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May 1999

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

HFC 10-43 mee

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

HFC 43-10mee

1. APPLICANT

Du Pont (Australia) Ltd of 49-59 Newton Road WETHERILL PARK NSW 2164 has submitted a standard notification statement in support of their application for an assessment certificate for HFC 43-10mee.

2. IDENTITY OF THE CHEMICAL

Chemical Name: pentane, 1,1,1,2,2,3,4,5,5,5-decafluoro

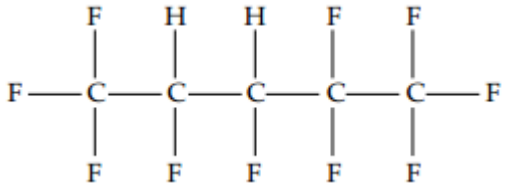
Chemical Abstracts Service (CAS) Registry No.: 138495-42-8

Other Names: HFC 43-10mee

Trade Name: Vertrel XF

Molecular Formula: $C_5H_2F_{10}$

Structural Formula:



Molecular Weight: 252

Method of Detection and Determination: Gas chromatography, Infra-Red spectroscopy

Spectral Data: peaks by Fourier Transfer IR Spectroscopy: (exempt information)

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C, 101.3 kPa:	colourless liquid
Melting point:	- 83.7°C
Boiling Point:	55°C
Specific Gravity:	1.58 g/cm^3
Viscosity:	0.67 cps
Vapour Pressure:	2.48 x 10^4 Pa at 20°C, 3.13 x 10^4 Pa at 25°C (moderate to high)
Water Solubility:	140 mg/L at 25°C (low)
Partition Co-efficient (n-octanol/water):	log P_{ow} = 2.70
Hydrolysis as a Function of pH:	not determined (see comments below)
Adsorption/Desorption:	not determined (see comments below)
Dissociation Constant:	no dissociation observed
Flash Point:	none observed up to 71°C (see comments below)
Flammability Limits:	not flammable in air
Autoignition Temperature:	not applicable
Reactivity/Stability:	thermally stable to 300°C, does not oxidise or degrade
Surface tension:	66.7 mN/m for 120 ppm aqueous solution
Ozone Depleting Potential (ODP):	0
Global Warming Potential (GWP):	1300 (100 year ITH[1])

[1] Integrated Time Horizon.

Atmospheric Lifetime: 17.1 years

Tests were performed according to EEC/OECD test guidelines at facilities complying with OECD Principles of Good Laboratory Practice.

Hydrolysis is not expected to be a significant degradation pathway as the chemical contains no groups which are generally considered to be hydrolysable. This is confirmed by modelling undertaken by the notifier which estimates the hydrolytic half lives at pH 7 and 8 to be 2.4 x 10^5 and 2.4 x 10^4 years, respectively (Gannon JT 1998).

The adsorption/desorption behaviour of HFC 43-10mee has not been investigated. The notifier has justified this omission on the basis of Mackay modelling (see Section 8.2, Environmental Fate) which indicates that almost none of the chemical is expected to partition to the soil compartment. Due to the volatility and water solubility of the chemical, little would be expected to partition to the soil. However, estimation of the log K_{OC} using the US EPA ASTER program (US EPA 1998) gave a value of 2.63, indicating that the chemical would be expected to bind moderately to soils.

Due to its low boiling point, HFC 43-10mee was only tested up to 71°C in the standard EC flash point test.

4. PURITY OF THE CHEMICAL

Degree of Purity: > 98% (isomer ratio not provided)

Toxic or Hazardous Impurities: none known

Non-hazardous Impurities (> 1% by weight): each below 1%

Additives/Adjuvants: none

5. USE, VOLUME AND FORMULATION

The notified chemical will not be manufactured or reformulated in Australia but will be imported in 20 L drums made of mild steel. The notifier estimates that less than 20 tonnes per year of the notified chemical will be imported in the first two years and less than 10 tonnes per year in the next three years.

The notified chemical will be used as a solvent degreaser to remove process lubricants and sub

micron particles from metal surfaces prior to further processing and soldering flux and ionic contamination from high reliability long life military electronics. The notified chemical is designed to be used in closed systems (vapour degreasers).

The notified chemical is currently in use at two sites in Australia under a NICNAS commercial evaluation permit granted under section 21G of the Act. Its use may extend to a further 3 or 4 sites in the future.

6. OCCUPATIONAL EXPOSURE

HFC 43-10mee is a volatile liquid at room temperature. Inhalation of HFC 43-10mee may occur through exposure to vapours emitted from liquid or by exposure to aerosols. Activities such as heating or agitation of the liquid will increase the emission of vapours and the likelihood of exposure. Skin contact with the notified chemical may also occur during handling of the liquid.

Guidance material for the safe handling of the notified chemical was provided by the notifier, namely *Safe Handling of Vertrel Cleaning Agents* (DuPont 1996) and *Vertrel Cleaning Agents – Recommended Work Practices* (DuPont 1996).

Transport and Storage

It is expected that drums of the notified chemical will be delivered directly to customers without being opened. Therefore, exposure to the notified chemical is unlikely during transportation unless leakage occurs from the drums.

Repacking

In the event of repacking into smaller containers, exposure to the notified chemical by inhalation and skin contact could occur during transfer of the chemical and during any spillage. The guidance material provided by the notifier indicates that gloves, goggles and safety footwear are to be worn when handling drums, with the addition of an impervious apron when handling open drums.

Solvent Degreasing

The notified chemical will be contained within commercially built vapour degreasers incorporating vapour and safety controls which comply with the Association of Fluorocarbon Consumers and Manufacturers (AFCAM) *Code of Practice for the Minimisation of Chlorofluorocarbon (CFC) Emissions from Degreasing/Cleaning Plants Using CFC 113 Solvents* (AFCAM Code of Practice) (AFCAM 1990) and the prescribed requirements for the safe operation of vapour degreasing plant described in AS 2661 (Standards Australia 1983). The work area is ventilated in accordance with AS 1668.2 (Standards Australia 1994).

Between 7 to 10 workers are involved in degreasing tasks at each site where the notified

chemical is currently in use under the commercial evaluation permit.

The cleaning operation involves workers placing the workpieces[2] to be cleaned into baskets. This activity is carried out in a room away from the degreaser. Upon operator command, an automatic conveyor transports the baskets for loading into the degreaser. A wash cycle typically takes 15 to 20 minutes to complete. At one site, from 20 to 30 wash cycles occur per day with a washload of 5 to 10 kg per wash. The solvent capacity of the bath at this site is 100 kg. At the second site, there are 5 to 10 wash cycles with a washload of 2 to 5 kg. During the wash cycle, exposure to the notified chemical is not expected under normal conditions as the lid of the tank remains sealed and operator attendance is not required. Losses of the notified chemical to the workplace atmosphere from the tank and consequently potential for inhalation exposure can occur from the freeboard zone[3] and vapour zone[4] as the lid is opened, and from drag-out[5]. Losses can also occur from leaks in pump seals, valves and pipe joints. The notifier states that infrequent, short-term (less than one minute) operator exposure to vapours (> 5 ppm) may occur during the loading and unloading of baskets into and from the degreaser tank. Skin contact with liquid HFC 43-10mee may occur during handling of degreased workpieces containing trapped solvent in pockets and recesses.

Replenishment, Cleaning and Maintenance

Degreasers are replenished with fresh solvent as required, with an expected monthly top up of 10 to 15% of the bath volume if the bath is continually heated and operating. Fresh solvent is pumped from closed head containers to below the existing liquid level in the tank, via a filling port. During clean-out of the degreaser (removal of sludge and contaminated solvent from the sump[6]), the sump contents are pumped into high density polyethylene containers and sent for recycling. Exposure to vapours and drips and spills may occur during refilling and clean-out.

For maintenance purposes, the notifier states that the equipment can be completely emptied with no opportunity for exposure to the notified chemical.

Solvent Reclamation

The notifier indicates that solvent recycling by distillation will be undertaken by Du Pont (Australia) Limited. The notifier was not able to provide any details of occupational exposure during recycling, as recycling to date has only been trialled on a small scale and under laboratory conditions. The notifier has indicated however, that solvents will be reclaimed and recycled in accordance with the AFCAM Code of Practice (AFCAM 1990).

[2] Workpiece - the object, in this case metal item or electronic device/component to be cleaned in the equipment.
[3] Freeboard zone – the space within the equipment between the vapour/air interface and the upper rim of the equipment.
[4] Vapour zone – the space within the equipment filled with saturated solvent vapour between the level of liquid solvent and the vapour/air interface.
[5] Drag out – the action of removing solvent, in liquid or vapour form, from the equipment when withdrawing the washload after processing.
[6] Sump – processing tank within the equipment containing the liquid solvent.

Atmospheric Monitoring

The notifier indicates that no atmospheric monitoring has been conducted at the two sites where the notified chemical has been in use in Australia. However, the notifier's submission contains atmospheric monitoring data (in summary form) for various activities and modes of equipment operation. The data are presented below in the following four tables.

Table 1: Vapour concentrations during charging of empty vapour degreaser

Table 2: Summary of vapour concentrations adjacent to vapour degreaser

Table 3: Vapour concentrations around area where luber[7] used

Table 4: Vapour concentrations during use of luber

The vapour concentrations in Tables 1, 3 and 4 are from area monitoring with most readings obtained from grab samples. Table 2 lists readings from short term Time Weighted Average (TWA) sampling (< 2 hours). The result of only one 8-hour TWA analysis was available (in Table 4).

Grab sampling was conducted using either a Foxboro OVA 128 portable gas chromatograph or a Foxboro Miran IB2 infra-red analyser. The TWA analyses were conducted by air sampling through charcoal tubes using constant flow air sampling pumps, followed by gas chromatographic analysis.

Table 1 - Vapour Concentrations During Charging of Empty Vapour Degreaser

Method of Charging	***Vapour concentration (ppm)[a]***
Pour from _ inch valve on 5 gal pail	26
Pump using hand piston pump (hose)	35
Pour from 1 gallon glass jug	46
Pump using electric pump	48
Pour from open _ inch bung	71
Pump using hand piston pump (no hose)	82
Pour from open beaker	94

a Instantaneous Vapour in Air Concentrations Using Foxboro OVA 128 Portable Gas Chromatograph.

[7] Note that a luber is a machine that uses a fluorocarbon (e.g. the notified chemical) and a fluorolubricant to deposit a thin film of the lubricant onto a computer hard drive disk. Although it is not envisaged that the notified chemical will be used in this way in Australia, the emissions data give some idea of the vapour concentrations that can occur during end-use. Vapour concentrations during spillage of the notified chemical are included.

Table 2 - Summary of Vapour Concentrations Adjacent to Vapour Degreaser

Sample Location	*Duration (h. min.)*	Operating Conditions	*Vapour in Air (ppm)*	
			Range	*Average*
In Front and Behind Degreaser	1 h. 35 min.	Degreaser idling with lid open	2.3 – 18.0	7.0
In Front of Degreaser (without measurements made 60 cm behind unit)	1 h. 35 min.	Degreaser idling with lid open	2.3 to 12.0	6.0
60 cm Behind Degreaser at Midpoint of Degreaser	14 min.	Degreaser idling with lid open	4.9 to 18.0	9.6
60 cm Behind Degreaser at Midpoint of Degreaser	1 h. 30 min.	Cleaned 8 basketloads of parts. Degreaser lid open at all times	1.6 to 31.0	8.4
60 cm Behind Degreaser at Midpoint of Degreaser	27 min.	Cleaned 4 basketloads of parts. Degreaser lid closed during idling	0.6 to 38.0	8.5

Table 3 - Vapour Concentrations Around Area Where Luber Used

	Vapour Concentration (ppm)
Operating Step	
Pour into luber, breathing zone	7.9
Pour into tank, 30 cm above tank	13.4, 167.5
Return to bottle, 20 cm above funnel	6.9, 7.4
Floor Spill ~ 500 mL spill	
15 cm above floor	21.7, 130.1, 37.4
20 cm above floor	27.6, 43.6
30 cm above floor	11.4, 9.6
Remove and drain tank, breathing zone	27.6
Squirt and wipe table, breathing zone	5.1, 14.2

Table 4 - Vapour Concentrations During Use of Luber

Sample Spot	*Luber Step*	*Vapour Concentration (ppm)* *High*	*Low*	*Average*
1	Closed	9.0	0.7	3.0
1	Open to Load	10.9	2.2	6.6
1	Closing with load	9.6	2.8	6.4
1	Open when finished	11.5	1.5	4.9
2	Closed	1.7	0.5	1.2
2	Open to Load	24.8	1.1	10.2
2	Closing with load	16.5	3.1	7.5
2	Open when finished	4.1	0.9	3.0
3	Closed	18.6	3.9	10.5
3	Open to Load	82.2	5.5	55.5
3	Closing with load	20.2	1.7	11.3
3	Open when finished	21.5	6.7	14.6
	8-hour TWA			4

For use of the notified chemical in vapour degreasers, grab sample results showed that vapour concentrations during charging of the degreaser ranged from 94 ppm (open pouring from a beaker) down to 26 ppm (charging via a small valve). Short-term TWA readings taken during degreaser use indicated that vapour concentrations averaged approximately 6 to 10 ppm in the vicinity of the degreaser. Most of these readings were taken with the degreaser lid open, reflecting a worst case scenario. Higher individual readings were obtained when the degreaser was being used, however, the average was similar for each location, irrespective of the number of washloads or whether the lid was open or closed.

Based on grab sampling results during luber use, high vapour concentrations can occur during spillage and pouring (up to 167.5 ppm).

7. PUBLIC EXPOSURE

The public will not make contact with the notified chemical because the items treated will be free of all traces of the chemical by the time the articles reach the public domain.

The potential for public exposure to the notified chemical during transport and industrial use or from disposal is assessed as negligible.

8. ENVIRONMENTAL EXPOSURE

8.1 Release

Under normal conditions, release of HFC 43-10mee is not expected during storage and transportation. The MSDS contains adequate instructions for handling a spill should one occur.

The major release of the chemical would be through volatilisation from vapour degreasing/cleaning plants during use and from residual solvent on washed items. The notifier states that this will be kept to a minimum through operators working in accordance with the AFCAM Code of Practice.

The notifier has indicated that for a continuously operating process with a high volume of material passing through the bath, it is expected that losses to the atmosphere would be between 10-15% per month, due to volatilisation from solvent baths, solvent residues on washed items and the solvent reclamation process. However, based on current work practices at the trial sites (baths operating 8 hours per day on 2 to 4 days a week with a low volume of work passing through the bath), the loss of chemical may be as high as 30% (corresponding to approximately 5 tonnes of chemical per annum at the maximum rate of import).

The notifier anticipates that the empty import drums will be used to return contaminated notified chemical for recycling. Residues remaining in containers is expected to be less than 0.5%. Any excess containers will be reused by the solvent recycling firm after ensuring that the drums have been cleaned and relabelled.

8.2 Fate

Given its high volatility, any HFC 43-10mee released to the environment will partition almost entirely to the atmosphere. The notifier indicated that Level I Mackay modelling predicted over 99% of HFC 43-10mee would partition to the air. This result was confirmed using a four compartment Level I Mackay calculation which indicated that at equilibrium approximately 0%, 0%, 0.01% and 99.99% will be partitioned to soil, sediment, water and air, respectively. The notifier has also determined an environmental partitioning of 0.7%, 0.7%, 51.1% and 47.5% to soil, sediment, water and air compartments, respectively using the Mackay Equilibrium Criterion (EQC) model - Level III (Gannon JT 1998). The partitioning is dependent on how the chemical is discharged to the environment and as a result will vary with the assumptions made.

Any chemical entering water would not be expected to undergo biodegradation at significant rates as degradation by activated sludge in a closed bottle test (OECD TG 301D, (Organisation for Economic Co-operation and Development 1995-1996) was minimal (28 day biological oxygen demand 4% of theoretical). The lack of biodegradability of HFC 43-10mee was confirmed by modelling provided by the notifier (Gannon JT 1998) using

the Standard Treatment Plant (STP) model (Syracuse Research Corp.). This model indicated that, if HFC 43-10mee was to enter a wastewater treatment plant, approximately 1% may adsorb to the sludge, less than 0.1% may biodegrade (in an unacclimated treatment plant) and approximately 99% may volatilise during the waste water treatment process. Biodegradability probability modelling indicated that the ultimate biodegradability of the chemical, when extrapolated to soils, sediments and wastewater sludge, was estimated to be greater than 6 months. A Henry's Law constant of 0.53 atm.m^3/mol was calculated, which indicates that the chemical would readily volatilise from water and is unlikely to repartition to water.

As noted above, the estimated atmospheric lifetime[8] is 17.1 years based on chloroform (IPCC 1996). Atmospheric oxidation modelling (Gannon JT 1998) provided by the notifier calculated a half-life of 3,138 days in air, corresponding to an atmospheric half-life of 12.4 years. Detailed atmospheric degradation pathways for HFC 43-10mee do not appear to have been elucidated. However, the expected main degradation pathway in the environment is reaction with tropospheric hydroxyl radicals, which abstract hydrogen. After the initial radical abstraction, further transformation and breakdown would be expected to lead to hydrophilic products that would be removed from the troposphere by dissolution in rain.

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Summary of the acute toxicity of HFC 10-43mee

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	LD_{50} > 5 000 mg/kg	(Karr MS 1996)
acute inhalation toxicity	rat	LC_{50} > 114.64 mg/L	(Ulrich CE 1996)
		ALC[7] > 51.64 mg/L	(Kelly DP 1993)
acute dermal toxicity	rabbit	ALD[8] > 5 000 mg/kg	(Sarver JW 1993)
skin irritation	rabbit	non-irritating	(Sarver JW 1993)
eye irritation	rabbit	non-irritating	(Sarver JW 1993)
skin sensitisation	guinea pig	non-sensitising	(Arcelin G 1996)
			(Moore GE 1995)
cardiac sensitisation	dog	no cardiac sensitisation potential	(Kenny TJ 1994)

[8] Atmospheric lifetime - the time necessary for 63% degradation; equal to half life divided by ln2 (= 0.69).
[7] ALC – approximate lethal concentration
[8] ALD – approximate lethal dose

9.1.1 Acute Oral Toxicity (Karr MS 1996)

Species/strain:	rat/Crl: CD BR
Number/sex of animals:	5/sex
Observation period:	15 days
Method of administration/dose:	5 000 mg/kg by gavage; dose volume of 3.16 mL/kg bodyweight; density of test substance 1 580 mg/mL
Test substance purity/Isomer ratio:	99.9%; 6.8% diastereomer A, 93.1% diastereomer B
Mortality:	all animals survived to termination
Clinical observations:	intermittent weight loss of up to approximately 6% of previously measured body weights were observed in some females during the study
Morphological findings:	no abnormalities detected
Test method:	limit test, according to OECD TG 401 (Organisation for Economic Co-operation and Development 1995-1996)
LD_{50}:	> 5 000 mg/kg
Result:	the notified chemical was of very low acute oral toxicity in rats

9.1.2 Acute Dermal Toxicity (Sarver JW 1993)

The purpose of this study was to determine an Approximate Lethal Dose (ALD) by skin absorption. The ALD is defined as the lowest dose of the test substance administered that caused the death of a test animal within 14 days post exposure. If two rabbits survive the maximum feasible dose of 5000 mg/kg, then the ALD will be reported to be greater than 5000 mg/kg.

Species/strain:	rabbit/New Zealand White
Number/sex of animals:	2/male
Observation period:	14 days

Method of administration/dose:	5 000 mg/kg applied to shaved, intact skin and held under occlusion for 24 hours, then excess test substance was washed away with warm water
Test substance purity/Isomer ratio:	99.9%; 6.8% diastereomer A, 93.1% diastereomer B
Mortality:	all animals survived to termination
Clinical observations/Signs:	no clinical signs of toxicity; slight erythema for one rabbit for two days following application of test substance
Morphological findings:	no abnormalities detected
Test method:	no regulatory methods/guidelines exist for this type of investigation
ALD:	> 5 000 mg/kg
Result:	the notified chemical was of very low dermal toxicity in rabbits

9.1.3.1 Acute Inhalation Toxicity (Ulrich CE 1996)

Species/strain:	rat/Crl:CD BR
Number/sex of animals:	5/sex/group
Observation period:	14 days
Method of administration/dose:	whole body exposure, for a single 4-hour exposure to the following nominal vapour concentrations: 5 000, 10 000 or 20 000 ppm; actual measured concentrations: 4 880, 10 800 and 19 400 ppm
Test substance purity/Isomer ratio:	99.7%; isomer ratio not stated
Mortality:	high dose: 5/sex; mid dose: 2/sex deaths occurred within 50 minutes of exposure
Clinical observations/Signs:	during exposure: mid and high dose: prostration,

	salivation and extremities pale in colour; low and mid dose: hyperactivity and intermittent convulsions; low dose: ataxia and intermittent convulsions; post exposure (1-hour): mid dose: hyperactivity in one female ; Day 14: no toxicologically significant clinical observations
Morphological findings:	decedents: high dose: dark red areas of lungs, dark red lung and stomach contents, haemorrhagic thymus gland, clear or red matting of external body surface; mid dose: mottled lungs, dark red lungs and red matting of external body surface; terminal kill: mid dose: dilated pelvis of the kidney and dark red lungs in one male and hair loss in one female; low dose: dark red areas of the lungs in one female
Test method:	According to OECD TG 403 (Organisation for Economic Co-operation and Development 1995-1996)
LC_{50}:	114.64 mg/L (11 100 ppm)
Result:	the notified chemical was of very low acute inhalation toxicity in rats

9.1.3.2 Inhalation Approximate Lethal Concentration (Kelly DP 1993)

The purpose of this study was to determine an inhalation Approximate Lethal Concentration (ALC) of the test substance in male rats. The ALC was defined as the lowest atmospheric concentration tested which caused the death of one or more rats on the day of exposure or within at least 14 days post exposure.

The study was conducted in two phases, an initial phase with a batch which was 99.8% pure (Batch I) and a second batch which was greater than 99.9% pure (Batch II). The purpose of the second phase was to verify the toxicity results of the first phase with a purer test sample.

Species/strain:	rat/Crl: CD BR
Number/sex of animals:	6 males/group
Observation period:	14 days

Method of administration:	the study was conducted in two phases using different batches of test substance, Batch I and Batch II; inhalation, nose-only exposure to test substance in vapour form
Dose/Study duration:	4-hour exposure to vapour concentrations of: Batch I: 5 200, 7 900, 10 200, 19 400 or 67 800 ppm; Batch II: 10 100 or 10 500 ppm
Test substance purity/Isomer ratio:	Batch I: 99.8% purity; 4.2% diastereomer A, 95.6% diastereomer B Batch II: 99.9% purity; 1.3% diastereomer A, 98.6% diastereomer B
Mortality:	Batch I: 4 at 10 200 ppm, 6 at 19 400 ppm and 5 at 67 800 ppm; Batch II: 3 at 10 100 ppm and 2 at 10 500 ppm
Clinical observations/Signs:	all test doses: surviving animals showed slight to severe weight loss one day post exposure followed by normal weight gain during the recovery period; Batch I: at 10 200 ppm clinical signs immediately after exposure were wet face, back and underbody, rapid breathing, passive behaviour and lethargy, clinical signs one day post exposure were hyper-activity, hunched posture and ruffled fur; at 67 800 ppm, the surviving animal showed hyperactivity for 8 days post exposure and hunched posture for 15 days post exposure;
Morphological findings:	no treatment related abnormalities detected
Test method:	no regulatory methods/guidelines exist for this type of investigation
ALC:	~ 103.28 mg/L (10 000 ppm) for Batch I > 51.64 mg/L (5 000 ppm) for Batch II;
Result:	the notified chemical was of very low acute inhalation toxicity in rats

9.1.4 Skin Irritation (Sarver JW 1993)

Species/strain:	rabbit/New Zealand White
Number/sex of animals:	3 (one male, two females)
Observation period:	37 days
Method of administration:	0.5 mL of test substance applied to a shaved site of the back and held under semi-occlusive dressing for 4-hours; following removal of the dressing, the test area was washed with soap, dried and re-wrapped for 20-hours; the test sites were examined for evidence of irritation at 1, 24, 48 and 72 hours after removal of the dressing
Test substance purity/ Isomer ratio:	97.6%; 2.3% diastereomer A, 97.6% diastereomer B
Test method:	according to OECD TG 404 (Organisation for Economic Co-operation and Development 1995-1996)
Comment:	no dermal irritation was observed in any rabbit one hour after patch removal; after 24 hours, the male rabbit exhibited slight erythema which cleared by 48 hours; no other dermal irritation was observed throughout the study
Result:	the notified chemical was non irritating to the skin of rabbits

9.1.5 Eye Irritation (Sarver JW 1993)

Species/strain:	rabbit/New Zealand White
Number/sex of animals:	3 females
Observation period:	3 days
Method of administration:	0.1 mL of test substance instilled into the lower conjunctival sac of the right eye; the left eye served as a control; eyes were examined 1, 24, 48 and 72 hours after treatment;

Test substance purity/ Isomer ratio:	97.6%; 2.3% diastereomer A, 97.6% diastereomer B
Irrigated eyes:	eyes remained unwashed following treatment
Test method:	according to OECD TG 405 (Organisation for Economic Co-operation and Development 1995-1996)
Comment	conjunctival redness reported in the test eye of one rabbit during the first 24 hours of the test period
Result:	the notified chemical was not irritating to the eyes of rabbits

9.1.6 Sensitisation

9.1.6.1 Skin Sensitisation – Maximisation Test (Arcelin G 1996)

Species/strain:	guinea pig/Himalayan spotted
Number of animals/Sex:	20 test and 10 control/ males
Test substance purity/Isomer ratio:	99%; isomer ratio not stated
Induction procedure:	Day 1: three pairs of intradermal injections (0.1mL per site) to a clipped area of the dorsal suprascapular region as follows: test group, 1:1 (v/v) mixture of Freund's Complete Adjuvant (FCA) and physiological saline; test substance diluted to 5% with PEG 400; test substance diluted to 5% by emulsion in a 1:1 (v/v) mixture of FCA and physiological saline. negative control group, same as above, but substituting test substance with PEG 400. positive control group, 2-mercaptobenzothiazole 50% in mineral oil; Day 7: clipped and shaved suprascapular area

	pretreated with 10% dilution of sodium lauryl sulfate in paraffin oil massaged into skin with a glass rod; Day 8: filter paper saturated with test substance (neat) and placed over injection sites of test animals and held under occlusive dressing for 48 hours; control animals remain untreated; reaction sites were assessed for erythema and oedema 24 and 48 hours after removal of dressing
Challenge procedure:	Day 22: filter paper saturated with test substance (neat) and placed on the clipped and shorn left flank of each animal and held under occlusive dressing for 24 hours; application sites were assessed for erythema and oedema 24 and 48 hours after removal of dressing
Test method:	Magnusson and Kligman maximisation test according to OECD TG 406 (Organisation for Economic Co-operation and Development 1995-1996)
Comment	Day 8 induction: very slight erythema in 8 animals at the 24 hour reading; no erythema or oedema at 48 hours; Day 22 challenge: no erythema or oedema at 24 or 48 hour readings;
Result:	the notified chemical was not sensitising to the skin of guinea pigs

9.1.6.2 Skin Sensitisation - Buehler Method (Moore GE 1995)

Species/strain:	guinea pig/Hartley
Number of animals:	20 test and 10 vehicle control males; 5 positive control males
Test substance purity/ Isomer ratio:	99.9%; 6.8% diastereomer A, 93.1% diastereomer B
Induction procedure:	Day 1: 0.5 mL of test substance or control applied to a clipped area of the left flank using a HillTop Chamber and held under occlusive dental dam for 6

	hours, then the test site was wiped with deionised water; the test sites were evaluated for irritation 24 and 48 hours after test substance application; this procedure was performed once a week for three weeks; the animals were then rested for 18 days
Challenge procedure:	Day 32: a challenge application using the same procedure as above was applied the clipped right flank; the test sites were evaluated for irritation and/or signs of elicited sensitisation 24 and 48 hours after test substance application;
Test method:	modified Buehler method similar to OECD test guidelines 406 (Organisation for Economic Co-operation and Development 1995-1996)
Comment	for test substance and vehicle control no dermal irritation was observed 24 and 48 hours following the induction or challenge phases; the test substance did not induce delayed contact hypersensitivity; the positive control was a skin sensitiser in this study
Result:	the notified chemical was not sensitising to guinea pig skin following repeated exposure

9.1.6.3 Cardiac Sensitisation Potential (Kenny TJ 1994)

The purpose of this study was to investigate the potential of the notified chemical to sensitise the heart to adrenaline in Beagle dogs. Cardiac sensitisation to adrenaline is a phenomenon associated with inhalation of a number of unsubstituted and halogenated hydrocarbons (Kenny TJ 1994). After inhalation of a sensitiser, challenge with adrenaline causes cardiac arrhythmias. A positive response, or signs of test substance related cardiac sensitisation is the appearance of a burst of multifocal ventricular ectopic activity or ventricular fibrillation on an ECG recording.

Species/Strain:	dog/Beagle
Number/sex of animals:	9 males selected initially, however, only 6 animals used for test substance administration; (dogs selected were previously tested and known to give the appropriate adrenaline response following inhalation of known cardiac sensitisers)
Dose:	0, 1 000, 5 000 and 10 000 ppm; positive control: CFC-11
Purity/Isomer ratio:	99.7%; 7.73% diastereomer A, 91.94% diastereomer B
Method of administration:	each animal was tested at each dose, receiving snout only inhalation exposure to 0, 1 000, 5 000 and 10 000 ppm (only one animal was tested at 10 000 ppm) as follows: Time Event 0 min start ECG recording 2 min 1st adrenaline challenge (iv) (baseline) 7 min test substance on 12 min 2nd adrenaline challenge (iv) 17 min test substance off; animals were rested for at least 24 hours between each exposure session; positive control: 2/9 dogs gave positive responses to known cardiac sensitiser CFC-11; 6 of remaining dogs gave positive responses to various test gases (identity not stated), indicating that test system can detect cardiac sensitisers

Summary of Cardiac Response

Dog Number	*Adrenaline Dose (μg/kg)*	*Test Substance Concentration (ppm)*	*Number of Ectopic Beats: 1st Adrenaline Challenge*	*Number of Ectopic Beats: 2nd Adrenaline Challenge*	*Clinical Response*
1	12	0	0	6	N
		1 000	0	9	NAD
		5 000	9	9	CS
		10 000	0	NP	CS
2	12	0	1	1	N
		1 000	0	2	NAD
		5 000	0	0	CS
3	4	0	16	8	N
		1 000	4	6	NAD
		5 000	12	0	CS
4	2	0	2	1 (+2)	N
		1 000	12	8	NAD
		5 000	4	6	CS
5	2	0	3	16	N
		1 000	2	18	NAD
		5 000	0	0	CS
6	1	0	11	9	N
		1 000	14	24	NAD
		5 000	11	0	CS

NP not performed
N negative response
NAD no abnormalities detected
CS clinical signs, including shaking, muscular rigidity, retching, vomiting, urinary and faecal incontinence

Clinical observations: severe clinical signs, namely convulsions, were observed in the animal tested at 10 000 ppm and therefore the 2nd adrenaline dose was not administered; this test concentration was not used in subsequent animals, thus preventing the assessment of cardiac sensitisation potential at this dose

Test method: no regulatory test methods/guidelines exist for this type of investigation; the design of this study is in accordance with accepted pharmacological principles and methods (Reinhardt et al 1971)

Comment: positive responses to either CFC-11 or other gases were recorded, indicating that the test system can detect cardiac sensitisers

Result: the notified chemical did not exhibit cardiac sensitisation potential in the dog at 1 000 ppm or 5 000 ppm (10.33 or 51.64 mg/L); severe

	convulsions prevented assessment of potential at 10 000 ppm (103.28 mg/L)

9.2 Inhalation Toxicity

9.2.1 Repeated Dose Toxicity –14 day Inhalation Study (Warheit DB 1992)

Species/strain:	rat/Crl:CD BR
Number/sex of animals:	treatment phase: 10 males/dose recovery phase: 5 males from each dose group
Method of administration:	inhalation, nose only exposure to vapour form of test substance;
Test substance purity/Isomer ratio:	97.6%; 2.3% diastereomer A, 97.6% diastereomer B
Dose/Study duration:	vapour concentrations of 0, 500, 1 000 or 4 000 ppm for 6 hours/day, 5 days/week for 2 weeks (10 exposures); 5 animals from each dose group were held over for a 14 day recovery period
Mortality	all animals survived to termination
Clinical observations/signs:	all test doses: clinical signs including nasal and ocular discharges and stained fur were observed during and/or immediately following exposure; high dose: one rat had significantly decreased mean body weight through to day 5 and showed hyperactive behaviour on test days 14 – 19; low dose: significantly decreased mean body weight through to day 5 and mean body weight gain on test days 13-14;
Functional observational battery assessment	following the 8th exposure, high dose: 3 rats exhibited either no reaction or exaggerated reactions to an approach and touch stimulus; low dose: exaggerated reactions to an auditory stimulus in 3; no dose response relationship was evident for these changes;

Clinical chemistry:	all test doses: mild increase in serum sodium but not dose-related; high dose: mild increase in urine volume and mild decrease in urine osmolality; mid dose: mild decrease in urine osmolality;
Haematology:	mid and high dose: significantly decreased mean leucocyte counts due to decreased neutrophil, monocyte and lymphocyte counts; significantly decreased monocyte counts persisted during recovery period for high dose recovery animals; low dose: slightly decreased, though not significant, neutrophil and monocyte counts; the magnitude of the white blood cell alterations suggests a dose-response relationship, although the study authors regarded the changes as not toxicologically important as decreased leucocyte counts have been reported as a typical stress response in rats and mice;
Organ weight	significant increase in mean relative brain weights in all treated animals following the 14 day recovery phase, however, mean absolute brain weights similar to controls
Histopathology:	inflammation of the nasal cavity and degeneration in the epithelium of the seminiferous tubules was evident in animals of the control and treated groups during both the treatment and recovery phases; no microscopic brain lesions observed
Test method:	similar to OECD TG 412 (Organisation for Economic Co-operation and Development 1995-1996)
Result:	treatment-related effects, namely decreased leucocyte counts and increased serum sodium, were seen at all doses and persisted during the recovery period for the high dose group; decreased urine osmolality was seen at mid and high dose groups. under the conditions of the study, a NOAEL of 4000 ppm (41.31 mg/L) was established by the study authors, based on the absence of any dose-related adverse effects; the authors could not establish a NOEL, based on decreased leucocyte

counts at all doses.

9.2.2 Repeated Dose Toxicity –90 day Inhalation Study (Malley LA 1996)

This study was conducted to determine the potential subchronic toxicity and neurotoxicity from repeated inhalation exposure to the notified chemical.

Doses selected for this 90-study were based on the results of a range finding study (study not provided by notifier). In the range finding study, rats exposed whole-body to target concentrations of 5 000 and 7 000 ppm showed clinical signs, namely seizure-like behaviour, suggestive of central nervous system involvement. The clinical signs were transient and occurred during the initial stage of the dosing period as the threshold concentration in the chamber was reached, but subsided during the remainder of the dosing period. The same signs were seen at the commencement of each subsequent exposure. The lowest concentration at which seizure like behaviour was observed was at 2 800 ppm (Reinhardt CF 1993), depending on the isomer ratio in the test material (diastereomer A concentration ranged from 1.0% to 44.85%). No further details on the results of the range finding study or effect of differing isomer ratios were given.

Species/strain:	rat/Crl:CD BR
Number/sex of animals:	20/sex/group
Method of administration:	inhalation, whole body exposure to vapour form of test substance
Test substance purity/ Isomer ratio:	two drums of test substance were supplied for the study, with the batches considered to be equivalent by the study authors: <u>Batch 1:</u> 8.39% diastereomer A, 91.29% diastereomer B <u>Batch 2:</u> 8.15% diastereomer A, 91.51% diastereomer B in vapour form, the concentration of diastereomer A varied between 8.6% and 9.6% during the study
Dose/Study duration::	nominal vapour concentrations of 0, 500, 2 000 or 3 500 ppm for 6 hours/day, five days/week for 90 days (65-67 exposures); actual (mean) achieved concentrations for the 90 day period were 0, 503.3, 1981.9, and 3472.6 ppm.
Mortality	five deaths from non test substance related causes

Clinical observations:	all doses: significantly higher incidence of stained fur (red discolouration of the fur on the head, neck, ears and/or facial region) in females; control group: discolouration observed in two females; no treatment related changes in weight gain, food and water consumption;
Neurobehaviour:	the design of the chamber precluded the quantification of the number of animals which exhibited clinical signs; high dose: treatment related, abnormal behaviour (jerking/jumping, pawing the air, flinching, abnormal gait, convulsions, tremors, excessive grooming and high activity) was typically observed within the first hour of exposure as the vapour concentration increased to the target concentration; significant treatment related decrease in motor activity (it was reported by the study authors that these clinical signs also occurred in the range-finding study); mid dose: same abnormal behaviour as for high dose animals; suggestive trend towards decreased motor activity, though not significant, was observed;
Clinical chemistry:	all doses: a concentration dependent significant decrease in peroxisomal beta-oxidation activity was observed in males; significant changes as follows: high dose: progressive decrease (significant at day 90) of serum albumin, and decreased mean bilirubin in all animals, decreased creatine kinase (CK) and sorbital dehydrogenase (SDH) in males and decreased blood urea nitrogen in females; mid dose: decreased SDH in all animals, increased mean glucose and CK in males; decreased CK in females; low dose: decreased mean triglyceride, total protein and plasma fluoride in males;
Haematology:	significant changes as follows:

	high dose: day 45, increased mean cell volume in males, decrease in mean erythrocyte count in females; day 90, increased mean neutrophil count in females; low dose: decreased mean cell haemoglobin concentration in males; non-significant, group mean increase in atypical lymphocytes in treated females;
Urinalysis:	mid and high dose: increased urine fluoride; high dose: females had significantly decreased urine osmolality and increased urine volume;
Organ weights:	high dose: significant increases in the mean absolute and relative weight of the adrenal glands in males, and livers and lungs of females; low dose: the mean relative weight of the kidney was significantly increased in males;
Histopathology:	high dose: increased incidence of unilateral retinal lesions (rosettes/folds); no pathologic changes in other organs; no neuropathologic changes;
Test method:	similar to OECD guidelines (Organisation for Economic Co-operation and Development 1995-1996); see neurotoxicity section for US test guidelines
Result:	the notified chemical did not produce specific organ toxicity; based on clinical signs of neurotoxicity at 2 000 ppm (20.66 mg/L) and above, a NOAEL of 500 ppm (5.16 mg/L) was established by the study authors; based on mild changes in clinical chemistry and haematological parameters at the lowest dose, no NOEL was achieved

9.2.3 Neurotoxicity Study (Malley LA 1995)

This study was conducted subsequent to the 90-day inhalation study (see Section 9.2.2) to further study the potential for developing clinical signs of neurotoxicity during exposure to the test substance between 500 ppm and 2000 ppm. The study was conducted in three phases:

. Phase 1 was a single, 2-hour exposure, in male rats to doses in the range 1000 to 3000 ppm, incorporating an abbreviated functional observational battery (FOB) assessment;

. Phase 2 was a single 2 hour exposure to 4000 ppm. It was initiated due to unexpected mortality which occurred at 2500 ppm and 3000 ppm during Phase 1. Three hypotheses were put forward as to the cause of the deaths: contamination of the test substance; formation of a contaminant in the test chamber; and that animals died as a result of effects which occurred during the convulsive episodes; and

. Phase 3 was a 14 day study in male rats to 0 or 1000 ppm. The 1000 ppm concentration was selected because no treatment related adverse clinical signs of toxicity were observed at 1000 ppm or 1500 ppm in Phase 1. Also, if excursions occurred during use, the atmospheric concentration would be unlikely to exceed 2000 ppm. No FOB assessment was conducted during this phase.

Species/strain:	rat/Crl:CD BR
Method of administration:	inhalation, whole-body exposure to vapour
Isomer ratio:	~8 % diastereomer A, ~91 % diastereomer B

Phase I

Number/sex of animals:	30 males/group
Dose/Study duration:	1 000, 1 500, 2 500 or 3 000 ppm for a single 2 hour exposure
Mortality:	one death each at 2 500ppm and 3 000 ppm
Clinical observations/Signs:	at 2 500 and 3 000 ppm clinical signs, including abnormal gait or mobility, lethargy, tremors, circling, eye discharge, stained mouth or nose;
Neurotoxic effects:	at 2 500 and 3 000 ppm, reduction in speed of the righting reflex and convulsions

Phase II:

Dose/Study duration:	4 000 ppm for a single 2 hour exposure
Number/sex of animals:	30 males

Mortality:	none
Clinical observations/Signs:	hyperactivity in one animal
Neurotoxic effects:	not evaluated
Phase III:	
Dose/Study duration:	0 or 1 000 ppm for 6 hours/day, 5 days/week for 2 weeks (10 exposures)
Number/sex of animals:	29 males in control group, 30 males in test group
Mortality:	none
Clinical observations/Signs:	alopecia in one animal in test and control groups, stained nose in one animal of the control group
Neurotoxic effects:	rats of both groups exhibited episodes of diminished or no response to an alerting stimulus, FOB not conducted, one animal in the test group exhibited transient labored breathing; all the above findings were not considered to be treatment related;
Test method:	no regulatory methods/guidelines exist for this type of investigation
Comment:	the findings did not help elucidate the cause of deaths observed in Phase 1
Results:	toxic neurological effects were observed at 2500 ppm and 3000 ppm following a single 2-hour exposure, with no effects at 1 500 ppm (15.49 mg/L) in the 10-day repeated exposure study, no treatment-related effects were observed at 1 000 ppm (10.33 mg/L), the only dose tested

9.2.4 Comparative Neurotoxicity Study (Malley LA 1996)

To improve its effectiveness in end use applications, the notified chemical is available blended with trans-1,2-dichloroethylene (DCE) to form an azeotrope. The purpose of this study was to compare the clinical signs of toxicity elicited during an acute inhalation exposure to the notified chemical or a 50/50 blend of the notified chemical and DCE (azeotrope). The exposure

concentrations selected were based on results observed in the 90-day inhalation study (see section 9.2.2)

Species/strain:	rat/Crl:CD BR
Number/sex of animals:	24 males/dose
Method of administration:	inhalation, whole body exposure to vapour form of notified chemical or azeotrope
Dose/Study duration:	notified chemical: 0, 1 000, 2 000, 3 000, 4 000, 5 000 or 6 000 ppm; actual measured concentration: 1 100, 2 000, 3 000, 4 000, 4 900, or 5 800 ppm; azeotrope, notified chemical/DCE: actual measured concentration: 980/ 2 600, 2 000/ 4 700, 2 900/ 6 800, 4 100/ 9 400, 5 000/12 000, 5 600/13 000 ppm; single 2 hour exposure
Test substance purity:	> 99%; isomer ratio not provided
Mortality:	all animals survived to termination
Clinical signs:	notified chemical, clinical signs at 4 000, 5 000 or 6000 ppm respectively: tremors (2/24, 0/24, 0/24) biting the cage (1/24, 0/24, 3/24) head jerking (2/24, 13/24, 4/24) seizure like behaviour (0/24, 6/24, 13/24) convulsions (0/24, 7/24, 1/24) a diminished response to an alerting stimulus was observed at 4 000 ppm and 5 000 ppm; azeotrope, clinical signs at 4 000, 5 000 or 6 000 ppm respectively: abnormal posture (23/24, 24/24, 24/24) hunched over (1/24, 2/24, 1/24) tremors (5/24, 14/24, 13/24) biting the cage (0/24, 1/24, 1/24) head jerking (24/24, 24/24, 24/24) seizure like behaviour (0/24, 1/24, 1/24)

	convulsions (0/24, 1/24, 1/24) lethargy (0/24, 0/24, 24/24) salivation and foaming from the nose (0/24, 0/24, 1/24) gasping (0/24, 1/24, 0/24); a diminished response to an alerting stimulus was observed at 4 000, 5 000 and 6 000ppm
Test method:	no regulatory methods/guidelines exist for this type of investigation
Result:	clinical signs of neurotoxicity were observed at 4000 ppm and above both for the notified chemical and azeotrope, but not at 3000 ppm (30.98 mg/L for notified chemical); compared to the notified chemical, the blend increased the variety of clinical signs observed (abnormal posture, hunched over, lethargy) and substantially increased the incidence of tremors and head jerking but there were no differences in the incidence of convulsions or seizure like behaviour between the notified chemical and the azeotrope

9.2.5 Developmental Toxicity (Murray SM 1994)

Species/strain:	rat/Crl:CD BR
Number/sex of animals:	25/females/group
Method of administration:	inhalation, whole body exposure to vapour form of test substance
Dose/Study duration:	nominal vapour concentrations of 0, 500, 2 000 or 3 500 ppm for 6 hours/day, from days 7 to 16 of gestation; actual measured (mean) concentration: 0, 501.8, 1940.3 and 3475.5 ppm
Test substance purity/ Isomer ratio:	99.7%; 8.39% diastereomer A, 91.29 % diastereomer B

Maternal in-life findings	mid and high dose: all animals survived to termination (day 22); significant dose related decreases in mean maternal body weight, reduced food consumption, increased perinasal staining, abnormal behaviour (convulsions, jerking, pawing the air, tremors and involuntary muscle reflexes) were observed in mid and high dose animals
Reproductive effects:	no treatment related effects on reproductive parameters were detected
Foetal findings:	high dose: mean foetal weight significantly reduced; there were no dead foetuses and no treatment related effects on the incidence of foetal variations or malformations
Test method:	similar to OECD TG 414 (Organisation for Economic Co-operation and Development 1995-1996)
Result:	based on clinical signs of neurotoxicity in dams at 2 000 ppm and above, the NOAEL for maternal toxicity was 500 ppm (5.16 mg/L); based on reduced bodyweight in foetuses at 3 500 ppm, the NOAEL for developmental toxicity was 2 000 ppm (20.66 mg/L); there was no evidence of teratogenicity in the study.

9.3 Genotoxicity

9.3.1 Reverse Mutation Assay with *Salmonella typhimurium* and *Escherichia coli* (Reynolds VL 1994)

Strains:	*S. typhimurium* TA 100, TA 1535, TA 97 and TA98; *E. coli* WP2uvr (pkM101)
Concentration range:	0 – 5 000 µg/plate
Test substance purity/ Isomer ratio:	99.68% 8.39% diastereomer A 91.29% diastereomer B
Metabolic activation system:	liver S9 fraction from rats pretreated with Aroclor 1254

Test method:	similar to OECD test guideline 471 (Organisation for Economic Co-operation and Development 1995-1996)
Result:	the notified chemical was not considered mutagenic to the bacterial strains tested with or without metabolic activation

9.3.2 Micronucleus Assay in the Bone Marrow Cells of the Rat (Gerber KM 1994)

Species/strain:	rat/Crl:CD BR
Number and sex of animals:	5/sex/control, low and mid dose groups; 6/sex/high dose group; 5/sex/positive control group
Doses:	nominal concentration: 0 2 000, 3 500 or 7 000 ppm for 6 hours/day for two consecutive days; actual (mean) measured concentration: Day 1: 0, 1986.9, 3 292.5, and 7125.2 ppm; Day 2: 0, 2 008.2, 3574.9 and 6983.7 ppm positive control: cyclophosphamide 25 mg/kg via intraperitoneal administration
Test substance purity/ Isomer ratio:	99.68%; 8.39% diastereomer A, 91.29% diastereomer B
Method of administration:	inhalation whole body exposure to test substance vapour; intraperitoneal injection of positive control
Metabolic activation system:	liver S9 fraction from rats pretreated with Aroclor 1254
Sampling schedule:	test groups were sacrificed either 24 or 48 hours after the second exposure; positive control group sacrificed 24 hours after the second exposure
Clinical observations:	Day 1: during exposure, mid dose – prostrate posture, lethargy, and convulsions which were more frequent during the first hour of exposure,

	high dose, same as for mid dose, and also piloerection, salivation and barrel rolling; post exposure high dose – hyperactivity and stained fur; Day 2: during exposure, low and mid dose –lethargy; high dose, same as for Day 1 high dose above, post exposure high dose – stained and/or ruffled fur;
Cytogenetic analysis:	no significant increase in micronucleated polychromatic erythrocytes (PCEs) or decrease in PCEs due to treatment with test substance at either sampling time; the positive control caused a significant increase in micronucleated PCEs
Test method:	similar to OECD TG 474 (Organisation for Economic Co-operation and Development 1995-1996)
Result:	the notified chemical did not induce a significant increase in micronucleated PCEs in bone marrow cells of the rat *in vivo*

9.3.3 Chromosomal Aberrations in Human Lymphocytes *In Vitro* (Gerber KM 1995)

Cells:	human lymphocytes freshly isolated from male and female donors
Doses:	test substance: 0, 2, 3, 4 and 5 mg/mL positive controls: mitomycin C 0.35 µg/mL (for cells treated with metabolic activation); cyclo-phosphamide 10 µg/mL (for cells treated without metabolic activation)
Purity of test substance:	99.9%; isomer ratio not provided
Metabolic activation system:	liver S9 fraction from rats pretreated with Aroclor 1254
Treatment regime:	cells stimulated to divide *in vitro* with phyto-haemagglutinin; test substance or positive controls added to cell cultures for 3 hour incubation with or without metabolic exogenous activation system;

	colcemid added 22 hours later to arrest cells in metaphase;
Test method:	similar to OECD TG 473 (Organisation for Economic Co-operation and Development 1995-1996)
Result:	the notified chemical did not induce a significant increase in chromosomal aberrations in human lymphocytes *in vitro* with or without metabolic activation

9.3.4 Induction of Germ Cell Damage

Claims were made and accepted for variation of the Schedule data requirements for this end point. The notifier stated that the test was not conducted on the basis that germ cell damage is improbable in light of:

. no significant mutagenic activity *in vitro* or *in vivo*,

. the atypical structure of the notified chemical compared to materials found to cause base-pair disruption in chromatin, and

. lack of evidence of teratogenicity in the developmental toxicity test (see Section 9.2.5).

9.4 Overall Assessment of Toxicological Data

Acute toxicity
The notified chemical has low acute toxicity. No mortality was observed in rats receiving a single oral dose: the LD_{50} is >5 000 mg/kg. The acute inhalation toxicity is low, with a 4-hour LC_{50} value of 114.6 mg/L (11 100 ppm) in rats, however, a severe treatment-related effect, namely, haemorrhage of the lung, was observed at all doses (5000 ppm and above). In a separate inhalation study with two batches of the notified chemical containing differing levels of diastereomer A, the approximate lethal concentration (ALC) for the two batches were 103.28 mg/L (10 000 ppm) and 51.64 mg/L (> 5 000 ppm). Dermal exposure of rabbits to 5 000 mg/kg caused no mortality, no signs of toxicity and shows no potential for significant skin absorption: the approximate lethal dose (ALD) is >5 000 mg/kg.

Irritation and Sensitisation
The notified chemical was not an irritant to the eye or skin of rabbits. Two skin sensitisation studies in the rabbit were negative.

In the dog there was no evidence of cardiac sensitisation (life threatening arrhythmia) in response to exogenous adrenaline challenge at exposure concentrations of

1 000 ppm (10.33 mg/L) or 5 000 ppm (51.64 mg/L). Clinical signs of toxicity were observed in dogs at 5 000 ppm. Toxic effects (convulsions) were observed in the one dog exposed to 10 000 ppm (103.28 mg/L) in this study; cardiac sensitisation potential at this exposure concentration was not determined in this dog.

Inhalation Repeated Dose Toxicity

In a 14 day inhalation study in rats exposed nose only to 0, 500, 1 000 and 4 000 ppm, no specific organ toxicity was observed. A dose related decrease in mean total white cell count occurred in all test animals, however, there was some doubt about the toxicological significance of these observations. Similarly, non dose related decreases in body weight and heightened responses to stimuli were observed. Based on these changes, the study authors could not establish a NOEL.

A 90-day inhalation study in rats exposed to 0, 500, 2 000 or 3 500 ppm revealed a significant, progressive decrease in serum albumin in animals of the high dose group. There were significant changes in some haematological and clinical chemistry parameters but these changes were isolated and in the absence of organ toxicity did not show evidence of being treatment related. Male rats at all test doses had a concentration dependent significant decrease in peroxisomal beta-oxidation activity. The biological significance of this finding is not apparent as there was no significant fatty change in the liver, and no changes in clinical chemistry parameters of lipid metabolism. Elevated urinary fluoride levels were found in the mid and high dose animals. Specific kinetic and metabolism studies on the notified chemical are lacking but the increased urinary fluoride level is indicative of absorption and some metabolic transformation. Evidence of treatment related diuresis was observed in females of the high dose group. The cause and mechanism of the diuresis is not known and occurred in the absence of changes in other parameters of kidney function. There were some significant changes in organ weights, however, these were isolated and occurred in the absence of specific organ toxicity. Unilateral retinal lesions were seen in high dose animals; no other pathological changes were seen. Clinical signs of neurotoxicity (seizure like behaviour, convulsions and flinching or jerking type of behaviour) were observed in animals at 2 000 ppm and above during exposure periods. Treatment related decrease in motor activity was observed in animals of the high dose group. Histopathological examination of the brain, spinal cord and sciatic nerve revealed no lesions at the concentrations tested. A NOAEL of 500 ppm (5.16 mg/L) based on clinical signs of neurotoxicity at and above 2 000 ppm was established for this 90-day study. Based on minor clinical chemistry and haematological findings at the lowest dose, no NOEL was established.

Neurotoxicity

The neurotoxicity potential of the notified chemical was investigated in a study which focused on concentrations between the low and mid doses in the 90-day inhalation study (50 to 200 ppm). The study consisted of an acute exposure phase (single, 2 hour exposure) using a range of concentrations 0 to 3 000 ppm and a repeated exposure phase (6-hours/day, 5 days/week for 10 exposures) using 0 or 1 000 ppm. No treatment related effects occurred in the repeated dose test. Clinical signs of neurotoxicity occurred in the acute exposure test at 2 500 and 3 000 ppm, which is consistent with the findings of effects at and above 2 000 ppm in the 90-day inhalation study. Unexplained deaths also occurred at these doses,

but not in a subsequent test conducted to investigate the cause of these deaths. No treatment-related effects were observed at 1 500 ppm (15.49 mg/L) and above in the acute study and at 1 000 ppm (10.33 mg/L), the only dose tested, in the repeated dose study.

A study of the neurotoxic effects of the notified chemical and an azeotrope (notified chemical/DCE, 50/50) revealed a threshold of 4 000 ppm for clinical signs of neurotoxicity for both substances following a single 2-hour exposure. Compared to the test substance, the azeotrope increased the variety of clinical signs (abnormal posture, hunched over, lethargy) and increased the incidence of tremors and head jerking, but not convulsions or seizure like behaviour. Clinical signs of neurotoxicity were observed at 4 000 ppm and above, however, no treatment-related effects were observed (for both the notified chemical and the azeotrope) at 3 000 ppm (30.98 mg/L for the notified chemical).

Developmental Toxicity
The notified chemical was not teratogenic in the rat up to 3 500 ppm. Evidence of foetal (developmental) toxicity, namely, reduced foetal weight, and significant dose-related maternal toxicity, namely, depressed body weight and behavioural changes, were seen at 3 500 ppm and 2 000 ppm respectively. The maternal NOAEL, based on neurotoxicity, was 500 ppm (5.16 mg/L) and the NOAEL for developmental toxicity was 2 000 ppm (20.66 mg/L).

Genotoxicity
The notified chemical was not mutagenic in bacterial studies. It did not induce chromosomal aberrations in human lymphocytes *in vitro* and an *in vivo* inhalation mouse micronucleus assay was negative.

Human Health Effects
The notified chemical is currently in use in Australia at two sites under a commercial evaluation permit granted under Section 21G of the Act. The notifier has not reported any adverse health effects from the use of the notified chemical during the evaluation period. The notifier states that no reported and validated health issues have arisen from its use overseas. A search of the scientific literature did not reveal any adverse health effects associated with use of the notified chemical.

Summary of Health Effects
The notified chemical has low acute oral, dermal and inhalation toxicity. In animals it is not a skin or eye irritant and is not sensitising to skin. At the doses tested the notified chemical did not show cardiac sensitisation potential in dogs. The notified chemical is not mutagenic in *in vivo* and *in vitro* test systems. The notified chemical was not teratogenic to the rat. Clinical signs of neurotoxicity at concentrations of 2 000 ppm (20.66 mg/L) and above were evident across all studies (acute, repeat dose) where exposure was via the inhalation route. A NOAEL of 500 ppm was determined in a 90-day inhalation study, however, a NOEL could not be established in the same study.

In most studies, the test substance consisted of approximately 92% diastereomer B and

approximately 8% diastereomer A, whereas for other studies, the isomer ratio was either unknown or not provided. Although the toxicology of both isomers would be expected to be similar, they may not necessarily be equivalent.

Health Hazard Classification
Based on the data provided, the notified chemical would not be classified as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC 1994).

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The following ecotoxicity studies were supplied by the notifier. The tests were carried out according to OECD Test Methods (Organisation for Economic Co-operation and Development 1995-1996).

Species	***Test***	***Concentrations**** (mg/L)	***Results*** (mg/L)	***Reference***
Fathead minnow *(Pimephales promelas)*	96 h static acute	0, 9.26, 14.1, 22.9, 36.8, 60.7, 108	LC50 = 27.2 (95% CI: 22.9-36.8) NOEC = 14.1	(Ward TJ Kowalski PL Boeri RL 1996)
Water Flea *(Daphnia magna)*	48 h static acute	0, 8.59, 13.9, 21.8, 37.1, 60.4, 98.2	EC50 = 10.6 (95% CI: 8.59-13.9) NOEC < 8.59	(Ward TJ Kowalski PL Boeri RL 1996)
Algae (*Selenastrum capricornutum)*	96 h growth	0, 7.28, 15.0, 26.5, 53.5, 120	E_RC50>120 E_BC50 > 120 NOEC = 120	(Ward TJ Kowalski PL Boeri RL 1996)

* Measured concentration

In the fish study, small fish were used to minimise loading in sealed test vessels. The average weight of the fish was 4.3 mg and the average total length was 9.5 mm. After 6 hour none of the 7 test animals were affected at any of the concentrations and no effects were observed at the two lowest test concentrations and the control throughout the 96 hour duration of the test. A single mortality was observed at 22.9 mg/L test level after 24 hours and complete mortality was observed at all higher concentrations. The LC_{50} value was determined using binomial-nonlinear interpolation and the given confidence limits correspond to the highest test concentration (showing no mortality) and the lowest concentration (total mortality). As a result, it is believed that the best estimate of the LC_{50} would be in the range 22.9 to 36.8 mg/L. Of the surviving test animals at 22.9 mg/L, all were noted as swimming erratically and/or lethargic from 24 hours onwards.

A single immobilised daphnia was observed at the lowest test concentration after 48 hours. At the 13.9 mg/L test concentration all daphnia were either immobilised or deceased after 48 hours. Higher concentrations resulted in 100% mortality. The EC_{50} value was determined using binomial-nonlinear interpolation and the given confidence limits correspond to the highest test concentration (showing no effect) and the lowest concentration (all affected). As a result, it is believed that the best estimate of the EC_{50} would be in the range 8.6 to 13.9 mg/L.

No effects (size difference, unusual cell shapes, colours, flocculations, adherence of cells to test container, or cell aggregation) were noted during the algal study.

The ecotoxicity data for HFC 43-10mee indicate that the chemical is slightly toxic to fish and daphnia and practically non-toxic to algae.

Acute toxicity data for HFC 43-10mee using QSAR calculations by ASTER (US EPA 1998), indicating that the chemical is slightly toxic to fish and daphnia, is in agreement with the experimental results. The ASTER results are summarised in the following table:

Species	***Duration* (hours)**	***LC_{50}* (mg/L)**
Bluegill sunfish (*Lepomis macrochirus)*	96	66
Fathead minnow (*Pimephales promelas)*	96	85
Channel catfish (*Ictalurus punctatus)*	96	37
Rainbow trout (*Oncorhynchus mykiss)*	96	37
Daphnia magna	48	45

ASTER also calculated a 32 day chronic maximum acceptable toxicant concentration (MATC) for the growth of fathead minnow *(Pimephales promelas)* of 13 mg/L and a bioconcentration factor of 30 for bluegill sunfish *(Lepomis macrochirus)*.

Halocarbons can affect the atmosphere. HFC 43-10mee does not contain either chlorine or bromine, and thus will not act as a source of ozone depleting halogen radicals in the stratosphere. Scientists from the US National Oceanic and Atmospheric Administration concluded recently that hydrofluorocarbons have negligible potential to destroy ozone (Ravishankara AR Turnipseed AA Jensen NR Barone S Mills M Howard CJ and Solomon S 1994).

Like other halocarbons, HFC 43-10mee adds to the global warming potential (GWP) of the atmosphere. The GWP of HFC 43-10mee is 1300 (100 year ITH), however, this is

considerably lower than the 9300 GWP (100 year ITH) for CFC-113, which the notified chemical is intended to replace (IPCC 1996).

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

Although HFC 43-10mee is slightly toxic to fish and daphnia, it is not expected to exert a direct effect on living organisms by analogy with other hydrofluorocarbons. The high volatility should ensure minimal exposure of aquatic and terrestrial compartments, and therefore minimal hazard to organisms inhabiting them.

The hazard to the atmosphere will be reduced when HFC 43-10mee replaces the previously used chlorofluorocarbons, such as CFC-113, as the replacement solvent will not carry chlorine or bromine to the stratosphere (hence, it has no potential for ozone depletion) and has a lower global warming potential. However, HFC 43-10mee retains significant global warming potential.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

The notified chemical has a very low acute toxicity. In animals it is not a skin or eye irritant, although the notifier's MSDS indicates that immediate eye or skin irritation may occur following acute exposure. HFC 43-10mee is not sensitising to the skin. At the doses tested, the notified chemical did not show cardiac sensitisation potential in dogs, however, the notifier's MSDS warns that, by analogy with other fluorocarbons, potential for cardiac arrhythmia (sensitisation) exists. The notified chemical is not mutagenic in *in vitro* and *in vivo* test systems and was not teratogenic in the rat. Developmental toxicity was observed only at doses above the maternotoxic dose. No data on dermal absorption were available.

The critical effect identified in both acute and repeated dose inhalation studies is neurotoxicity, with reported symptoms including stimulation and depression of the central nervous system, tremors and convulsions. In acute studies (2 hour exposure), neurotoxic signs were observed at and beyond 2500 ppm, whereas in repeated dose studies, neurotoxic signs were observed at 2000 ppm and above. In the 14-day repeated dose study, neurotoxic signs were not clearly observed. In the 14-day and 90-day studies, there was no evidence of organ toxicity at concentrations up to 4000 and 3500 ppm respectively. The NOAEL of 500 ppm is established in the 90-day inhalation study; a NOEL could not be established in the same study.

In addition, an asphyxiation hazard exists from displacement of air due to accumulation of the notified chemical in large amounts (> 10%).

The notified chemical is currently in use in Australia at two sites under a commercial

evaluation permit granted under Section 21G of the Act. The notifier has not reported any adverse health effects from the use of the notified chemical during the evaluation period. The notifier states that no reported and validated health issues have arisen from its use overseas. A search of the scientific literature did not reveal any adverse health effects associated with use of the notified chemical.

On the basis of the data provided, the notified chemical would not be classified as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC 1994).

Exposure Limit
An in-house occupational exposure standard (or Acceptable Exposure Limit (AEL) of 200 ppm (8 and 12-hour Time Weighted Average (TWA) and 400 ppm (Ceiling Limit) is used by the notifier (Brock WJ Malley LA 1995). The TWA is stated to be based on the NOAELs of 500 ppm observed in the developmental and 90-day repeated dose inhalation studies. This represents a safety factor of only 2.5, which may be insufficient to protect the health of workers. The basis of the 400 ppm Ceiling Limit (or peak concentration) is not apparent from the data provided by the notifier.

Occupational Health and Safety

The notified chemical is to be used as a solvent degreaser and will be used in vapour degreasing equipment. Occupational exposure to the chemical will be limited to degreaser plant operators, solvent reclamation workers and workers engaged in transport, storage and handling of the chemical. Workers involved in plant and equipment maintenance may also be exposed. As the notified chemical is a low boiling liquid, exposure to both the liquid and vapour may occur, particularly where heat is applied, e.g. during vapour degreasing.

Acute Effects
Atmospheric monitoring data (area sampling) provided in the submission included data for vapour degreasing. It was not stated whether local exhaust ventilation was in operation during sampling. Grab sample concentrations up to 94 ppm were obtained for charging an empty degreaser (Table 1) and short term concentrations up to 38 ppm (30-95 minutes) were obtained adjacent to an operating degreaser (Table 2). These concentrations are well below the no effect levels of 1500 and 3000 ppm obtained in acute inhalation studies. Assuming this data are representative of vapour degreasing operations in Australia, the risk of neurotoxic effects from inhalation exposure during normal operating conditions is low. Moreover, it is stated by the notifier that the vapour degreasers to be used with the notified chemical will conform to the requirements of the AFCAM Code of Practice and the relevant Australian Standards, including the provision of local exhaust ventilation to minimise vapour release into the work environment.

No monitoring data was available for exposure during solvent reclamation, however, it was claimed by the notifier that this work in Australia will be conducted in accordance with the requirements of the AFCAM Code of Practice. Similarly, cleaning and maintenance of

degreasers will be carried out under the same requirements.

Therefore, the risk of adverse health effects from acute inhalation exposure is largely confined to the frequency and duration of exposure to spills and leaks, particularly in confined areas, where high vapour concentrations may develop. This may include cleaning and maintenance activities. It is therefore recommended that respiratory equipment be available for use when required. Atmospheric monitoring during non-routine activities should also be considered, e.g. during cleaning and maintenance of degreaser tanks.

The risk of asphyxiation is considered to be low and would only exist in the event of major leakage, or where solvent leakage was allowed to accumulate in a confined space or low lying area.

Skin contact with liquid HFC 43-10mee may occur during use of the chemical, particularly during charging of degreaser tanks, handling workpieces, solvent reclamation, and the cleaning and maintenance of plant and equipment. Degreased workpieces taken from vapour degreasing tanks may contain trapped liquid solvent. The notified chemical may be a slight skin and eye irritant and its dermal absorption characteristics have not been reported. The risk of adverse health effects by skin and eye contact is likely to be low, however, as this is difficult to quantify, precautions should be taken to prevent contact. The MSDS states that impervious gloves and splash goggles should be worn when handling the chemical.

The risk of adverse health effects during normal storage and transport is considered to be low as the notified chemical is usually delivered directly to customers in 20 L drums.

Health Effects Due To Repeated Exposure
Insufficient results from longer duration personal monitoring, e.g. for 8 to 12 hour shifts, are available. However, for the purposes of determining a margin of exposure (MOE) for health effects following repeated exposure, a reasonable worst case personal monitoring value of 10 ppm TWA can be assumed. The 10 ppm value is taken from the results of short-term TWA sampling (14-95 minutes), where 9.6 ppm was the highest average obtained during vapour degreasing (section 6, Table 2). This mean was obtained for a degreaser left idle with the lid open. Using the lowest NOAEL of 500 ppm for neurotoxic effects from repeated inhalation exposure and 10 ppm as the reasonable worst case level of exposure, an MOE of 50 is obtained. Individual readings ranging from 0.6 ppm to 38 ppm were obtained during the vapour degreasing survey, both readings obtained near the degreaser during cleaning of parts. These isolated readings represent an MOE range of 833 to 13 respectively. The MOE obtained for both the average and high individual readings (50 and 13 respectively) indicate that effective exposure controls including local exhaust ventilation are required to maintain vapour concentrations below a TWA average of 5 ppm. These estimates do not take into account any contribution from dermal absorption.

It is therefore important that the use of HFC 43-10mee in vapour degreasing is well-controlled. Compliance with the AFCAM Code of Practice and the relevant Australian standards is essential to reduce inhalation and dermal exposure and consequently reduce health risks from exposure to the notified chemical. Only under these circumstances is the

health risk to workers expected to be acceptable.

Workers employed in solvent reclamation and cleaning and maintenance are likely to be at lower risk from chronic effects as exposure is expected to be less regular than for vapour degreaser operators. Cleaning and maintenance activities are conducted intermittently, therefore the risk of adverse health effects from chronic inhalation exposure is low.

Exposure from drum leakage and spills may occur but will generally be infrequent. Therefore, the risk of adverse health effects from repeated exposure from normal transport, storage and handling is considered negligible.

As mentioned above, the MOE calculations have taken into account inhalation exposure only and skin contact may occur during handling and use of the chemical. The operations involving HFC 43-10mee are largely controlled under the AFCAM Code of Practice and the relevant Australian standards, however, as the dermal absorption characteristics of the chemical have not been reported, precautions should be taken to prevent repeated skin contact.

As a means of assisting plant and equipment control and determining worker exposure, atmospheric monitoring of the work environment on a regular basis is advisable. For example, it would aid in the early detection of equipment malfunction and ensure adherence to good work practices. Personal monitoring over an entire shift should be conducted.

This assessment indicates that HFC 43-10mee needs to be referred to the NOHSC Hazardous Substances Sub-committee for consideration of an exposure standard. In the meantime, exposure to the notified chemical should be maintained well below the notifier's recommended Acceptable Exposure Limit (AEL) of 200 ppm TWA (8- and 12-hour) and 400 ppm Ceiling Limit.

Public Health

The notified chemical is for industrial use only and is unlikely to come into contact with the general public. According to the notifier, items treated by the notified chemical will be free of all traces of the chemical by the time it reaches the public domain. In addition, with the industrial controls to minimise environmental release, public exposure is likely to be low. Based on the use pattern and its toxicological properties, the notified chemical is considered not to pose a significant hazard to public health.

13. RECOMMENDATIONS

1. This assessment report and the health effects data submitted with this notification should be referred to the NOHSC Hazardous Substances Sub-committee to determine whether a NOHSC exposure standard should be set for HFC 43-10mee. In the meantime, exposure to the notified chemical should be maintained well below the

notifier's recommended Acceptable Exposure Limit (AEL) of 200 ppm TWA (8- and 12-hour) and 400 ppm Ceiling Limit.

2. Due to the current lack of exposure data and uncertainty about the validity of the notifier's exposure limits, it is recommended that a regular program of atmospheric monitoring be introduced to monitor the personal exposure of vapour degreaser operators. Both instantaneous and time-weighted average (over the full shift) measurements should be made. This data may need to be made available to the NOHSC Hazardous Substances Sub-committee at a later date.

3. To minimise occupational exposure to HFC 43-10mee, the following guidelines and precautions must be observed:

- Adhere to the AFCAM Code of Practice for the Minimisation of Chlorofluorocarbon Emissions from Degreasing/Cleaning Plants Using CFC 113 Solvents (AFCAM 1990);
- Adhere to the requirements for the safe operation of vapour degreasing plant described in Australian Standard 2661 (Standards Australia 1983);
- Select and fit safety goggles in accordance with Australian Standard (AS) 1336 (Standards Australia 1994) to comply with Australian/New Zealand Standard (AS/NZS) 1337 (Standards Australia/Standards New Zealand 1992);
- Wear industrial clothing conforming to the specifications detailed in AS 2919 (Standards Australia 1987) and AS 3765.1 (Standards Australia 1990);
- Wear impermeable gloves or mittens conforming to AS 2161 (Standards Australia 1998);
- Wear occupational footwear conforming to AS/NZS 2210 (Standards Australia/Standards New Zealand 1994);
- Avoid spillage of the notified chemical. Clean spills up promptly with absorbents which should then be put into containers for disposal;

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

14. MATERIAL SAFETY DATA SHEET

The MSDS for the notified chemical was provided in a format consistent with the NOHSC *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.

15. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the Act, secondary notification of the notified chemical shall be required if any of the circumstances stipulated under subsection 64(2) of the Act arise. No other specific conditions are prescribed.

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Attachment 1

The Draize Scale for evaluation of skin reactions is as follows:

Erythema Formation	*Rating*	*Oedema Formation*	*Rating*
No erythema	0	No oedema	0
Very slight erythema (barely perceptible)	1	Very slight oedema (barely perceptible)	1
Well-defined erythema	2	Slight oedema (edges of area well-defined by definite raising	2
Moderate to severe erythema	3	Moderate oedema (raised approx. 1 mm)	3
Severe erythema (beet redness)	4	Severe oedema (raised more than 1 mm and extending beyond area of exposure)	4

The Draize scale for evaluation of eye reactions is as follows:

CORNEA

Opacity	*Rating*	*Area of Cornea involved*	*Rating*
No opacity	0 none	25% or less (not zero)	1
Diffuse area, details of iris clearly visible	1 slight	25% to 50%	2
Easily visible translucent areas, details of iris slightly obscure	2 mild	50% to 75%	3
Opalescent areas, no details of iris visible, size of pupil barely discernible	3 moderate	Greater than 75%	4
Opaque, iris invisible	4 severe		

CONJUNCTIVAE

Redness	*Rating*	*Chemosis*	*Rating*	*Discharge*	*Rating*
Vessels normal	0 none	No swelling	0 none	No discharge	0 none
Vessels definitely injected above normal	1 slight	Any swelling above normal	1 slight	Any amount different from normal	1 slight
More diffuse, deeper crimson red with individual vessels not easily discernible	2 mod.	Obvious swelling with partial eversion of lids	2 mild	Discharge with moistening of lids and adjacent hairs	2 mod.
Diffuse beefy red	3 severe	Swelling with lids half-closed	3 mod.	Discharge with moistening of lids and hairs and considerable area around eye	3 severe
		Swelling with lids half-closed to completely closed	4 severe		

IRIS

Values	*Rating*
Normal	0 none
Folds above normal, congestion, swelling, circumcorneal injection, iris reacts to light	1 slight
No reaction to light, haemorrhage, gross destruction	2 severe