File No: NA/858

December 2000

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

OS-9000

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Director
Chemicals Notification and Assessment

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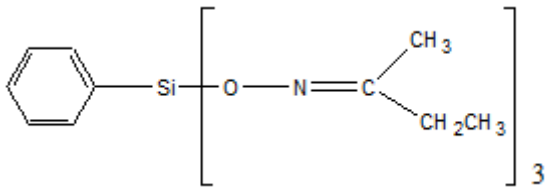
1. APPLICANT

Honeywell Polymers (Australia) Ltd of 71 Queens Rd, Melbourne VIC 3004 (ACN 008 423 096) and Parbury Technologies Pty Ltd of 7 Lucca Rd, Wyong NSW 2259 (ACN 069 961 968) have submitted a standard notification statement in support of their application for an assessment certificate for OS-9000. The notified chemical has previously been used in Australia, under Commercial Evaluation Permit 415 (CEC/448), dated 6 October 1999.

2. IDENTITY OF THE CHEMICAL

Chemical Name:	2-butanone, O,O',O''-(phenylsilylidyne)trioxime
Chemical Abstracts Service (CAS) Registry No.:	34036-80-1
Other Names:	phenyltris(methylethylketoximino)silane phenyl oximino silane PHOS
Marketing Name:	OS-9000
Molecular Formula:	$C_{18}H_{29}N_3O_3Si$
Structural Formula:	
Molecular Weight:	363.5
Method of Detection and Determination:	can be detected by GC and characterised by UV/visible, infrared (IR) and ^{1}H nmr spectroscopy
Spectral Data:	UV/vis λmax = 253, 258, 263, 270 nm

IR: 3074, 3042, 2974, 2935, 2876, 2848, 1640, 1593, 1448, 1431, 1367, 1224, 1128, 1091, 1072, 977, 927, 873, 797, 739, 699, 581, 514 476 cm^{-1}

^{1}H nmr 7.87, 7.82, 7.39, 7.35, 2.52, 2.48, 2.28, 2.23, 2.05, 1.98, 1.88, 1.08, 1.05, 1.02 ppm

^{13}C nmr 165.62, 165.57, 135.50, 135.41, 135.33, 130.36, 130.10, 129.89, 129.68, 127.39, 127.12, 126.88, 77.64, 77.01, 76.37, 29.15, 29.00, 22.62, 19.21, 14.04, 10.93, 10.65, 9.99 ppm

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C & 101.3 kPa:	colourless to light yellow low viscosity liquid
Melting Point:	< -25°C
Boiling Point:	60 - 306°C (decomposes)
Specific Gravity:	1.04
Vapour Pressure:	3×10^{-6} kPa at 25°C
Water Solubility:	not determined (see comments below)
Fat Solubility:	miscible in all proportions with standard fat HB307
Particle Size:	liquid under ambient conditions
Partition Co-efficient (n-octanol/water):	log P_{ow} = 11.05 (calculated)
Hydrolysis as a Function of pH:	$T_{1/2}$ at 20°C and pH 4.0, 7.0, 9.0 < 5 minutes
Adsorption/Desorption:	log K_{oc} = 7.39 (calculated)
Dissociation Constant:	not determined (see comments below)
Flash Point:	106°C (closed cup)
Flammability Limits:	not flammable
Autoignition Temperature:	320°C
Explosive Properties:	not explosive

Reactivity/Stability:	hydrolyses in contact with moisture hazardous polymerisation can occur at above 35°C, and in the presence of electrophiles such as ferric chloride

3.1 Comments on Physico-Chemical Properties

EEC Method A2, 103 (ebulliometric method) was used to determine the boiling point of the chemical. In the study (Young, 1999) it was found that the chemical began to decompose at 60ºC and continued until over 300ºC. A series of colour and state changes was observed over this temperature range.

The vapour pressure was determined using EEC Method A4, 104 (vapour pressure balance) (Young 1999). Four test runs using the same chemical sample (0.48 g) with a pressure of less than 0.0013 Pa, were done at temperatures between 25 and 49ºC. The vapour pressure was calculated using three of the runs as one of the runs was disregarded due to degree of variation.

In an attempt to determine the water solubility of the chemical a modified test based on OECD method 105 was conducted (Young 1999). However, because of the reactivity of the notified chemical with water this was not possible.

The partition coefficient n-octanol/water could not be measured because of the reactivity of the notified chemical with water. Syracuse Research Corporation software (Syracuse Research Corporation) estimated log P_{ow} at 11.05 at 20ºC. This indicates that the chemical is hydrophobic and may have the potential to bioaccumulate. The notifier has agreed this appears high and probably the result of the computer estimation program overestimating log P_{ow} of some aliphatic compounds with a high alkyl carbon content.

Soil adsorption/desorption could not be measured because of the reactivity of the notified chemical with water. Young (1999) calculated an estimated soil adsorption coefficient for the notified chemical using the formula log K_{oc} = 0.544 log P_{ow} + 1.377. With a value of 11.05 being used for log P_{ow}, log K_{oc} was estimated to be 7.39 ($K_{oc}=2.44\times10^7$). This result indicates that the chemical is likely to be immobile in soil or sediments. The notifier acknowledges the result is high.

Due to the reactivity of the notified chemical with water, the dissociation constant was not determined. The compound and its reaction products with water contain no acidic or basic groups, and dissociation constant data is not relevant.

A fat solubility test was also done by Young (1999), in which a mixtures of standard fat HB307 and the notified chemical (6.9 to 94.6 %) were used. Visual inspections were done to determine if a homogenous phase had been formed. In all mixtures it was found that the chemical was miscible with standard fat.

4. PURITY OF THE CHEMICAL

Degree of Purity:	typically 95.5 % (range 89.0 – 96.9 %)

Hazardous Impurities:

Chemical name:	n-hexane
CAS No.:	110-54-3
Weight percentage:	0.1 – 0.7
Toxic properties:	harmful: danger of serious damage to health by prolonged exposure through inhalation (NOHSC, 1999b)
Regulatory controls:	NOHSC exposure standard 50 ppm TWA (NOHSC, 1995)

Chemical name:	toluene
CAS No.:	108-88-3
Weight percentage:	0 – 0.9
Toxic properties:	harmful by inhalation (NOHSC, 1999b)
Regulatory controls:	NOHSC exposure standard 100 ppm TWA, 150 ppm STEL (NOHSC, 1995)

Chemical name:	2-butanone oxime
Synonyms:	methyl ethyl ketoxime, MEKO
CAS No.:	96-27-9
Weight percentage:	0.4 – 0.9
Toxic properties:	irritating to eyes may cause sensitisation by skin contact (NOHSC, 1999b)
Exposure limit:	the notifier has indicated that exposure limits of 3 ppm TWA, 10 ppm STEL will be applied for this chemical

Chemical name:	2,2-bis(2-butanoneoximino)butane
CAS No.:	
Weight percentage:	0.2 – 1.5
Toxic properties:	not known

In addition, a number of reaction products of silanes with 2-butanone oxime, closely related to the notified chemical, have been identified by GC. The toxicity of these reaction products is expected to be similar to that of the notified chemical, due to the similar reactivity of all of these chemicals. The identified impurities were present in the samples used for toxicity testing.

Chemical name	*Weight Percentage*
2-butanone, O, O'-(methylphenylsilylene)dioxime	0 – 0.7
phenyl(2-butoxy)bis(2-butanoneoximino)silane	0.05 – 0.35
cyclohexyltris(2-butanoneoximino)silane	0 – 0.8
either methyltris(2-butanoneoximino)silane or vinyltris(2-butanoneoximino)silane or tetrakis(2-butanoneoximino)silane	0 – 0.9
phenyl(4-methyl-2-pentanoneoximino)bis(2-butanoneoximino)silane	0 – 0.5
diphenylbis(2-butanoneoximino)silane	0 – 0.55
(2-butanoneoximino)silane terminated phenyl siloxanes	2 – 4.6

Non-hazardous Impurities (> 1% by weight): none

Additives/Adjuvants: none

5. USE, VOLUME AND FORMULATION

The notified chemical is used as a crosslinking agent for silicone sealants, coatings and adhesives. It is incorporated in silicone formulations at a level of < 4 %. In the presence of moisture, it causes the formulations to crosslink, producing rubber-like materials.

The notified polymer is imported as the pure liquid, with no additives, in 50 – 200 kg epoxy phenolic lined steel drums. It will be reformulated in Australia to produce the silicone sealants, which contain < 4 % notified chemical, by blending with other silicone raw materials. The sealants will be packaged in 300 mL polyolefin cartridges and 20 L steel drums. The sealants are applied to joints in concrete roads and pavements by professional sealant applicators.

The notifier estimates that the import volume will be less than 100 tonnes per annum during the first five years of importation.

6. OCCUPATIONAL EXPOSURE

Transport and Storage
Waterfront, transport and warehouse workers are not expected to be exposed to the notified chemical except in the case of an accident involving spillage of the notified chemical. Handling, transporting and storage of drums of notified chemical will involve 2 cargo unloaders, 2 customs clearance agents, 1 truck driver and 2 storage workers. One truck driver will also be involved in loading and transporting used drums. Transport and storage workers will also be involved in handling the formulated sealant, containing < 4 % notified chemical. No exposure is expected except in the case of an accident.

Reformulation
The reformulation of pure notified chemical to produce the sealant formulations will occur at

one site. Mixing will occur in a closed head planetary mixer. The notified chemical (28 kg per batch) will be weighed into a small plastic drum, dedicated for this purpose, and added to the ingredients in the mixer. Dermal exposure to the pure notified chemical will be possible during decanting of the notified chemical from the import drum and during addition to the mixer. The finished formulation will be sampled for quality control testing, then transferred to the final packaging.

Reformulation will involve quality assurance staff, manufacturing operators and packaging operators. During quality control testing, small quantities of formulated sealant (< 4 % notified chemical) are expected to be handled under laboratory conditions.

The reformulation process will involve 2 manufacturing operators, who will be involved in dispensing and blending pure notified chemical for 1 hour per day, 30 days per year. Dermal exposure to drips and spills of the pure notified chemical may occur during weighing out and addition of notified chemical to the mixer. Inhalation exposure to the notified chemical and decomposition products, particularly 2-butanone oxime, may also occur. After reformulation, the finished sealants will be handled by 2 packaging operators, for 1 hour per day, 30 days per year. Dermal exposure to drips and spills of the sealant, containing < 4 % notified polymer, may occur, although the potential will be limited by the paste-like consistency of the finished sealant.

Reformulation workers will wear impervious gloves (butyl rubber, neoprene or nitrile) and goggles and overalls. In addition, a butyl rubber apron and full face shield will be used if splashes are likely, and a respirator with organic vapour filter or air fed respirator will be used in confined spaces.

Drum Reconditioning
After emptying, the import drums will be transported to a drum reconditioner, where residues will be disposed of by incineration. Little or no exposure to the notified chemical is expected. The drum reconditioning is expected to involve handling the notified chemical for 1 hour per day, 10 days per year.

End Use
The notified polymer will be used by skilled tradespeople for application to expansion joints in concrete roads and pavements. Application will be either directly from the cartridge, using a caulking gun, or from drums, using a pump. Exposure is expected to be limited because of the paste-like consistency of the finished sealant, which will reduce the likelihood of spills. After application, the sealant will harden due to reaction of the notified chemical with atmospheric moisture, and the notified chemical will be consumed and encapsulated in the silicone in crosslinked form. The notifier has not provided details of the numbers of workers involved or exposure frequencies.

7. PUBLIC EXPOSURE

Products containing the notified chemical will only be used by professional tradespeople and they will not be available to the general public. Exposure of the general public as a result of transport and disposal of the notified chemical and products containing the notified chemical

is assessed as being negligible. The general public may make dermal contact with sealant containing the notified chemical after it has been cured, but this is likely to occur only infrequently.

Any unreacted notified chemical is likely to be trapped within a polymer matrix and the concentration of notified chemical present on the surface of the cured sealant is likely to be very low or negligible. Therefore it is unlikely that dermal contact with the cured material will result in significant exposure to the notified chemical.

8. ENVIRONMENTAL EXPOSURE

8.1 Release

Since the chemical is a viscous liquid, release during handling and sealant manufacture is expected to be minimal. The notifier has estimated that less than 1 % of the contents would be left as residue in the import drums. A licensed waste disposal contractor will either recondition or incinerate the drums. No percentage has been provided for loss due to spills. Due to the nature of the chemical this is likely to be quite small (possible less than 1 %, ie a maximum of 1 tonne per annum). However, any spilt material will react with the moisture in the atmosphere to form 2-butanone oxime. Less than 1 % of the sealant product (containing approximately 4 % of the notified chemical) will remain in the production equipment and resultant effluent. This equates to a maximum of 1 tonne of notified chemical per annum, which should hydrolyse quickly.

After application, the majority of the chemical will be bound into the cured sealant matrix, which in turn would be intimately associated with the road/pavement construction materials. The notifier expects that the residues in the empty sealant containers will be less than 1 %. Sealant containers are expected to be disposed of by specialised waste contractors. It is expected that the residual sealant in the containers will cure into a highly cross linked rubbery mass prior to disposal.

8.2 Fate

The majority of the silicone sealants, containing the notified chemical cross-linked within the sealant matrix, will share the fate of the construction material to which they have been applied. After demolition of the roads, most of the sealant would be deposited with rubble into landfill. Silicone sealants are resistant to biological and abiotic degradation, but over a very long time it is likely that they would be degraded.

Incineration of the sealant would result in decomposition of the silicone polymers and consequent production of silica. This would be assimilated into ash and slag which could also be expected to eventually be placed into landfills.

Barnes (1999) undertook a study of the ready biodegradation of the chemical using OECD Guideline 301B (Modified Sturm Test). The chemical was added to two vessels inoculated with activated sludge, while a reference vessel was set-up with sodium benzoate. The nominal exposure concentration of the chemical was 10 mg(C)/L. The vessels were incubated for 36 days at 20-24ºC, and aerated with CO_2 free air. Any CO_2 emitted from the vessels was

collected in Dreschel bottles. Sodium benzoate had undergone 67 % degradation on day 6 and 91 % on day 36. The notified chemical had undergone 10 % degradation at 7 days and 62 % after 36 days, indicating that it is not readily biodegradable.

The estimated log P_{ow} and observed fat solubility suggests that the chemical has the potential to bioaccumulate, however this is unlikely to occur due to the high reactivity of the notified chemical with water.

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Summary of the acute toxicity of OS-9000

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	LD_{50} > 2000 mg/kg	(Bonnette, 1998)
acute dermal toxicity	rat	LD_{50} > 2000 mg/kg	(McRae, 2000a)
skin irritation	rabbit	persistent irritant	(McRae, 2000c)
eye irritation	rabbit	slight irritant	(McRae, 2000b)
skin sensitisation	guinea pig	moderate sensitiser	(Coleman, 2000)

9.1.1 Oral Toxicity (Bonnette, 1998)

Species/strain:	rat/Sprague-Dawley Crl:CDBR VAF/Plus
Number/sex of animals:	5/sex/dose
Observation period:	14 days
Method of administration:	gavage, doses 100, 500, 2000 mg/kg, notified chemical administered as received
Test method:	OECD TG 401
Mortality:	one female in the 2000 mg/kg group died on day 1
Clinical observations:	prostration, decreased activity, wobbly gait, rigidity on handling, breathing abnormalities, urine stains, decreased defecation, partially closed eyelids and dark material around the eyes observed until day 4 for the 2000 mg/kg group wobbly gait and decreased activity observed until day 2 for the 500 mg/kg group
Body weight:	reduced body weight gain was observed for the males and body weight loss for the females in the 2000 mg/kg group between day 0 and day 1; recovery occurred by day 4; no

	other significant body weight changes were observed
Morphological findings:	for the animal that died, abnormal content in the trachea, digestive tract and urinary bladder, reddened mucosa in the small intestine, mottled lung, stained mucosa in the stomach and dark red foci in the thymus were observed for the surviving animals, blackish purple spleens and an increase in spleen weight relative to body weight (statistically significant in males only) were observed for the 500 and 2000 mg/kg animals
Comment:	significant toxicity was observed at 500 and 2000 mg/kg
LD_{50}:	> 2000 mg/kg
Result:	the notified chemical was of very low acute oral toxicity in rats

9.1.2 Dermal Toxicity (McRae, 2000a)

Species/strain:	rat/Hsd: Sprague-Dawley (CD)
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	semi-occlusive patch; 24 hr exposure; dose 2000 mg/kg; notified chemical used as received
Test method:	OECD TG 402
Mortality:	there were no premature decedents during the study
Dermal observations:	no cutaneous reactions were observed
Clinical observations:	no clinical signs of toxicity were observed
Body weight:	body weight gain was unaffected by treatment except for a low body weight gain in one female on day 8 only
Morphological findings:	no gross pathological abnormalities were observed at necropsy
LD_{50}:	> 2000 mg/kg
Result:	the notified chemical was of low dermal toxicity in rats

9.1.3 Inhalation Toxicity

No acute inhalation toxicity study was submitted.

9.1.4 Skin Irritation (McRae, 2000c)

Species/strain: rabbit/New Zealand White

Number/sex of animals: 3 male

Observation period: 10 days

Method of administration: semi-occlusive patch; 4 hr exposure; dose 0.5 mL; notified chemical used as received

Test method: OECD TG 404

Draize scores:

	Time after application (days)																			
Animal	***½ hr***		***1***		***2***		***3***		***4***		***5***		***6***		***7***		***8***		***9***	
	E	***O***	***E***	***O***	***E***	***O***	***E***	***O***	***E***	***O***	***E***	***O***	***E***	***O***	***E***	***O***	***E***	***O***	***E***	***O***
1	1[a]	1	1	1	1	0	1	0	2	0	2	0	1	0	1	0	1	0	0	0
2	1	1	2	2	2	2	2	0	2	0	2	0	1	0	1	0	1	0	0	0
3	0	0	0	0	0	0	0	0												

[a] see Attachment 1 for Draize scales

Comment: in animals 1 and 2, patchy erythema was observed for 8 days, while desquamation characterised by dryness and sloughing was observed for 9 days in animal 2

Result: the notified chemical was a persistent irritant to the skin of rabbits

9.1.5 Eye Irritation (McRae, 2000b)

Species/strain: rabbit/New Zealand White

Number/sex of animals: 3 female

Observation period: 4 days

Method of administration: 0.1 mL of notified chemical was instilled in the conjunctival sac of one eye; the untreated eye served as control

Test method: OECD TG 405

Draize scores of unirrigated eyes:

	Time after instillation									
Animal	***1 hour***		***1 day***		***2 days***		***3 days***		***4 days***	
Cornea	all Draize scores after the 1 hr observation were zero									
Iris	all Draize scores were zero									
Conjunctiva	***r***	***c***	***r***	***c***	***r***	***c***	***r***	***c***	***r***	***c***
1	2[1]	2	2	0	1	0	1	0	0	0
2	2	2	1	0	1	0	0	0		
3	2	2	1	0	1	0	0	0		

[1] see Attachment 1 for Draize scales
r = redness c = chemosis

Comment: dulling of the cornea was observed for animal 1 at 1 hr

Result: the notified chemical was slightly irritating to the eyes of rabbits

9.1.6 Skin Sensitisation (Coleman, 2000)

Species/strain: guinea pig/Dunkin-Hartley

Number of animals: 10 female (test group)
5 female (control group)

Induction procedure:

test group:

day 0 on a prepared area of skin from the shoulder region of test animals, three pairs of intradermal injections were administered as follows:

1. 0.1 mL of Freund's Complete Adjuvant (FCA) 50 % v/v in water;
2. 0.1 mL 1 % notified chemical in 5 % acetone in Alembicol D;
3. 0.1 mL 1 % notified chemical in 5 % acetone in Alembicol D 50 % v/v with FCA

day 6 local irritation was induced at the shaved test site for both test and control groups by application of 0.5 mL of 10 % sodium lauryl sulphate in petrolatum

day 7 notified chemical as supplied (approximately 0.4 mL) was applied by occlusive patch to the same site that received the intradermal injections for 48 hours; application sites were observed for irritation 24 hours subsequently

control group:

day 0 1. 0.1 mL of Freund's Complete Adjuvant (FCA) 50 % v/v

in water;
2. 0.1 mL 5 % acetone in Alembicol D;
3. 0.1 mL 5 % acetone in Alembicol D 50 % v/v with FCA

day 6, 7 — a similar topical induction procedure to that for the test animals was used but the notified chemical was omitted

Challenge procedure:

day 21 — patches of approximately 2 cm square were saturated with approximately 0.2 mL of a 25 % or 50 % concentration of notified chemical in acetone and applied to the shaved left flank of each animal under occlusive conditions for 24 hr;

dermal reactions were scored at 24, 48 and 72 hours after patch removal

Test method: OECD TG 406 (Magnusson and Kligman Method)

Challenge outcome:

	Test animals			***Control animals***		
Challenge concentration	***24 hours****	***48 hours****	***72 hours***	***24 hours****	***48 hours****	***72 hours***
25%	**0/10	0/10	0/10	0/5	0/5	0/5
50%	4/10	6/10	6/10	0/5	0/5	0/5

* time after patch removal
** number of animals exhibiting positive response

Comment: necrosis was seen at the sites injected with FCA; slight irritation was observed at the sites injected with acetone in Alembicol D (for both test group and control group); no irritation was observed following topical application

the study authors indicated that, in error, the maximum non-irritant concentration of notified chemical (100 %) was not used in the challenge phase, but in light of the positive results at a 50 % concentration, the study results were not affected

Result: the notified chemical was moderately sensitising to the skin of guinea pigs

9.2 Repeated Dose Toxicity (Rush, 2000)

Species/strain: rat/Sprague-Dawley Crl: CD(SD)IGS BR

Number/sex of animals: 5/sex/group

Method of administration:	gavage; notified chemical diluted in corn oil; dose volume 2 mL/kg care was taken to avoid moisture induced degradation of the notified chemical to produce 2-butanone oxime and other products prior to dosing, including use of dried corn oil, nitrogen blanketing of the test material, daily preparation of the dose suspensions and use within 1 hr, and use of a high test material concentration and resultant low dose volume
Dose/Study duration:	0, 10, 150, 300 mg/kg/day for 28 days; additional groups at 0 and 300 mg/kg/day were allowed a 14 day recovery period
Test method:	OECD TG 407
Mortality:	there were no premature decedents during the study

Clinical observations:
A number of clinical signs of toxicity were observed in the 150 and 300 mg/kg/day groups. Clear wet matting or red matted material around the nose and mouth and salivation were observed in a dose related manner in both the males and females. Pale extremities were observed in the 300 mg/kg/day females. These signs were not observed during the recovery period.

No statistically significant differences in the functional observation battery or in body weight gains were observed.

Clinical chemistry/Haematology
Decreased red blood cells, haemoglobin and haemocrit, and increased mean corpuscular volume, mean corpuscular haemoglobin, platelets, nucleated red blood cells and leukocytes were observed in the 150 and 300 mg/kg/day groups. Abnormalities in red blood cell morphologies, including polychromasia, basophilic stippling, anisocytosis and macrocytes, were observed in the 150 and 300 mg/kg/day groups. In the 300 mg/kg/day animals after the recovery period, red blood cell morphologies were normal, and a reduction in the severity of the haematological changes was observed. Statistically significant differences in red blood cell counts, mean corpuscular volume, mean corpuscular haemoglobin and eosinophils were found.

In the 10 mg/kg/day group, no statistically significant changes in any individual haematological parameters were observed, although, for the majority of the parameters mentioned above, slight differences from controls in the direction of the statistically significant changes at higher doses were observed.

An increase in serum bilirubin was seen in the 150 and 300 mg/kg/day groups at the end of the 28 day treatment period. In addition, there was a decrease in potassium (300 mg/kg/day males and females), globulin (300 mg/kg/day males) and cholesterol (150 mg/kg/day males) and an increase in phosphorus and aspartate aminotransferase (AST) (300 mg/kg/day males), blood urea nitrogen (BUN) (10 mg/kg/day males) and albumin (300 mg/kg/day females). No statistically or toxicologically significant differences in clinical chemistry were observed in the 300 mg/kg/day animals after the 14 day recovery period.

Gross pathology:
Enlarged, blackish red spleens were observed in all 150 and 300 mg/kg/day animals at the end of the 28 day treatment period. After the 14 day recovery period, enlarged, blackish red spleens were seen in one of five females and four of five males. No other morphological abnormalities were observed.

An increase in absolute and relative spleen weights was observed in all 150 and 300 mg/kg/day animals at the end of the 28 day treatment period. Absolute and relative liver weights were statistically increased in 300 mg/kg/day females. Absolute and/or relative heart weights were increased in 150 and 300 mg/kg/day females and 300 mg/kg/day males. At the end of the 14 day recovery period, absolute and relative spleen weights were increased in 300 mg/kg/day males, and absolute and relative heart weights were increased in 300 mg/kg/day females.

Histopathology:
All tissues from the 300 mg/kg/day groups and controls after the 28 day treatment period and the spleen and liver of the 10 and 150 mg/kg/day animals were examined.

The spleens of the 300 mg/kg/day animals showed extramedullary haematopoiesis and accumulation of numerous haemosiderin laden macrophages in the red pulp. Similar findings but to a lesser extent were observed for the 150 mg/kg/day animals. Minimal extramedullary haematopoiesis was also observed in the 10 mg/kg/day animals, at levels slightly above background. The livers of the 300 mg/kg/day animals showed multiple scattered foci of extramedullary haematopoiesis within sinusoids and accumulation of numerous haemosiderin laden macrophages (Kupffer cells) lining sinusoids. Similar findings but to a lesser extent were observed for the 150 mg/kg/day animals. No abnormalities were found in the livers of the 10 mg/kg/day animals. No histopathological changes to the heart, despite the increased heart weights, or in other organs, were observed.

Comment:
The haematological changes in the 150 and 300 mg/kg/day animals were considered by the study authors to be indicative of a dose related anaemia. Serum bilirubin, indicative of red cell lysis, was elevated in these animals. The haemosiderin laden macrophages were also considered indicative of red blood cell degradation. The recovery animals showed an improvement in the haematological parameters indicating that the anaemia was reversible.

The histopathological observations in the spleens of the 10 mg/kg/day animals were all of minimal severity, and were at an incidence only slightly above controls and normal background levels. Haematological changes in the same direction as those observed for the higher doses were also observed for a majority of parameters at this dose level, indicating that similar anaemia may be occurring to a minimal degree.

Result:
A No Observed Adverse Effect Level (NOAEL) of 10 mg/kg/day was established in this study.

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium and Escherichia coli* Reverse Mutation Assay (Wagner & Klug, 1997)

Strains:	*Salmonella typhimurium* TA98, TA100, TA1535 and TA1537; *Escherichia coli* WP2uvrA(pKM101)
Metabolic activation:	10 % rat liver S9 fraction (Aroclor 1254-induced) in standard cofactors
Concentration range:	5000, 1800, 600, 200 and 75 μg/plate, dissolved in dimethyl sulphoxide (DMSO) and plated as a 50 μL aliquot
Positive controls:	with S9: 2-aminoanthracene TA98, TA100, TA1535, TA1537: 1.0 μg/plate WP2*uvr*A: 10 μg/plate without S9 TA98: 2-nitrofluorene 1.0 μg/plate TA100,TA1535: sodium azide 1.0 μg/plate TA1537: 9-aminoacridine 75 μg/plate WP2*uvr*A: methyl methanesulphonate 1000 μg/plate
Test method:	OECD TG 471 and 472 (plate incorporation method)
Comment:	all concentrations were tested in triplicate and concurrent positive and negative controls responded appropriately; two independent assays were performed precipitation was observed at 1800 μg/plate and above; no signs of appreciable toxicity manifested in thinning of the background lawn were observed; a reduction in the number of spontaneous revertants was seen for the highest concentration for TA1537 in the absence of metabolic activation, indicating slight toxicity no positive responses were observed with any tester strain in the presence or absence of metabolic activation large increases in the number of revertant colonies were seen for the positive controls in all cases, indicating that the test system responded appropriately
Result:	The notified chemical was non mutagenic under the conditions of the test

9.3.2 Chromosomal Aberration Assay in Human Lymphocytes (Akhurst, 1999)

Cells:	human lymphocytes

Metabolic activation system: 10 % rat liver S9 fraction (Aroclor 1254-induced) in standard cofactors

Dosing schedule:

Metabolic Activation	Experiment/ Study Number	Test concentration (μg/mL)	Controls
-S9	1	treatment time = 3 hr with 18 hr recovery 12.5, 25, 50, 100, 200, 400*, 800*, 1600*	Positive: mitomycin C 0.4, 0.8 μg/mL
	2	treatment time = 21 hours 200, 400*, 800*, 1600*	Negative: DMSO
+S9	1	treatment time = 3 hr with 18 hr recovery 12.5, 25, 50, 100, 200, 400*, 800*, 1600*	Positive: CP 25, 30 μg/mL
	2	treatment time = 3 hr with 18 hr recovery 400*, 800*, 1600*	Negative: DMSO

CP - cyclophosphamide
DMSO – dimethylsulphoxide
* - cultures selected for metaphase analysis

Test method: OECD TG 473

Comment: colcemid (0.1 μg/mL) was added 2 hr before harvest to arrest cells in metaphase

in the first test, in the presence or absence of metabolic activation, no reduction in mitotic index compared with solvent control was observed; in the second test, a reduction to 52 % was observed for the highest concentration in the absence of metabolic activation; no reduction was observed in the presence of metabolic activation

no statistically significant increases in the percentage of cells with structural chromosomal aberrations or in the incidence of polyploidy was observed in either experiment in the presence or absence of metabolic activation

the positive controls causes large, statistically significant increases in the proportion of aberrant cells in all cases, indicating that the test system responded appropriately

Result: the notified chemical was non clastogenic under the conditions of the test

9.3.3 Micronucleus Assay in the Bone Marrow Cells of the Mouse (Proudlock, 1999)

Species/strain:	mouse/CD-1
Number and sex of animals:	10/sex/group (vehicle control and 2000 mg/kg) 5/sex/group (500, 1000 mg/kg, positive control)
Doses:	500, 1000, 2000 mg/kg in corn oil; dose volume 10 mL/kg
Method of administration:	intraperitoneal injection
Positive control:	mitomycin C; 12 mg/kg by gavage; dose volume 20 mL/kg in water
Test method:	OECD TG 474
Comment:	2000 immature erythrocytes per animal from the femur bone marrow were examined 24 and 48 hours (vehicle control and 2000 mg/kg only) after dosing a small but statistically significant decrease in the proportion of immature erythrocytes was observed in animals treated with the notified chemical at the 48 hr examination; the value was within the historical control range no substantial increase in the proportion of micronucleated immature erythrocytes was seen at any dose at either sampling time a large statistically significant increase in micronucleated immature erythrocytes was seen for the positive control, indicating that the test system responded appropriately
Result:	the notified chemical was non clastogenic under the conditions of the test

9.4 Assessment of Toxicological Data for 2-Butanone oxime

2-Butanone oxime is a major decomposition product of the notified chemical in the presence of moisture, and inhalation of this chemical may occur upon exposure of the notified chemical to moist air.

A summary of the toxicity of 2-butanone oxime (National Institute of Occupational Safety and Health, 1997) indicates that it has an oral LD_{50} of 930 mg/kg in rats and 1000 mg/kg in mice. On inhalation of > 50 g/m^3 for 4 hours, rats showed somnolence. It was found to be a severe eye irritant.

It was considered carcinogenic or an equivocal carcinogen in rats by RTECS criteria (liver tumours) on inhalation of 75 ppm for 6 hours intermittent for 26 months in rats and 18 months in mice. On inhalation by rats or mice of 400 ppm for 6 hours intermittent for 4

weeks or 1000 ppm for 6 hours intermittent for 8 weeks, somnolence, changes in liver and spleen weight and methaemoglobiemia-carboxyhaemoglobin were observed.

9.5 Overall Assessment of Toxicological Data

Due to the reactivity of the notified chemical with water, many of the toxicological responses are likely to have resulted from the effects of 2-butanone oxime or from the reactivity of the notified chemical.

The notified chemical was found to have very low acute toxicity in rats (LD_{50} > 2000 mg/kg) although some signs of toxicity including enlarged discoloured spleens and one death at 2000 mg/kg were observed. It was found to have low acute dermal toxicity (LD_{50} > 2000 mg/kg). No inhalation toxicity study for the notified chemical was submitted. On exposure of the notified chemical to air, 2-butanone oxime is produced. This chemical shows significant toxicity on inhalation, and is a possible carcinogen based on animal studies by this route. 2-Butanone oxime is on the NOHSC *List of Designated Hazardous Substances* (NOHSC, 1999b) and is classified as irritant with the risk phrases R36: Irritating to eyes and R43: May cause sensitisation by skin contact.

The notified chemical was found to cause skin irritation which persisted for 9 days although at low levels. The presence of persistent irritation results in the notified chemical being classified as a skin irritant, with the risk phrase R38, in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (Approved Criteria) (NOHSC, 1999a). It was found to be a slight eye irritant. The notified chemical was found to be a moderate skin sensitiser, which is consistent with the R43 classification of the decomposition product, 2-butanone oxime. The notified chemical should therefore be classified as a hazardous substance, with the risk phrase R43, 'May cause sensitisation by skin contact'.

In a 28 day oral repeat dose study in rats, a NOAEL of 10 mg/kg/day was established. At higher doses (150 and 300 mg/kg/day), reversible dose related anaemia was observed, along with histopathological changes in the spleen and liver. Minimal changes in haematology parameters and histopathological changes in the spleen at 10 mg/kg/day indicated that these effects were occurring to a slight degree at this dose level, as well. These effects are similar to the reported effects for 2-butanone oxime, which is likely to be formed by decomposition of the notified chemical on ingestion.

The notified chemical was not found to be genotoxic in three *in vitro* and *in vivo* studies. 2-Butanone oxime was considered carcinogenic or an equivocal carcinogen in rats by RTECS criteria (liver tumours) on inhalation of 75 ppm for 6 hours intermittent for 26 months. On inhalation by rats or mice of 400 ppm for 6 hours intermittent for 4 weeks or 1000 ppm for 6 hours intermittent for 8 weeks, somnolence, changes in liver and spleen weight and methaemoglobiemia-carboxyhaemoglobin were observed. Degenerative effects on the olefactory epithelium were also observed. 2-Butanone oxime has also been classified as a carcinogen (MAK-2) in Germany. The European Union CMR Working Group (http://www.hse.gov.uk/hthdir/noframes/chip/chip7.htm) has recently revised the health effects classification for 2-butanone oxime and the risk phrase R40(3): 'Possible risk of irreversible effects' is assigned to 2-butanone oxime.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The following ecotoxicity studies have been supplied by the notifier. The tests were carried out according to OECD Test Methods.

Species	Test	Concentrations[a] (mg/L)	Result (mg/L)	Reference
Rainbow trout *(Oncorhynchus mykiss)*	96 h semi-static acute	100	LC_{50} > 89.8 NOEC > 89.8	(Jenkins, 2000b)
Water Flea (*Daphnia magna*)	48 h acute	100	EC_{50} > 101 NOEC > 101	(Jenkins, 2000a)
Algae (*Selenastrum capricornutum*)	96 h growth inhibition	6.25, 12.5, 25, 50 and 100	E_RC_{50} > 22 E_BC_{50} > 13.8 NOEC = 4.34	(Jenkins, 1999)

[a] nominal concentration
NOEC - no observable effect concentration

After a range finding test using 1, 10 and 100 mg/L it was determined that the nominal concentration for the studies on fish and daphnia should be 100 mg/L. Due to the reactivity of the notified chemical with water no attempt was made to maintain the concentration of the chemical in the media through out the study, however the media was replaced daily.

The fish toxicity study was conducted using OECD method 203 (Jenkins, 2000b). In this study 10 fish were placed in tanks holding 14 L of diluent water and 1.4 g of the chemical. The reaction of the chemical with water produces 2-butanone oxime and phenylsiloxane. To ascertain the exposure level of the chemical the concentration of 2-butanone oxime was determined via GLC analysis. The following parameters were maintained throughout the study: temperature 15±2ºC, a photoperiod of 16 hrs light/8 hours dark, and no feeding. Daily measurements of temperature, pH and dissolved oxygen were taken along with observation of morality and behaviour. The overall mean concentration of the notified chemical (determined from the measured concentration of 2-butanone oxime) was 89.9 mg/L. There were no mortalities or significant changes in behaviour, therefore the NOEC was equal to or greater than 89.8 mg/L and the LC_{50} was greater than this. This indicates that the chemical is at worst slightly toxic to fish.

OECD method 202 was used to study the effect of the notified chemical on daphnia (Jenkins, 2000a). The 48 hr study consisted of four replicates with five daphnia per vessel with the temperature maintained at 20±2ºC, photoperiod of 16 hours light/8 hours dark, and no feeding. The nominal concentration was 100 mg/L, with the overall mean concentration of the notified chemical (determined from measured concentration of 2-butanone oxime) was 101 mg/L. Daily observations of behaviour and measurements of temperature, pH and oxygen were taken. There were no mortalities/behaviour changes and no significant changes in environmental parameters. The NOEC is therefore equal to or greater than 101 mg/L, with the LC_{50} being greater than 101 mg/L. This indicates that the chemical is practically non-toxic to daphnia.

OECD method 201 was used to determine the effect of the chemical on algae (Jenkins, 1999). The study was run in triplicate, with the algae being exposed to notified chemical dissolved in

the nutrient medium. The hydrolysis product 2-butanone oxime was measured via GLC to ascertain the actual exposure concentration, thus it was determined that the overall mean concentrations were 4.34, 11.0, 21.7, 44.5 and 89.4 mg/L. The temperature was maintained between 21 and 25ºC and the other environmental parameters did not vary significantly. The algal cell density was determined daily. The E_RC_{50} was greater than 22 mg/L, the E_BC_{50} was greater than 13.8 mg/L, and the NOEC was estimated to be 4.34 mg/L. This indicates that the chemical is slightly toxic to algae.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The notified chemical is a minor component of a specialist silicone sealant. It reacts rapidly with moisture, and this is the basis for its catalytic action in inducing the cross linking of silicone polymers. Approximately 100 % of the sealant will be used in the construction of roads/pavements.

Since the cured silicone sealant will be associated with other road/pavement construction materials, it will be finally disposed of as rubble and most likely placed into landfill. In landfill, the cured sealant is expected to be very inert. After a very long time some degradation may occur. Incineration of the sealant would produce silica which would become part of the ash or furnace slag, and would also be eventually placed into landfill.

Since the notified chemical is highly reactive with atmospheric moisture, any residual pure chemical/product will quickly form either 2-butanone oxime or a rubbery inert mass. This waste and any other usage waste is likely to end up in landfill, where the majority will be in an inert matrix.

Neither hydrolysis product is toxic to aquatic organisms. The environmental hazard from the new compound is assessed to be low when used in the indicated manner, as a catalyst for silicone polymers in road/pavement construction sealants.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Hazard Assessment
The notified chemical is of very low oral toxicity in the rat (LD_{50} > 2000 mg/kg), although signs of toxicity and one death occurred at 2000 mg/kg. It is of low dermal toxicity in rats (LD_{50} > 2000 mg/kg). The notified chemical was found to cause skin irritation which persisted for 9 days although at low levels. The presence of persistent irritation results in the notified chemical being classified as a skin irritant, with the risk phrase R38, in accordance with the Approved Criteria. It was found to be a slight eye irritant. The notified chemical was found to be a moderate skin sensitiser, and is classified as a skin sensitiser, with the risk phrase R43, in accordance with the Approved Criteria. The notified chemical was not found to be genotoxic in three *in vitro* and *in vivo* studies.

In a 28 day oral repeat dose study in rats, a NOAEL of 10 mg/kg/day was established. At higher doses, reversible dose related anaemia was observed, along with histopathological changes in the spleen and liver. Similar but minimal changes were observed at 10 mg/kg/day indicated that these effects were also occurring to a slight degree at this dose level.

On exposure to moist air, 2-butanone oxime is produced by decomposition of the notified chemical. 2-Butanone oxime is a skin sensitiser, and on repeated oral dosing has been shown to produce similar changes to those observed in the 28 day repeat dose study for the notified chemical. 2-Butanone oxime shows significant toxicity on inhalation, with degenerative effects on the olefactory epithelium. It is a possible carcinogen based on animal studies by inhalation. 2-Butanone oxime is on the NOHSC *List of Designated Hazardous Substances* (NOHSC, 1999b) and is classified as irritant with the risk phrases R36: Irritating to eyes and R43: May cause sensitisation by skin contact. Due to the observed effects in animal carcinogenesis studies, the EU (http://www.hse.gov.uk/hthdir/noframes/chip/chip7.htm) has recently revised the health effects classification for 2-butanone oxime and the risk phrase R40(3): 'Possible risk of irreversible effects' is assigned to 2-butanone oxime. Because of the potential of release of 2-butanone oxime from the notified chemical, this risk phrase should also be applied to the notified chemical.

Human exposure to the notified chemical will occur under conditions where 2-butanone oxime is produced, by contact of the notified chemical with moist air or body fluids. The notified chemical contains approximately 71 % 2-butanone oxime which could potentially be released under these conditions, and, in the absence of appropriate toxicity data on the notified chemical for assessment, the risk phrase R40(3) should apply to the notified chemical.

The MSDS for the notified chemical indicates that it is a hazardous substance. Apart from the health effects described above, the notified chemical may also react violently with electrophiles such as ferric chloride. The MSDS for the formulated sealant, containing < 4 % notified chemical, indicates that it is also a hazardous substance, with health effects including skin sensitisation, due to the notified chemical, and degenerative effects of vapours on mucous membranes if inhaled, due to the presence of 2-butanone oxime.

Occupational Health and Safety

There is little potential for significant occupational exposure to the notified chemical in the transport and storage of OS-9000 or the silicone sealants containing the notified chemical. There may be exposure during the reformulation of the notified chemical and during use of silicone sealants containing the notified chemical.

During reformulation and end use, the main exposure route for the notified chemical will be dermal. The notified chemical has low volatility, but there is significant potential for exposure to 2-butanone oxime by inhalation upon contact of the notified chemical with moist air. While the mixing occurs in a closed system, exposure to drips and spills of the notified chemical and to vapours of 2-butanone oxime is possible during weighing and addition of the notified chemical. It is therefore necessary for a high level of respiratory protection to be used during reformulation of the notified chemical, including exhaust ventilation, and where this is not adequate to reduce 2-butanone oxime levels sufficiently, a respirator with organic vapour filter or air fed respirator. A high level of skin protection is also required due to the sensitising potential of the notified chemical.

Exposure to drips and spills of the silicone sealant (< 4 % notified chemical) is also possible during packing and use of the sealants. The formation of drips and spills of the sealants is

expected to be limited due to the paste-like consistency of the finished sealant. Exposure to 2-butanone oxime vapours should be reduced by the slow reaction of the paste with atmospheric moisture and the outdoor use of the sealant product. On use of the sealants in confined spaces, use of respiratory protection to reduce exposure to 2-butanone oxime may be required.

The notifier has recommended an exposure limit of 3 ppm TWA, 10 ppm STEL for 2-butanone oxime. Respiratory protection should be used if the exposure limit is exceeded. The MSDS also indicates that butyl rubber, neoprene or nitrile gloves and a butyl rubber apron should be used to reduce the possibility of skin sensitisation on handling the notified chemical. Butyl rubber, neoprene or PVA gloves are recommended for handling the sealants.

Public Health
Products containing the notified chemical will only be used by professional tradespeople and will not be available to the general public. Exposure of the general public as a result of transport and disposal of the product containing the notified chemical is assessed as being negligible. The general public may make dermal contact with sealant containing the notified chemical after it has been cured. However, the notified chemical is not likely to be present because it is completely reacted in the cured sealant products. Therefore public exposure to the notified chemical is likely to be negligible.

Based on the above information, it is considered that OS-9000 will not pose a significant hazard to public health when used in the proposed manner.

13. RECOMMENDATIONS

To minimise occupational exposure to OS-9000 and the decomposition product 2-butanone oxime the following guidelines and precautions should be observed:

- Where engineering controls and work practices do not reduce 2-butanone oxime vapour exposure to safe levels, an air fed respirator should be used;
- Butyl rubber, neoprene or nitrile gloves, safety goggles, chemical resistant industrial clothing and footwear should be used while handling the notified chemical; where splash hazards exist, a butyl rubber apron and full face shield should also be used;
- Butyl rubber, neoprene or PVA gloves, safety goggles, chemical resistant industrial clothing and footwear should be used while handling the sealants containing the notified chemical;
- Spillage of the notified chemical should be avoided. Spillages should be cleaned up promptly with absorbents which should then be put into containers for disposal;
- A copy of the MSDS should be easily accessible to employees.

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

Guidance in selection of goggles may be obtained from Australian Standard (AS) 1336 (Standards Australia, 1994) and Australian/New Zealand Standard (AS/NZS) 1337 (Standards Australia/Standards New Zealand, 1992); for industrial clothing, guidance may be found in AS 2919 (Standards Australia, 1987) and AS 3765.2 (Standards Australia, 1990); for impermeable gloves or mittens, in AS 2161 (Standards Australia/Standards New Zealand, 1998); for occupational footwear, in AS/NZS 2210 (Standards Australia/Standards New Zealand, 1994); for respirators, in AS/NZS 1715 (Standards Australia/Standards New Zealand, 1994) and AS/NZS 1716 (Standards Australia/Standards New Zealand, 1994).

The following regulatory action is recommended:

- Consideration of 2-butanone oxime by the National Occupational Health and Safety Commission for adoption of the EU carcinogenicity health effects classification and for consideration of a national exposure standard.

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.

15. REQUIREMENTS FOR SECONDARY NOTIFICATION

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

16. REFERENCES

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Attachment 1

The Draize Scale (Draize, 1959) 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 (Draize *et al*., 1944) 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.
		Swelling with lids half-closed	3 mod.	Discharge with moistening of lids and hairs and considerable area around eye	3 severe
Diffuse beefy red	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

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