $t_{1/2}$ is estimated as 6.7×10^7 seconds, or approximately 2.12 years. The difference between the literature value and the calculated value for $t_{1/2}$ is attributable to the choice of the average concentration of atmospheric hydroxy radicals.

Water and biodegradation

Only small quantities of the compound are expected to enter the water compartment, and due to the high value of Henry's Law constant most of this would volatilise to the atmosphere. Nevertheless the notifier provided a test report on the biodegradation of the notified chemical by microorganisms in aqueous media (Solvay Pharmaceuticals, 1999e). The test was carried out in accordance with OECD TG 301D, Closed Bottle Test.

The test used inoculum separated from sewage sludge collected from RWZI Horstermeer, Nederhorst den Berg, The Netherlands. Four stock solutions were prepared by dissolving the test substance (50 mg) in the closed bottle medium (320 mL). The test substance was introduced into purified water and inoculum in 280 mL BOD bottles. The concentration of the test substance in solution is 5.58 mg/L. The test substance was left to cultivate (degrade) in a closed vessel for a period of 28 days, at a temperature of 20°C. After 28 days, 14% biodegradation of the test substance was observed. Over the same period the reference substance, sodium acetate, exhibited 67% degradation. The test substance was found not to be degraded by microorganisms under these test conditions.

The biodegradation tests suggest that microorganisms will not degrade the notified chemical once it is released. However, given its relatively low boiling point, and high values of vapour pressure and log H, the notified chemical is expected to be very volatile from water. Hence under normal atmospheric pressures and temperatures, the notified chemical is not expected to remain dissolved either in the effluent water, or in natural water bodies, and hence is not expected to pose a threat to aquatic organisms once released into the environment via stormwater drains.

Bioaccumulation

Little of the chemical will reach the water compartment and so exposure to aquatic organisms will be low. Nevertheless, due to the relatively high water solubility and modest value for Log Kow, the potential for bioaccumulation is considered to be low (Connell, 1990).

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Summary of the acute toxicity of Solkane 365mfc

Test	Species	Outcome
acute oral toxicity	rat	LD50 > 2 000 mg/kg
acute inhalation toxicity	rat	LC50, 4hour > 100 000 ppm
skin irritation	rabbit	Not irritating
eye irritation	rabbit	Very slightly irritating
skin sensitisation	guinea pig	Not sensitising

9.1.1 Oral Toxicity (Solvay, 1997)

Species/strain: Rat/Sprague-Dawley (CRL:CD(SD)BR)

Number/sex of animals: 5/sex

Observation period: 14 days

Method of administration: 2000 mg/kg suspended in 1.25% tragacanth by gavage in a

dose volume of 10 mL/kg

Test method: OECD TG 401

Mortality: Nil

Clinical observations: A slightly hunched gait was observed in 5/5 males 0 - 0.5 h

after dosing and in 2/5 females 0 - 1.5 h after dosing. Dark coloured faeces were observed in males at 1.5 h after dosing,

and in females at 3 h after dosing. At 3 h after dosing and thereafter there were no abnormalities observed in males. In females there were no abnormalities observed at 6 h after dosing and thereafter.

Morphological findings: No abnormalities were noted at necropsy.

LD50: > 2000 mg/kg

Result: The notified chemical was of low acute oral toxicity in rats.

9.1.2 Dermal Toxicity

No acute dermal toxicity study was submitted.

9.1.3 Inhalation Toxicity (Solvay, 1997)

Species/strain: Rat/Sprague-Dawley

Number/sex of animals: 10 females, 14 males

Observation period: 14 days

Method of administration: Animals were exposed nose only to test substance vapour.

Animals in Groups 1 and 2 received a single exposure only. Animals in Group 3 were exposed to increasingly higher doses of the notified chemical according to the table below:

Group	Number/ Sex of animals	Target concentration (ppm)	Mean actual concentration (ppm)	Exposure period	Mortality
1	5/sex	300 000	316 257	25 min*	5/5 females,
2	5/sex	100 000	102 788	4 hours	5/5 males 0/5 females, 0/5 males
3	4 males	0	0	30 min	0/4
		100 000	108 875	30 min	0/4
		200 000	221 610	30 min	1/4
		300 000	327 415	7 min**	2/4

^{*}Exposure was terminated after 25 minutes due to the death of test animals.

Test method: OECD TG 403

Mortality: In Group 1, animals died within 15 minutes from the

commencement of exposure. In Group 2 death occurred after 30 minutes exposure. In Group 3 death occurred within 4 to 6 minutes after the commencement of

exposure.

^{**}The interval of exposure for Group 3 animals to 300 000 ppm of test substance was terminated after seven minutes due the death of three animals in total (two animals at the 300 000 ppm exposure and one animal at the 200 000 ppm exposure)

Clinical observations:

Observation of clinical symptoms was limited due to restraining of the animals.

During exposure

Depression of respiratory rates (possibly due to the anaesthetic properties of the test substance) was observed at all exposure levels. Depression of respiratory rate was noted at 100 000 ppm and above, without any clinical signs of irritation to the upper respiratory tract such as gasping or struggling during exposure. The depression observed at 100 000 ppm was comparable in Groups 2 and 3. The depression at 200 000 ppm in Group 3 was slightly higher than the depression in Group 1. At the end of the exposure period, no respiratory movements were noted in one (live) animal in Group 3 at 300 000 ppm. All animals had bluish discoloration of the paws.

Post exposure

No clinical symptoms were observed in survivors from the end of the exposure period to the end of the observation period. Slight growth retardation in surviving females was observed.

Morphological findings:

In-study decedents of Group 1 showed pulmonary damage characterised by red areas on the lungs and pulmonary oedema. In-study decedents of Group 3 showed cyanosis of the skin and a full urinary bladder. A slight increase in mean absolute and relative liver and lung weights compared with those of historical control animals was noted.

At necropsy no abnormalities were detected in Group 2 animals. The remaining Group 3 animal showed a small right testicle but this was not considered treatment related.

LC50: > 100 000 ppm (607 mg/L) (4-hour exposure)

Result: The notified chemical was of low acute inhalation

toxicity in rats

9.1.4 Skin Irritation (HLS, 1998)

Species/strain: Rabbit/ New Zealand white

Number/sex of animals: 3 females

Observation period: 4 days

Method of administration: A single 4-hour, occluded application of 0.5 mL of the test

substance as supplied to intact skin.

Test method: OECD TG 404; EC Method B4

Comment: No dermal response (all Draize scores were zero) to the

treatment was observed in any animal throughout the study. There were no signs of toxicity or ill health during the

observation period.

Result: The notified chemical was not irritating to the skin of rabbits.

9.1.5 Eye Irritation (HLS, 1998)

Species/strain: Rabbit/ New Zealand white

Number/sex of animals: 3 females

Observation period: 3 days

Method of administration: A single instillation of 0.1 mL of test substance as supplied

into the lower everted lid of one eye of each animal. The eyelid was held together for one second before releasing. The

untreated eye served as the control.

Test method: OECD TG 405; EEC Method B5

Comment: Transient hyperaemia (Grade 1) of the blood vessels noted in

the three treated eyes had resolved by day one after instillation. No iridial or conjunctival effects were noted.

Result: The notified chemical was very slightly irritating to the eyes

of rabbits.

9.1.6 Skin Sensitisation (HLS, 1998)

Species/strain: Guinea pig/Dunkin Hartley

Number of animals: 10 male test and 5 male control animals

Induction procedure: Intradermal Injection

Test animals:

Day 1: Three pairs of intradermal injections (0.1 mL) into the dorsal skin of the scapular region:

• Freund's Complete Adjuvant (FCA), diluted with an equal volume of water for irrigation;

• The test substance, as supplied;

• The test substance, as supplied in a 50:50 mixture of FCA and Alembicol D.

Topical Induction:

Day 7: A 48 hour occluded application of filter paper loaded with the test substance as supplied (approximately 0.4 mL) to the treated area;

Control Animals:

Treated similarly to the test animals, excepting that the test substance was omitted from both the intradermal injections

and the topical application.

Challenge procedure: Test and Control animals:

Day 21: A 24 hour, occluded application of the test substance as supplied (approximately 0.2 mL) to an anterior site on the left flank of each animal, and 50% v/v in Alembical D

applied in a similar manner to the posterior site.

Test method: OECD TG 406; EC Method B6; Magnusson and Kligman

Maximisation Method

Challenge outcome: Slight irritation was seen in test animals receiving the test

substance as supplied and in control animals receiving Alembicol D by intradermal injection. No erythema was observed in test or control animals as a result of the topical applications. No skin reactions were observed in the test animals by the challenge application at the 24 or 48-hour

observation period.

Result: The notified chemical was not sensitising to the skin of

guinea pigs.

9.2 Repeated Dose Toxicity

9.2.1 14-Day Repeated Dose Inhalation Study (Solvay, 1998)

Species/strain: Rat/Sprague-Dawley (CRL:CD(SD)BR)

Number/sex of animals: 20 males

Method of administration: Inhalation: nose only exposure

Dose/Study duration: 10 animals were exposed to a target concentration (vapour)

of 50 000 ppm (actual daily mean concentration ranged between 48 371 and 49 862 ppm) for 6 hours/day, 5 days/week for 2 weeks. A control group of 10 animals was exposed to air only. Animals were killed 24 hours after their

last exposure.

Test method: OECD TG 407

Clinical observations:

No clinical symptoms due to exposure to the test substance were observed. Body weights and body weight gains were reduced over the total treatment period. Growth retardation and a slight loss in body weight in a number of the exposed animals during days 5 to 8 of treatment was considered to be a transient effect of the treatment, as only one animal showed weight loss between days 12 to 15. There were no observed effects of the treatment on food consumption. During days 5 to 8 of treatment one animal showed extreme weight loss accompanied by low food and water consumption, though no signs of bad health were observed. This finding was not considered to reflect a toxicological action of the test substance- a disturbance of the water supply was regarded as the most likely cause. Excluding this animal when calculating the standard deviation of the water consumption for days 5 to 8 revealed values comparable to those obtained at other time periods during the study. No other effects on water consumption were observed.

Pathology:

Macroscopic abnormalities (spots on the lung lobes, dark colour on the lung lobes) were observed in two treatment and two control animals, and were not considered to be treatment effects. No treatment related effects on absolute organ weights were observed, however significant increases in the relative weights of the testes, liver and kidney of test animals were observed. This was likely to be due to the slightly lower (<10%) necropsy body weights of the treated animals. The loss of body weight was regarded as of minor toxicological importance, and the increases in relative organ weights were considered to be secondary to the treatment.

Result:

The acceptable upper level of the dose range to be used in future subchronic toxicity studies was determined to be 50 000 ppm (303.3 mg/L).

9.2.2 28-Day Repeated Dose Inhalation Study (HLS, 1998)

Species/strain: Rat/Sprague-Dawley CD

Number/sex of animals: 5/sex/group

Method of administration: Inhalation: nose only exposure

Dose/Study duration: Treatment animals were exposed to the test substance vapour

for 6 hours/day, 5 days/week for 4 weeks. A control group was exposed to air only. Animals were killed 3 days after

their last exposure.

Treatment animals were divided into three groups. The

exposures are listed in the table below:

Group	Target concentration	Mean actual	concentration
	(ppm)	ppm	mg/L
Group 1	0	0	0
Group 2	10 000	9 685	58.7
Group 3	25 000	24 747	150.1
Group 4	50 000	50 486	306.2

Test method: OECD TG 412, EEC Method B8

Mortality:

There were no unscheduled deaths during the study.

Clinical observations:

Coldness to touch and piloerection were noted post exposure in Group 4 only, and were first noted in the second week of treatment. These signs resolved before the next exposure to the test substance, and were judged to be treatment related. Other post exposure signs noted in all groups, including control animals included wet fur, red staining around the snout/eyes and brown staining on the head/dorsal surface. These were attributed to the method of restraint and generally resolved overnight.

Mean bodyweight gain was significantly reduced (P<0.05) over the study period in Group 4 animals compared to control animals. Associated with this was a very small reduction in cumulative food consumption over the study period by Group 4 animals compared to control animals.

Clinical chemistry/Haematology/Urinalysis

Haematology

Statistically significantly higher mean packed cell volumes and haemoglobin concentrations were obtained for males in Groups 2, 3 and 4 when compared with controls. Lower reticulocyte, mean lymphocyte, eosinophil and basophil counts, and a lower mean white blood cell count reached statistical significance in females.

Biochemistry

Statistically significantly higher glutamic-pyruvic transaminase values were obtained for Group 4 animals when compared with controls, however, values were within the normal background range. Statistically high urea nitrogen levels were observed in Group 4 males, and statistically lower albumin and total protein levels were observed in Group 4 females. Males in Groups 2, 3 and 4 had statistically higher sodium levels, however, the increases were not dose-related.

Urinalysis

A statistically lower pH in males of Groups 3 and 4, and statistically higher volume and lower protein in females of Group 4 was observed.

Group 4 animals and male rats in Group 3 had statistically higher total outputs of urinary fluoride when compared with controls. This was considered to be treatment related.

Pathology:

No treatment related changes in organ weights were observed. Also, there were no significant macroscopic findings.

Histopathology:

Lesions were detected in the incisor teeth. An increased incidence of ameloblastic dysplasia in animals from Group 4 was observed, with the effect being more pronounced in males. This was possibly related to the hydrogen fluoride content of the test substance. All other lesions were not considered to be of toxicological importance.

Comment:

There was a significant reduction in bodyweight gain of Group 4 animals over the treatment period. This reduction was considered to be treatment related.

Differences in clinical chemistry and haematology between groups were generally small and inconsistent between males and females. Thus, they were not considered to be of toxicological importance, even when statistical significance was reached. Of the investigations performed, only an increase in the total output of urinary inorganic fluoride in females of Group 4 and in males of Groups 3 and 4 were considered to be treatment related. Post study analysis of the residual test substance revealed that between 0.2 and 0.3 ppm hydrogen fluoride was present in the test substance. This was considered likely to have contributed to the increased output of urinary fluoride, and may have contributed to

the dental fluorosis. An indication of hydrolysis at pH 7 may additionally have contributed to the phenomenon.

Result:

Based on increased urinary fluoride levels at 50 486 ppm, the no observed adverse effect level (NOAEL) was determined to be 24 747 ppm (150 mg/L).

9.3 Genotoxicity

9.3.1 Salmonella typhimurium Reverse Mutation Assay (Pharmaco LSR Ltd, 1998)

Strains: Preliminary toxicity tests: TA 98

Main test: TA 98, TA 100, TA 1535, TA 1537

Metabolic activation: The main test was conducted both with and without

activation from rat liver (S-9) mix.

Concentration range:

Preliminary toxicity test 1: Vapour concentrations of 10, 20, 30, 40, 50, 60 and 70% v/v (nominal) for an exposure period of 48 hours.

Preliminary toxicity test 2: Vapour concentrations of 0.1, 0.5, 1.0, 2.5, 5.0 and 7.5% v/v (nominal) for an exposure period of 48 hours.

Main test: Vapour concentrations of 0.5, 1.0, 2.5, 5.0 and 7.5% v/v (nominal) for an exposure period of 48 hours. Each test in each strain was conducted twice.

Test method: OECD TG 471

Comment:

Revertant colonies did not develop in preliminary toxicity test 1 and were observed at concentrations less than 10% v/v in preliminary toxicity test 2. Their numbers were reduced at 7.5% so this was chosen as the top exposure level in the main test.

No increase in revertant colonies was obtained in any of the strains tested either with or without metabolic activation. At 7.5% v/v all strains showed slight toxicity.

Positive control substances induced marked increases in the number of revertant colonies.

Result: The notified chemical was not mutagenic under the

conditions of the test.

9.3.2 Micronucleus Assay in the Bone Marrow Cells of the Mouse (HLS, 1999)

Species/strain: Mouse/Specific Pathogen Free CD-1

Number and sex of animals: 5/sex/group

Method of administration: The treatment groups received a single, 6 hour, whole body

inhalation exposure to the test substance (vapour). The

concurrent negative control group received clean air only, while the concurrent positive control group received mitomycin C by gavage.

Doses:

Doses received are shown in the table below:

Treament	Exposure level ^a	Kill time after dosing
Negative control: air	-	24 or 48 hours
Notified chemical	20 000 ppm 50 000 ^b ppm	24 hours 24 or 48 hours
Positive control: mitomycin C	12 mg/kg bodyweight	24 hours

^aNominal dose levels only. Mean achieved levels were 19 178 and 48 868 ppm

Test method:

OECD TG 474; EC Method B12

Clinical observations:

Most animals in the high dose group were motionless with their eyes shut after 30 minutes exposure to the test substance. Those moving had an unsteady gait. At 90 minutes and thereafter until the end of the exposure period, a decrease in respiratory rate was also observed.

No adverse clinical signs were observed after the completion of the exposure period in high dose animals, or for the duration of the test in control and low dose animals.

Mortality:

Post mortem examination indicated that the death of one female treated with Mitomycin C might have been due to mis-dosage.

Micronuclei score:

At least 1000 erythrocytes were scored for each animal. There was no statistically significant increase in the number of micronucleated immature erythrocytes due to the test substance at either the 24-hour or 48-hour sampling times (P>0.01), nor did the test substance cause any substantial increases in the incidence of micronucleated mature erythrocytes. Bone marrow toxicity was not observed - there were no significant decreases in the proportion of immature erythrocytes due to the test substance.

The positive control Mitomycin C caused highly significant increases in the frequency of micronucleated immature erythrocytes (P<0.001), and statistically significant decreases in the proportion of immature erythrocytes (P<0.001).

Result:

The notified chemical was not clastogenic under the conditions of the test.

^bMaximum practical exposure level

9.4 Overall Assessment of Toxicological Data

The notified chemical is of low acute oral toxicity (LD_{50} > 2 000 mg/kg) in rats. At high concentrations acute inhalatory exposure of rats induced adverse effects on the respiratory system (reduced respiratory rate and pulmonary damage), growth retardation and slight effects on liver and lung weights, with mortality observed at 200 000 ppm and upwards. The LC50 was established at greater than 100 000 ppm (607 mg/L). The notified chemical is not a skin irritant in rabbits, and did not cause delayed contact hypersensitivity in guinea pigs in a maximisation skin sensitisation study. The notified chemical was observed to be slightly irritating to the eyes of rabbits. No reports on acute dermal toxicity were provided.

Two repeat dose inhalation studies in rats were provided. The upper limit for the dose range in subchronic inhalation toxicity studies was determined to be 50 000 ppm from the range-finding 14-day study. The NOAEL from the 28-day study was determined to be 24 747 ppm (150 mg/L) based on increased urinary fluoride levels at the top dose (50 486 ppm). Lesions of the incisor teeth were also observed in animals at the top dose.

The notified chemical was not mutagenic in a reverse mutation assay in bacteria, and not clastogenic in an *in vivo* mouse micronucleus study.

Hazard Classification

Based on the data provided, the notified chemical is not classified as a hazardous substance under the NOHSC Approved Criteria for Classifying Hazardous Substances (NOHSC, 1999).

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

10.1 Toxic Effects on Aquatic Organisms

Although very little of the compound will be released to water the notifier provided test reports on the toxicity of the notified chemical to fish, *Daphnia* and algae.

Test	Species	Results
96 h Acute Toxicity	Zebra fish	LC ₅₀ not determined
OECD TG 203	• Brachydanio rerio	NOEC = 150 mg/L
48 h Acute Toxicity	• Daphnia magna	LC ₅₀ not determined
OECD TG 202 (part 1)		NOEC = 100 mg/L
72 h Algal Growth	Selenastrum capricornutum	E _b C ₅₀ and E _r C ₅₀ not determined
Inhibition		$NOEC_b = 13.2 \text{ mg/L}$
OECD TG 201		

^{*} NOEC - no observable effect concentration

The tests on fish (Solvay Pharmaceuticals 1998b) were performed using a static methodology in a closed system. Observations were performed at 0, 3, 24, 48, 72 and 96 hours. The test was performed using seven specimen fish per test concentration at a temperature of 23 °C. The tests were conducted using nominal concentrations of 100, 150 and 200 mg/L. The

results of the definitive study showed that no mortalities or sub-lethal effects were observed in any of the test vessels containing less than 150 mg/L of the notified chemical after 96 h. After 96 h, 50% immobility was observed at a test concentration of 200 mg/L. Analysis of the test solutions after 96 h showed the concentration of the notified chemical at the nominal concentrations of 100, 150 and 200 mg/L to be 95, 126 and 153 mg/L, respectively. The 96-hour NOEC for the notified chemical as calculated by Fisher's Exact Test to *Brachydanio rerio* is therefore 150 mg/L.

The immobilisation tests with *Daphnia* (Solvay Pharmaceuticals 1998c) were also performed under static conditions in a closed system with observations performed at 24 and 48 hours. The test was performed using 10 daphnids per flask at a temperature of 20 °C. The tests were conducted using nominal concentrations of 100, 150 and 200 mg/L. After 48 h, no immobilised daphnids were observed in the test vessels with less than 100 mg/L of the notified chemical and 7 and 13% immobility was observed after 48 h at test concentrations of 150 and 200 mg/L, respectively. Analysis of the test solutions after 48 h showed the concentration of the notified chemical at the nominal concentrations of 100, 150 and 200 mg/L to be 93, 132 and 185 mg/L, respectively. No 48-hour EC₅₀ for the notified chemical to *Daphnia magna* could be calculated. The 48-hour NOEC for the notified chemical as calculated by Fisher's Exact Test to *Daphnia magna* is 100 mg/L.

Algae were exposed to the test substance in a closed system at concentrations of 3, 10, 30, 100 and 300 mg/L for 72 h at 24°C under constant illumination and shaking (Solvay Pharmaceuticals 1998d). Analysis of the test solutions after 72 h showed the concentration of the notified chemical at the nominal concentrations of 3, 10, 30, 100 and 300 mg/L to be 1.58, 3.5, 8.9, 26.4 and 81.1 mg/L, respectively After 72 h, the percentage inhibition of biomass for the test vessels containing 3, 10, 30, 100 and 300 mg/L of the notified chemical was 3.1, 2.2, 3.8 7.9 and 13.8%, respectively, and the percentage inhibition of growth rate was 1.8, 0.5, 1.0, 2.0 and 5.0%, respectively. The 72 h E_bC₅₀ and E_rC₅₀ for the notified chemical to *Selenastrum capricornutum* could not be calculated. The NOEC based on the biomass intergral and determined with Williams' Test is 13.2 mg/L.

The ecotoxicity data indicates the notified chemical is practically non-toxic to fish, daphnia and algae. Furthermore, the notified chemical's volatility suggests that the notified gas will not remain dissolved in water bodies under normal atmospheric pressures and in temperature ranges found in Australian aquatic environments.

10.2 Ozone Depletion Potential

The ozone depletion potential (ODP) of a gaseous compound is a measure of its ability to migrate to the stratosphere, together with its ability to degrade (through direct and indirect photolysis) to radical species which are able to react with and destroy ozone molecules. The most damaging chemicals in this regard are compounds which contain chlorine and/or bromine, and this has been a characteristic of various chlorinated hydrocarbons (CFCs) and hydrochlorofluorocarbon (HCFCs) compounds which have been used as foam blowing agents in the past. The ODP of such compounds is roughly related to the content of chlorine (or bromine) in the compounds together with its atmospheric lifetime (Verschueren, 1996). Although the atmospheric lifetime of the notified chemical is appreciable at 10.8 years, since

it contains no chlorine or bromine¹, it is expected to have zero or very low ODP.

The new compound is intended as a replacement for blowing agents such as HCFC-141b (CH₃CFCl₂) which contains chlorine and has an ODP of 0.1 compared with the reference compound trichlorofluoromethane (CFC-11, Verschueren, 1996). Consequently, the introduction of the new compound as a replacement blowing agent is expected to be beneficial in respect of stratospheric ozone destruction.

10.3 Global Warming Potential

The Global Warming Potential (GWP) of a gaseous compound is a composite measure of its ability to absorb radiation in the infrared (IR) spectral region (typically 500-1200 cm⁻¹), together with its expected atmospheric lifetime (Verschueren, 1996). Effectively the GWP of a chemical compares the amount of IR radiation absorbed by unit weight (eg 1 tonne) of the chemical over a given time (taking into account its removal through degradation processes) with that absorbed by an equivalent weight of emitted CO₂. Because of atmospheric degradation of compounds (eg through reaction with OH• radicals) the GWP decreases with time, and it is usual to estimate the GWP using 20, 100 and 500 year horizons. By determining the IR absorption cross section from the measured IR spectrum of the notified chemical between 600 and 1500 cm⁻¹ together with an estimation of the atmospheric half life, 20, 100 and 500 year global warming potentials for the notified chemical were derived as 2210, 790 and 250 compared with CO₂, respectively. However, the International Committee on Climate Change has revised these values indicating the 20, 100 and 500 year global warming potentials for the notified chemical are 2600, 890 and 280 compared with CO₂, respectively.

Although these GWP figures are subject to some uncertainty they may nevertheless be used to gain some insight into the effects of using the chemical in Australia. In the worst case, assuming that 20 tonnes of the notified chemical is used and released to the atmosphere each year in Australia, when averaged over a 100 year period this is roughly equivalent to releasing $20 \times 890 = 17800$ tonnes of CO_2 . This calculation could obviously be refined, but this CO_2 emission equivalent is relatively small compared with Australia's overall annual greenhouse gas emissions which were estimated as approximately 460 million tonnes of CO_2 equivalent in 1999 (Australian Greenhouse Office, 2001). So the use of 20 tonnes per annum of the notified chemical would represent an annual increase of approximately 0.004% to consolidated emissions over 100 years.

However, it should be noted that as a blowing agent, the notified chemical will be used as a replacement for other compounds such as hydrochlorofluorocarbons (HCFCs) including HCFC-141b (CH₃CFCl₂) which themselves have significant GWP in addition to ozone depleting potential by virtue of the contained chlorine (see above). If it is assumed that the notified chemical is to replace HCFC-141b on a mole for mole basis, then 20 tonnes would replace approximately 20 tonnes of HCFC-141b. The 100 year horizon GWP of HCFC-141b is 700 (WMO, 1999) so replacement by the notified chemical would increase greenhouse gas emissions by approximately 6740 tonnes release of CO₂ equivalent. Consequently, the net release of additional CO₂ equivalent resulting from introduction of notified chemical as a blowing agent represents an increase of 0.002% in Australia's total greenhouse gas

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¹ Although fluorine is a halide and is in many ways chemically similar to chlorine and bromine, the ozone depletion potential of fluorine in the stratosphere is accepted as being negligible.

emissions.

However, HCFC-141b is not currently considered in the National Greenhouse Gas Inventory (NGGI)², and so the full 17800 tonnes of CO₂ equivalent originating from release of the notified chemical will be included in the NGGI. As the emissions of the notified chemical are not replacing an existing greenhouse gas, they equate to approximately 0.06% of Australia's permitted increase in emissions under the Kyoto Protocol.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The new compound is a volatile liquid and its use pattern as a blowing agent for production of polyurethane foams indicates that it will be released mainly to the atmosphere, although diffusion from the polymer foam may be extended over several years.

Only minor releases to the water and soil compartments are expected, and due to the high values of vapour pressure and Henry's Law constant any compound released to water or soil is expected to quickly evaporate to the atmosphere. Consequently exposure to aquatic organisms will be low, but in any case, the available test data indicates that the compound is of low toxicity to aquatic species, and would also have little potential for bioaccumulation.

The compound will slowly degrade in the atmosphere through reaction with hydroxy radicals, and will eventually degrade to HF and CO₂. However, due to its relatively long anticipated atmospheric half life (estimated in the literature as 10.8 years), together with its large infrared cross section, the most environmentally significant effect resulting from use of the compound will be its contribution to global warming. On a 100 year horizon basis, use of the compound as a foam blowing agent at the indicated import quantities are estimated to annually add around 17800 tonnes of CO₂ equivalent to Australia's greenhouse gas emission inventory, which (based on 1999 data) represents a contribution of approximately 0.004% to Australia's total greenhouse gas emissions. However, when it is considered that the new compound will replace HCFC-141b as a blowing agent, and that this compound also has significant global warming potential, the net additional annual release of CO₂ equivalents will only increase 0.002%. However, HCFC-141b is not currently considered in the National Greenhouse Gas Inventory (NGGI)³, and so the full 17800 tonnes of CO₂ equivalent originating from release of the notified chemical will be included in the NGGI. As the emissions of the notified chemical are not replacing an existing greenhouse gas, they equate to approximately 0.06% of Australia's permitted increase in emissions under the Kyoto Protocol..

Due to the absence of chlorine and bromine in the chemical, it is not expected to have potential for removing ozone from the stratosphere, and this represents a definite environmental advantage over blowing agents such as HCFC-141b for which the new chemical is intended as a replacement.

When used in the indicated manner in the production of polymer foams the new compound is

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² Because the hydrochlorofluorocarbons such as HCFC-141b are ozone depleting substances and regulated under the Ozone Protection Act 1989, they are not considered in Australia's greenhouse gas inventory, despite the fact that these compounds have global warming potential in addition to their ozone destroying properties.

³ Because the hydrochlorofluorocarbons such as HCFC-141b are ozone depleting substances and regulated under the Ozone Protection Act 1989, they are not considered in Australia's greenhouse gas inventory, despite the fact that these compounds have global warming potential in addition to their ozone destroying properties.

not expected to be a hazard to the aquatic or soil environmental compartments, but will increase Australia's greenhouse gas emissions.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Hazard assessment

The notified chemical is a volatile liquid and highly flammable. It is a Class 3 dangerous good (National Road Transport Commission, 1998). It may decompose at high temperatures to liberate hydrogen fluoride.

The notified chemical is of low acute toxicity. It is a slight eye irritant in rabbits but not a skin irritant. It is not a skin sensitiser in guinea-pigs. In a 28-day repeated dose inhalation study in rats, the NOAEL for the notified chemical was 24747 ppm (150 mg/L), based on increased urinary fluoride levels at the highest dose. The notified chemical is not classified as a hazardous substance in accordance with the NOHSC Approved Criteria for Classifying Hazardous Substances (NOHSC, 1999).

Occupational health and safety

The notified chemical is used as a blowing agent in polyurethane foams. It is firstly blended in a closed system with other additives to manufacture the polyol blend, which is then blended with isocyanate resin for foam production. These processes are largely enclosed, with occupational exposure confined to scenarios such as product transfer, vessel cleaning and spill cleanup. Local exhaust ventilation is employed in production areas and low pressures are utilised to minimise foam splashing. Incidental exposure may arise during laboratory testing and cleaning and maintenance of blending vessels and foam machinery. The notified chemical is highly flammable so all ignition sources must be avoided. There is a risk of eye irritant effects when handling the notified chemical so eye protection is required.

Once the foam is produced, the risk of eye irritation is low as the notified chemical is largely trapped within the closed cell nature of the foam matrix.

Conclusion

The risk of adverse health effects arising from exposure to the notified chemical is low. There is a high fire risk so precautions are required when handling the chemical.

Public Health

Refrigerant products eg. fridges and eskies, containing polyurethane foam insulating material with 1-7.5% of the notified chemical will be sold onto the domestic market. Once trapped within the final foam, the notified chemical is unavailable for release. Also, the foam used in the manufacture of domestic products is sealed. Consequently, there will be no public contact with the notified chemical during normal use of domestic refrigerant products. The public hazard therefore, from exposure to the notified polymer through all phases of its life-cycle is considered to be negligible, except in the event of an accidental spill. Based on the above information, it is considered that the notified chemical will not pose a significant hazard to public health when used in the proposed manner.

13. RECOMMENDATIONS

Regulatory controls

- The NOHSC Chemicals Standards Sub-committee should consider the following physico-chemical hazard classification for the notified chemical:
 - R11 Highly flammable
 - S16 Keep away from sources of ignition No smoking
- The notified chemical should be classified as follows under the ADG Code:
 - Class 3 Packaging Group II
- Suppliers should label the notified chemical as a Class 3 dangerous good with the signal words Flammable Liquid and the risk and safety phrases listed above.
- Due to the global warming potential of the notified chemical and the expected substantial releases to the atmosphere, the notifier should report annual data on import quantities to the Australian Greenhouse Office.

Control Measures

Occupational Health and Safety

- Employers should implement the following engineering controls to minimise occupational exposure to the notified chemical:
 - Enclosure of processes as much as possible; otherwise local exhaust ventilation required
- Employers should implement the following safe work practices during handling of the notified chemical:
 - Use sparkproof tools and machinery
 - Keep away from heat and ignition sources
- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical:
 - Overalls, neoprene gloves and goggles/safety glasses
 - Respiratory equipment in confined spaces

Guidance in selection of personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

• A copy of the MSDS should be easily accessible to employees.

If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999), workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Storage

• The notified chemical must be stored away from heat and ignition sources.

Disposal

• Industrial waste containing the notified chemical should be sent to an industrial incinerator equipped with a hydrogen fluoride neutraliser.

Secondary notification

The Director of Chemicals Notification and Assessment must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under subsection 64(1) of the Act; if

 The notified chemical is to be used in substantial quantities in more open systems such as use as a solvent, or

(2) Under subsection 64(2) of the Act:

- if any of the circumstances listed in the subsection arise.

The Director will then decide whether secondary notification is required.

14. MATERIAL SAFETY DATA SHEET

The MSDS for the notified chemical was provided in a format consistent with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC 1994).

This MSDS was provided by the applicant as part of the notification statement. It is reproduced here as a matter of public record. The accuracy of this information remains the responsibility of the applicant.

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