File No: NA/866

February 2001

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

Bis(2,4-dicumylphenyl) pentaerythritol diphosphite (Doverphos S-9228)

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Director
Chemicals Notification and Assessment

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FULL PUBLIC REPORT

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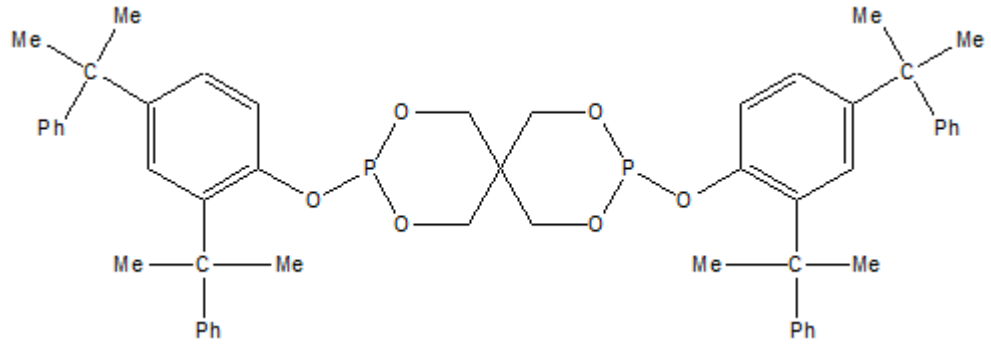
1. APPLICANT

B F Specialty Chemicals (Australia) Pty Ltd of Unit 9, 43-51 College St, Gladesville, NSW 2111 (ABN 31 051 283 866) has submitted a standard notification statement in support of their application for an assessment certificate for bis(2,4-dicumylphenyl) pentaerythritol diphosphite. No exempt information has been requested.

2. IDENTITY OF THE CHEMICAL

Chemical Name:	2,4,8,10-tetraoxa-3,9-diphosphaspiro[5.5]undecane, 3,9-bis[2,4-bis(1-methyl-1-phenylethyl)phenoxy]-
Chemical Abstracts Service (CAS) Registry No.:	154862-43-8
Other Names:	bis(2,4-dicumylphenyl) pentaerythritol diphosphite
Marketing Name:	Doverphos S-9228
Molecular Formula:	$C_{53}H_{58}O_6P_2$

Structural Formula:



Molecular Weight:	852
Method of Detection and Determination:	may be determined by extraction in methylene chloride and HPLC separation characterised by: UV/visible spectroscopy

IR spectroscopy
^{31}P nmr spectroscopy

Spectral Data:

UV/vis
λ_{max} = 274 nm, $\varepsilon = 3.6 \times 10^4$
λ_{max} = 241 nm, $\varepsilon = 3.87 \times 10^4$ (chloroform solution)

IR
3083, 3057, 3026, 2971, 2931, 2885, 1607, 1580, 1548, 1499, 1471, 1453, 1441, 1400, 1364, 1303, 1288, 1257, 1234, 1211, 1193, 1166, 1154, 1100, 1088, 1036, 1011, 968, 921, 900, 878, 834, 814, 789, 770, 739, 723, 698, 677, 645, 604, 573, 554, 523, 463, 413 cm^{-1}

^{31}P nmr
117.65 ppm

3. PHYSICAL AND CHEMICAL PROPERTIES

All physical and chemical properties were measured for the pure notified chemical.

Appearance at 20°C & 101.3 kPa: off white, free flowing powder or compacted pellets

Melting Point: 221 - 230°C

Specific Gravity: 1.26

Vapour Pressure: < 10^{-6} kPa at 25°C

Water Solubility: < 0.05 mg/L at 20°C

Particle Size:

size range (μm)	mass %
< 0.42	0.31
0.42 – 0.87	1.07
0.87 – 1.80	4.06
1.80 – 3.59	6.49
3.59 – 7.19	10.94
7.19 – 13.97	17.54
13.97 – 28.64	24.32
28.64 – 63	35.27
> 63	0

Partition Co-efficient (n-octanol/water): log P_{ow} > 6 at 22ºC

Hydrolysis as a Function of pH: not determined due to low water solubility

Adsorption/Desorption: log K_{oc} > 4.64 (calculated)

Dissociation Constant:	no dissociable groups are present
Flash Point:	not applicable
Flammability Limits:	not flammable
Autoignition Temperature:	> 440°C
Explosive Properties:	not explosive
Reactivity/Stability:	stable under normal environmental conditions

3.1 Comments on Physico-Chemical Properties

The physico-chemical properties were determined using accepted OECD test methods.

The melting range was determined using differential scanning calorimetry with a heating rate of 1 K/min, and the strongest endothermic heat effect was observed in the range 221-230ºC. The notified chemical decomposes without boiling at temperatures above 240ºC (Grothe, 1996a).

The relative density was determined at 20ºC using a gas comparison pycnometer. Triplicate measurements were performed on two test samples (Grothe, 1996b).

The vapour pressure was estimated based on the calculated boiling point (740ºC by the Meissner method) using the Modified Watson Correlation (Grothe, 1996c). Also, the vapour pressure was calculated from the decomposition temperature of > 240ºC, resulting in a value of < 0.61 Pa.

The water solubility was estimated in a preliminary test using a simplified flask method to be < 10 mg/L. Therefore the column elution method was used for the definitive test and it was concluded that the water solubility of the main component of the substance was < 0.05 mg/L at 20ºC (Grothe, 1996d).

Hydrolysis of the notified chemical could not be determined due to its low water solubility. The saturation concentrations of the substance in pH 4, 7 and 9 buffers containing 1 % acetonitrile were determined to be < 0.1 mg/L (Grothe, 1996e). Hydrolysis of the phosphorus-oxygen bond is however likely to occur slowly under environmental conditions.

The n-octanol/water partition coefficient was determined using the HPLC method, where the retention time of the test compound on a reversed-phase column was compared with those for six reference compounds with known values for P_{ow} (Grothe, 1996f). The reference compounds included nitrobenzene, bromobenzene, 1,4-dichlorobenzene, biphenyl, 1,2,4-trichlorobenzene and 2,4-DDT. From the retention times of the notified chemical on the column, Log P_{ow} was determined to be > 6, indicating high affinity for the oil phase.

The value for Log K_{oc}, which is a measure of the compound's ability to bind to the organic component of soils and sediments, was estimated using regression equations relating K_{oc} with water solubility and molecular weight (Volkel, 2000). A further estimation was calculated

using a regression equation relating K_{oc} with P_{ow}. This high value for Log K_{oc} indicates that the chemical will bind strongly to the organic component of soils and sediments.

4. PURITY OF THE CHEMICAL

Degree of Purity: 98 %

Hazardous Impurities: none

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

Chemical name:	phenol, 2,4-bis(1-methyl-1-phenylethyl)-
Weight percentage:	< 2
CAS No.:	2772-45-4

Additives/Adjuvants: none

5. USE, VOLUME AND FORMULATION

The notified chemical is to be used as an antioxidant/stabiliser for thermoplastic engineering polymers, including polyethylene, polypropylene, polyamides, polyesters, polyethers and polycarbonates. It may be used in a wide variety of applications, particularly where thermal stability is required, such as in dishwashers, toasters and dryers. In Australia, the majority of the notified chemical is expected to be used in the polyolefin and polystyrene industry. Products to be made from plastics including the notified chemical include containers for food, clothing and other items, food wrap, household appliances and automotive parts.

The notified chemical will be imported in pure form, as powder or compacted pellets, in 50 kg metal foil lined fibre drums. It will be reformulated in Australia by blending with solid polymer along with other additives, melting and extruding as pellets for sale to the end users. The notified chemical will be present in the finished polymer blend at 0.05 – 0.15 % by weight.

The notifier estimates that the import volume for the notified chemical will be 0.5 tonnes in the first year, increasing to 1 tonne per annum after one year and 2 tonnes per annum after three years.

6. OCCUPATIONAL EXPOSURE

Transport and Storage
No details of the numbers of workers involved or the frequency of exposure were given by the notifier. These workers are not expected to be exposed to the notified chemical except in the case of an accident involving rupture of the packaging.

Extrusion Operator
The notifier estimates that 10 workers will be exposed to the notified chemical, for 2 hours per day. The extrusion operators will transfer the notified chemical from the imported drums into the automated feed hopper of the extruder, and also clean the extruder by purging with pure polymer resin. The extrusion equipment will be automated, and after extrusion, the pellets will be packaged in bags or drums, or shipped in bulk to fabricators. The notified chemical will be present at low concentrations (0.05 – 0.15 %) and encapsulated in the polymer pellets. Exposure is therefore expected to be negligible after extrusion.

Exposure will be mainly by the dermal route only if compacted pellets are used, however inhalation exposure is possible if the notified chemical is used in powder form. The notifier indicates that workers will wear protective clothing and gloves while handling the compacted pellets, and that a dust mask will also be used if the notified chemical is handled in powder form.

The Material Safety Data Sheet (MSDS) for Doverphos S-9228 indicates that hazardous chemicals including phosphorous acid and phosphine may be formed on thermal decomposition (above 240ºC) of the notified chemical, and care should be taken to ensure that residual polymer containing the notified chemical in the extruder nozzle is not overheated.

Packaging Disposal
The notifier indicated that 4 workers will be involved in collecting empty drums for transport to incineration or landfill, for 1 hour per day. Little exposure is expected for these workers as the drums would be reclosed after emptying.

Plastics Fabrication
The notifier did not provide estimates of the number of workers or of exposure details for fabrication of plastic articles containing the notified chemical. Articles will be manufactured by extrusion, moulding, blow moulding or film blowing at a number of fabrication plants. Polymer pellets and the final articles will contain the encapsulated notified chemical at low concentrations. Exposure for these workers is therefore expected to be negligible.

7. PUBLIC EXPOSURE

The notified chemical is not available for sale to the public and will be used as a an ingredient in plastics manufacture. The potential for public exposure to the notified chemical during transport, reformulation or disposal is assessed as negligible. The public may make dermal contact with some plastic products containing the notified chemical and may eat or drink foodstuffs that have been in contact with plastics containing the notified chemical.

8. ENVIRONMENTAL EXPOSURE

8.1 Release

Release of the notified chemical during the reformulation process is expected to be of low volume and this should only be sent to landfill or for incineration. No release is expected from spills or equipment cleaning as any spills will be cleaned up and recycled into the next

batch of polymer as will the polymer purge used to clean the equipment after use. The only release anticipated by the notifier is the residue remaining in the import drums after emptying. These residues are estimated to be up to 2 g per 50 kg drum or 80 g per annum at the maximum import volume of 2 tonnes per annum.

Very little release of the chemical is anticipated during use of the formulated granules in the preparation of the moulded, or extruded plastic products. No release is expected from equipment cleaning and spills and all polymer waste from these routes will be recycled into the next batch of polymer. The notifier did not indicate the fate of empty polypropylene bags, but it is expected that these would be either incinerated or placed into landfill. The notifier estimates that approximately 0.2 % of the polymer pellets will remain as residues in the bulk sacks after emptying and this equates to a maximum disposal volume of 4 kg per annum of the notified chemical at the maximum import volume.

Articles containing the notified chemical are likely to have a wide distribution throughout the community which indicates that long term release of the chemical (eg as result of discarding old consumer products, electrical equipment or car parts) would be very diffuse.

Some release of the chemical is likely as a result of "blooming" from the manufactured articles during day to day use. The notified chemical will slowly diffuse from the interior of the plastic article to the surface, where it may be removed through cleaning processes, and released in waste water (presumably mainly to sewer). However, release through this route is expected to be diffuse and at very low levels.

While recycling of the plastic in discarded articles is theoretically possible, this is not anticipated to take place on a large scale. Consequently, the majority of the imported chemical will be discarded with old plastic articles at the end of their useful lives, and these are likely to be either incinerated or be placed into landfill.

8.2 Fate

A test for ready biodegradability conducted according to the Modified Sturm Test (OECD TG 301B) indicated that the chemical was practically non-biodegradable under the conditions of the test (Grutzner, 1996a). Biological Oxygen Demand (BOD) measurements after 28 days incubation of the test substance with sewage sludge indicated 0.2 – 2 % degradation. The reference compound used during this test was aniline, which was 97.2 % degraded over the 28 day test period. The result of this test indicates that the notified chemical is not readily biodegradable.

Although little of the notified chemical is likely to be released during manufacturing processes, any that is released is likely to be placed into landfill or incinerated. The eventual fate of the majority of the imported chemical will be strongly linked to that of discarded plastic articles, which are likely to be either placed into landfill or be incinerated.

Notified chemical disposed of into landfill will be incorporated in a solid polymer matrix (ie the plastic article) where it will be immobilised. However, the polymer matrix will be slowly degraded through the biological and abiotic processes operative in landfills, and this would release the notified chemical. Diffusion of the polymer to the surface of broken pieces of plastic ("blooming") would contribute to this mode of release.

The compound has a large estimated value for K_{oc} (Log K_{oc} > 4.3) indicating strong affinity for the organic component of soils and sediments, and the strong binding indicates that it would have low mobility in these media. The chemical is not readily biodegradable, but when bound to, or otherwise associated with, soils and sediments it could be expected to be slowly degraded through the agency of biological and abiotic processes operative within landfills.

Complete combustion of the chemical in the presence of excess oxygen would be expected to destroy the material with production of water vapour and oxides of carbon. Some solid phosphate salts would also be formed, and these would become incorporated with the waste incinerator ash.

The high value for Log P_{ow} (> 6) and low water solubility (<0.05 mg/L) indicate large potential for bioaccumulation (Connell, 1990). However, the moderate molecular weight (852) and the low and diffuse release volumes along with the fact that the chemical is unlikely to enter the water compartment mitigate the risks associated with bioaccumulation.

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Summary of the acute toxicity of bis(2,4-dicumylphenyl) pentaerythritol diphosphite

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	LD_{50} > 5000 mg/kg	(O'Meara, 1994a)
acute dermal toxicity	rat	LD_{50} > 2000 mg/kg	(Arcelin, 1996a)
skin irritation	rabbit	non-irritant	(O'Meara, 1994b)
eye irritation	rabbit	slight irritant	(O'Meara, 1994c)
skin sensitisation	guinea pig	non-sensitiser	(Arcelin, 1996b)

9.1.1 Oral Toxicity (O'Meara, 1994a)

Species/strain: rat/Sprague-Dawley ZML:SD (MBM)

Number/sex of animals: 5/sex

Observation period: 14 days

Method of administration: gavage; notified chemical dissolved in 0.5 % aqueous

	methylcellulose; dose 5000 mg/kg, dose volume 20 mL/kg
Test method:	OECD TG 401
Mortality:	there were no premature decedents during the study
Clinical observations:	light coloured faeces were observed for all animals on day 1; decreased faeces were observed for one female on days 10 and 11; no other clinical signs of toxicity were observed
Morphological findings:	mottled lungs were observed in one animal at necropsy; no other gross pathological finding were made
LD_{50}:	> 5000 mg/kg
Result:	the notified chemical was of very low acute oral toxicity in rats

9.1.2 Dermal Toxicity (Arcelin, 1996a)

Species/strain:	rat/HanIbm: WIST (SPF)
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	semi-occlusive patch; notified chemical used as a 50 % (w/v) solution in polyethylene glycol (PEG 400); dose level 2000 mg/kg
Test method:	OECD TG 402
Mortality:	there were no premature decedents during the study
Dermal observations:	no local effects at the application site were observed
Clinical observations:	one female lost weight during the first week of the study; no other clinical signs of toxicity were observed
Morphological findings:	no gross 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 inhalation toxicity data was submitted by the notifier.

9.1.4 Skin Irritation (O'Meara, 1994b)

Species/strain:	rabbit/ New Zealand White
Number/sex of animals:	3/sex
Observation period:	3 days
Method of administration:	semi-occlusive patch; 0.5 g notified chemical moistened with 0.5 mL deionised water; 4 hr exposure; remnant notified chemical removed with moistened paper towel
Test method:	OECD TG 404
Observations:	one animal showed very slight erythema (Draize score 1) at the 1 hr observation; all other Draize scores were zero
Result:	the notified chemical was non-irritating to the skin of rabbits

9.1.5 Eye Irritation (O'Meara, 1994c)

Species/strain:	rabbit/ New Zealand White
Number/sex of animals:	3/sex
Observation period:	7 days
Method of administration:	0.08 g (0.1 mL) solid notified chemical was placed in the conjunctival sac of one eye; the other eye was used 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***			***7 days***		
Cornea	All Draize scores were zero																	
Iris	All Draize scores were zero																	
Conjunctiva	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***
1♂	2	1	2	2	0	0	1	0	0	1	0	0	1	0	0	0	0	0

2♂	2	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3♂	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4♀	2	1	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5♀	2	2	2	2	0	1	0	0	0	0	0	0	0	0	0	0	0	0
6♀	2	1	2	2	0	1	1	0	0	0	0	0	0	0	0	0	0	0

[1] see Attachment 1 for Draize scales
o = opacity a = area r = redness c = chemosis d = discharge

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

9.1.6 Skin Sensitisation (Arcelin, 1996b)

Species/strain: guinea pig/Ibm: GOHI: SPF

Number of animals: test group: 20 male
control group: 10 male

Induction procedure:

test group:

day 1 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 physiological saline;
2. 0.1 mL 5 % test substance in ethanol;
3. 0.1 mL 5 % test substance emulsion in physiological saline 50 % v/v with FCA

day 7 local irritation was induced at the shaved test site by application of 0.5 mL of 10 % sodium lauryl sulphate in paraffinum perliquidum

day 8 test substance (50 % in ethanol) was applied by occlusive patch to the same site that received the intradermal injections for 48 hours

control group:

day 1 on a prepared area of skin from the shoulder region of test animals, three pairs of intradermal injections were administered as follows:

4. 0.1 mL of Freund's Complete Adjuvant (FCA) 50 % v/v in physiological saline;
5. 0.1 mL ethanol;
6. 0.1 mL 1:1 (w/w) ethanol in physiological saline 50 % v/v with FCA

day 7 local irritation was induced at the shaved test site by

	application of 0.5 mL of 10 % sodium lauryl sulphate in paraffinum perliquidum
day 8	ethanol was applied by occlusive patch to the same site that received the intradermal injections for 48 hours

Challenge procedure:

day 22	patches of approximately 2 cm square were saturated with test substance (50 % in ethanol) and applied to the shaved left flank of each animal under occlusive conditions for 24 hr; patches with ethanol only were applied to the right flank
	dermal reactions were scored at 24 and 48 hours after patch removal

Test method: OECD TG 406

Challenge outcome:

	Test animals		***Control animals***	
Challenge concentration	***24 hours****	***48 hours****	***24 hours***	***48 hours***
50%	0/20	0/20	0/10	0/10

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

Result: the notified chemical was not sensitising to the skin of guinea pigs

9.2 Repeated Dose Toxicity (Allard, 1996)

Species/strain: rat/IcoIbm:OFA (Sprague-Dawley), outbred, SPF

Number/sex of animals: low and mid dose: 5/sex
control and high dose: 10/sex

Method of administration: gavage; test substance dissolved in corn oil; dose volume 5 mL/kg

Dose/Study duration: control: 0 mg/kg/day
low dose: 50 mg/kg/day
mid dose: 200 mg/kg/day

high dose: 500 mg/kg/day
study duration 28 days; 5 animals per sex in control and high dose groups were given a 14 day recovery period following completion of dosing

Test method: OECD TG 407

Clinical observations:
One 500 mg/kg/day male showed a smaller left eye due to crusts and corneal opacity; opthalmic examination found abnormalities including corneal opacity and degeneration of the eye in a small proportion of animals across all groups. No other clinical signs of toxicity were observed.

Food Consumption/Body Weights
Males in the 500 mg/kg/day group showed slightly higher food consumption from day 8 to the end of the recovery period; this group had higher food consumption in the pretest period. No effect of treatment on body weight was observed.

Clinical chemistry/Haematology
No haematological differences between the treated and control animals were seen after the treatment period.

After the recovery period, the treated animals (500 mg/kg/day) showed slightly decreased erythrocyte count, marginally increased mean corpuscular haemoglobin and slightly shortened activated partial thromboplastin time in both sexes; marginally decreased haemoglobin concentration, slightly decreased haemocrit, slightly increased mean corpuscular volume, slightly decreased total leucocyte count and a slight dcrease in segmented neutrophils and lymphocytes in males; and marginally increased mean corpuscular haemoglobin concentration in females.

After the treatment period, the 500 mg/kg/day males showed increased uric acid level and aspartate aminotransferase activity, and marginally increased total bilirubin level. An increase (not statistically significant) in total bilirubin level was also seen in the 500 mg/kg/day females.

After the recovery period, the treated animals (500 mg/kg/day) showed slightly increased creatinine level, total cholesterol level, phospholipid level and gamma-glutamyltransferase acitivity, and marginally lower sodium level in both sexes. The changes observed in males after the treatment period were not statistically significant after the recovery period, although the total bilirubin level was higher than controls for both males and females, and aspartate aminotransferase activity was higher in the treated males than the controls.

Gross Pathology:
Some statistically significant differences in organ weights were observed. After the treatment period, the relative heart weight was lower in both sexes at 50 mg/kg/day, the relative thyroid weight and relative adrenal weight were lower in the 200 mg/kg/day females and the relative spleen weight was lower in the 500 mg/kg/day females.

After the recovery period, a lower relative adrenal weight was observed for the 500 mg/kg/day males.

Macroscopic pathological findings were occasional occurrences, or scattered across all groups. These included dilated renal pelves, reddish discolouration in various organs and dilated uterine horns, and also accentuated lobular pattern of the liver in 3 control animals and 14 treated animals.

Histopathology:
For animals which showed accentuated lobular pattern of the liver, multifocal or diffuse hepatocellular vacuolation was observed, at minimal to moderate severity. This was observed in all groups. For the males, the incidence and severity was greater for the 500 mg/kg/day animals than for the controls, while the opposite was observed in the females. This finding was also observed after the recovery period.

Remaining microscopic findings were occasional occurrences, or scattered across all groups.

Comment:
The differences between control and treated animals were generally slight, and within the range of historical control data for this strain of rat. The liver observations were attributed by the study authors to slight hepatic lipidosis, resulting from the use of corn oil as the delivery vehicle.

Result:
A No Observed Effect Level (NOEL) of 200 mg/kg/day was established in this study, based on the changes in clinical biochemistry observed in the 500 mg/kg/day males at the end of the treatment period.

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* and *Escherichia coli* Reverse Mutation Assay (Wollny, 1996b)

Strains:	*Salmonella typhimurium*: TA98, TA100, TA1535, TA1537 *Escherichia coli*: WP2, WP2 *uvrA*
Metabolic activation:	rat liver S9 fraction from animals pretreated with phenobarbital and β-napthoflavone, 15 % (v/v) in standard cofactors
Concentration range:	33, 100, 333, 1000, 2500 and 5000 μg/plate as suspension
Positive controls:	with S9: 2-aminoanthracene

	2.5 μg/plate (*S. typhimurium* strains) 10 μg/plate (*E. coli* strains) without S9 TA98, TA1537: 4-nitro-o-phenylenediamine 10 μg/plate TA100,TA1535: sodium azide 10 μg/plate WP2, WP2*uvr*A: methyl methanesulphonate 5 μL/plate
Test method:	OECD TG 471 and TG 472
Comment:	two independent tests were performed in triplicate, using both the plate incorporation and pre-incubation methods no toxic effects, either in the presence or absence of metabolic activation, occurred at the dose levels used 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 HPRT Gene Mutation Assay in Chinese Hamster Ovary Cells (Wollny, 1996a)

Cells:	Chinese hamster ovary (CHO)
Metabolic activation system:	rat liver S9 fraction from animals pretreated with Arochlor 1254, 0.75 % protein, in standard cofactors
Dosing schedule:	

Metabolic Activation	Experiment/ Study Number	Test concentration (μg/mL)	Controls
-S9	1	treatment time = 4 hr 10*, 30*, 100*, 300*, 1000, 3000	Positive: EMS 0.6 mg/mL
	2	treatment time = 4 hours 10, 30*, 100*, 200*, 300*	Negative: DMSO

+S9	1	treatment time = 4 hr 10*, 30*, 100*, 300*, 1000, 3000*	Positive: DMBA 3.85 μg/mL
	2	treatment time = 4 hr 10*, 30*, 100*, 300*, 5000*	Negative: DMSO

EMS - ethylmethanesulphonate
DMBA - 7.12-dimethylbenz(a)anthracene
DMSO - dimethylsulphoxide
* - cultures selected for metaphase analysis

Exponential cell growth was allowed for 7 days to allow mutant expression, following which the cells were incubated in media containing 6-thioguanidine (6TG) to select for mutant colonies.

Test method: OECD TG 476

Comment: precipitation occurred for concentrations of 300 μg/mL and above; toxic effects evident as a reduction in cloning efficiency were seen in the absence of metabolic activation at concentrations of 300 μg/mL and above

no significant increase in the number of mutant colonies was observed for any of the cultures examined

a large increase in the number of mutant colonies was seen for the positive controls, indicating that the system responded appropriately

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

9.3.3 Chromosomal Aberration Assay in Chinese Hamster Ovary Cells (Czich, 1996)

Cells: Chinese hamster ovary (CHO)

Metabolic activation system: rat liver S9 fraction from animals pretreated with Arochlor 1254, 0.75 % protein, in standard cofactors

Dosing schedule:

Metabolic Activation	Experiment/ Study Number	Test concentration (μg/mL)	Controls
-S9	1	treatment time = 22 hr 3*, 10*, 30*, 300, 1000*, 5000 treatment time = 30 hr 30*, 300, 1000*, 5000	Positive: EMS 0.6 mg/mL

	2	treatment time = 22 hr 1*, 3*, 5, 10*, 30*, 1000 treatment time = 30 hr 5*, 10, 30, 1000*	Negative: DMSO
+S9	1	treatment time = 4 hr with 18 hr recovery 3*, 10*, 30*, 300, 1000, 5000* treatment time = 4 hr with 26 hr recovery 30*, 300, 1000, 5000*	Positive: CP 0.71 μg/mL
	2	treatment time = 4 hr with 18 hr recovery 1*, 3*, 5, 10*, 30*, 5000 treatment time = 4 hr with 26 hr recovery 5*, 10, 30, 5000*	Negative: DMSO

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

Test method: OECD TG 473

Comment: colcemid (0.1 μg/mL) was added 3 hr before harvest to arrest cells in metaphase

precipitation occurred for concentrations of 30 μg/mL and above; cytotoxicity occurred at 300 μg/mL in the absence of S9 and at 3000 μg/mL and above in the presence of S9

in the absence of metabolic activation, in the first test a reduction in mitotic index to 78.4 % compared with solvent control was observed at 1000 μg/mL after 22 hr; in the second test, a reduction to 73.2 % was observed at 1000 μg/mL after 30 hr; in the presence of metabolic activation, slight cytotoxicity was seen in the first test at 3 and 10 μg/mL (mitotic index 74.5 % and 77.7 % compared with controls, respectively); a large reduction in mitotic index was observed after treatment with 5000 μg/mL (between 0 and 44 % of controls for the two tests at 22 and 30 hr)

in the first test at 22 hr in the absence of S9, the increase in aberrant cells was statistically significant (2 % compared with 0 % in the controls) but within the normal range of solvent control values; no other 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 caused 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

9.4 Overall Assessment of Toxicological Data

The notified chemical is of very low acute oral toxicity in rats (LD_{50} > 5000 mg/kg) and of low acute dermal toxicity in rats (LD_{50} > 2000 mg/kg). It is non-irritant to rabbit skin, and a slight irritant to rabbit eyes, with conjunctival effects clearing by 48 hours in four out of six animals, and by 72 hours in one of the remaining animals; in the sixth animal, conjunctival redness persisted to 4 days. It is not sensitising to the skin of guinea pigs.

In a 28 day repeat dose oral toxicity study, a NOEL of 200 mg/kg/day was established. Some changes in clinical biochemistry indicative of metabolic disturbance were observed in the males at 500 mg/kg/day, but similar changes with the exception of a non-statistically significant increase in total bilirubin level were not observed in the females. These changes were at least partly reversible after a 14 day recovery period. The biological significance of the changes is not clear as the values are all within historical control ranges. No changes in haematological parameters were observed in animals treated at 500 mg/kg/day after the treatment period, but some statistically significant differences were observed after a 14 day recovery period. It is not clear whether these differences were related to treatment with the notified chemical.

The notified chemical was not found to be mutagenic or clastogenic in three *in vitro* genotoxicity tests.

The notified chemical is not classified as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substance* (Approved Criteria) (NOHSC, 1999).

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The notifier provided the following ecotoxicity data. Tests were performed in accordance with OECD Test Guidelines.

Test	***Species***	***Results (Nominal)***
Acute Toxicity [OECD 203]	*Brachydanio rerio* (Zebra fish)	LC_{50}(96 h) > 0.22 mg/L NOEC > 0.22 mg/L
Acute Immobilisation [OECD 202]	*Daphnia magna*	EC_{50}(48 h) > 0.20 mg/L NOEC = 0.06 mg/L
Inhibition of Algal Growth [OECD 201]	*Selanastrum subspicatus*	E_bC_{50} (72 h) > 0.49 mg/L $E_\mu C_{50}$ (72 h) > 0.49 mg/L NOEC > 0.49 mg/L
Inhibition of Bacterial Respiration [OECD 209]	Activated sludge bacteria	Not inhibitory – see notes below.

* NOEC - no observable effect concentration

In the above tests, supersaturated stock suspensions were prepared by stirring 100 mg/L of the notified chemical in water for 2 hours. These suspensions were filtered through coarse filter paper and used without dilution. The measured concentrations of the notified chemical in the tests were well above the water solubility of the chemical. Thus, the test solution contained finely dispersed particles of the notified chemical. This is reflected in substantial decreases (up to 48.5%) of the concentrations of the notified chemical measured during the tests, as a result of the deposition of the particles of the chemical.

Fish

The acute test on rainbow trout (Memmert, 1996a) was a semi-static limit test (renewal of test medium at 48 h) performed over 96 hours using the filtered stock solution, which had measured concentrations of 0.24-0.31 mg/L at the start of the test, dropping to 0.16-0.17 mg/L by the end of the test (calculated average 0.22 mg/L). The test was performed in a 3 L aquarium using seven fish in the test vessel. A solvent control was also run in parallel, also using seven fish. During the tests the temperature was controlled at 21.0-22.0ºC, while the pH was always between 7.8 and 8.1, dissolved oxygen between 8.0 and 9.6 mg/L.

All test fish survived over the 96 hour test period. Further, no physical or behavioural anomalies were observed during the test period, and accordingly it was concluded that the new chemical is non toxic to zebra fish up to the limits of its water solubility.

Daphnia

The tests on *Daphnia magna* (Memmert, 1996b) were conducted over a 48 hour period, as a static limit test. As with the fish test above, a stock solution was prepared. The stock filtrate was also diluted 1:2, 1:4, 1:8 and 1:16 and these dilutions were also tested. The measured concentration of the stock solution at the start of the test was 0.33 mg/L and at the end of the test it was 0.17 mg/L (calculated average 0.25 mg/L). The concentrations of the dilutions were measured and found to have decreased in the same proportion. Twenty daphnia in four groups of five animals (each group in 50 mL test medium in a 100 mL glass beaker) were introduced to each test vessel containing one of the four replicates of the dilutions or stock solution, together with the four solvent controls. During the tests the temperature was controlled at 20.4-20.9ºC, while the pH was always between 7.7 and 7.8 and dissolved oxygen above 8.2 mg/L.

Dilution	***No. daphnia tested***	***No. daphnia immobilised***		***% daphnia immobilised***	
		24 h	***48 h***	***24 h***	***48 h***
Control	20	0	0	0	0
1:16	20	0	0	0	0
1:8	20	0	0	0	0
1:4 (0.06 mg/L)	20	0	0	0	0
1:2 (0.12 mg/L)	20	2	6	10	30
Stock (0.25 mg/L)	20	4	12	20	60

An attachment to the test report refers to the undissolved material remaining in the test solution and dilutions, and the observed biological effects at 0.12 and 0.25 mg/L being possibly due to physical effects of the undissolved material. Thus the study authors have

concluded that the EC_{50} (48 h) is above the water solubility limit of the chemical and cannot be determined.

Algae
A static limit test on the inhibition of algal growth (Memmert, 1996c) was conducted on *Scenedesmus subspicatus* over a 72 hour incubation period using a supersaturated stock solution prepared as described above. The solution had a measured concentration of 0.60 mg/L at the start of the test, dropping to 0.37 mg/L by the end of the test (calculated average 0.49 mg/L). The test was started by inoculation of a biomass of 10000 algal cells/mL test medium. Three replicate tests were conducted in 50 mL Erlenmeyer flasks, together with six control flasks containing no chemical. The flasks were continuously stirred to maintain the algal cells in suspension. The pH of the test solutions rose from around 8.0 at the start of the period, to a value of 10.4 after 72 hours and the temperature remained between 23.0-24.2°C. The growth of algal biomass was determined over the test period by measurement of the cell densities and was at all counting dates slightly higher than the control. Consequently it was concluded that the new compound is not inhibitory to growth of algae up to the limits of its water solubility.

Sewage Bacteria
A test on the inhibition of bacterial respiration was also conducted (Grutzner, 1996b). The test substance was suspended in chloroform by ultrasonication to produce a stock solution of 5 mg/mL. Aliquots were taken, the chloroform evaporated off and the test substance diluted to produce test solutions of nominal loadings of 10, 20, 32, 50 and 100 mg/L using a 1 minute period of sonication to assist dispersion. The test flasks were inoculated with 16 mL sewage sludge bacteria and then aerated for 30 minutes. Following aeration aliquots of the test solutions were taken at 10 minute intervals for measurement of oxygen concentration. The rate of oxygen consumption was measured for the dispersions, and compared with that in a control vessel. None of the tests indicated any significant inhibition of bacterial respiration compared with the controls, and it was concluded that the new chemical is not toxic to sewage bacteria up to the limits of its water solubility.

In contrast to tests with the new chemical, a reference test conducted with 3,5-dichlorophenol showed inhibition of bacterial respiration of 10.3 % at a test concentration of 3.2 mg/L, and 77.9 % at 50 mg/L.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The environmental hazard from the notified chemical is not expected to be high when it is used for the manufacture of household plastic articles and motor vehicle parts as indicated in the notification.

Very little of the notified chemical is expected to be released during manufacturing processes. The notifier estimates that this release would be 4 kg per annum at the maximum import volume of 2 tonnes (0.2 %). However, some slow release of the chemical may occur as a result of everyday use and cleaning of the polymer articles, and this is likely to enter the sewer system with discarded cleaning water. In the sewer the compound will become strongly associated with sediments.

Plastic articles containing the notified chemical such as containers, food wrap, household

appliances or automotive parts are unlikely to be recycled, and consequently at the end of their useful lives will be discarded. The discarded articles are most is likely to be placed into landfill or incinerated.

If placed into landfill, the compound is likely to be slowly released as a consequence of the slow degradation of the polymer matrix in which it is encapsulated. Once released in this manner it is expected to become associated with the organic component of soils and sediments. The chemical is not readily biodegradable. However, once released and adsorbed to soils and sediments in a landfill it is expected to be slowly degraded through the biological and abiotic processes operative in these situations.

Very little of the notified chemical is expected to enter the water compartment and so exposure to aquatic organisms is expected to be low. The chemical is not toxic to those aquatic species against which it has been tested up to the limits of its water solubility, and so any release to the water compartment would entail a low environmental hazard. The notified chemical is not readily biodegradable and the high value for Log P_{ow} and low water solubility indicate high potential for bioaccumulation. However, any potential for bioaccumulation will be mitigated by the expected low exposure to the water compartment and the moderate molecular weight (852).

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Hazard Assessment
The notified chemical is of very low acute oral toxicity in rats (LD_{50} > 5000 mg/kg) and of low acute dermal toxicity in rats (LD_{50} > 2000 mg/kg). It is non-irritant to rabbit skin, and a slight irritant to rabbit eyes. It is not sensitising to the skin of guinea pigs. The notified chemical was not found to be mutagenic or clastogenic in three *in vitro* genotoxicity tests.

In a 28 day repeat dose oral toxicity study, a NOEL of 200 mg/kg/day was established. Some changes in clinical biochemistry indicative of metabolic disturbance were observed in the males at 500 mg/kg/day, but similar changes with the exception of a non-statistically significant increase in total bilirubin level were not observed in the females. Some statistically significant differences in haematological parameters were observed for animals treated at 500 mg/kg/day after a 14 day recovery period, but it is not clear whether these differences were related to treatment with the notified chemical.

The notified chemical is not classified as a hazardous substance in accordance with the Approved Criteria (NOHSC, 1999). It has been approved for use in polymers intended for food contact by the US Food and Drug Administration (US Federal Register, 1999), as well as in Canada, the EU, Switzerland, Japan and Brazil.

The MSDS for the notified chemical indicates that it is not a hazardous substance, but that skin and eye irritation may occur on prolonged or repeated contact. Respiratory irritation on exposure to dust and gastric disturbance if swallowed may also occur. Hazardous

decomposition products may be formed if the notified chemical is overheated (above 240ºC).

Occupational Health and Safety
There is little potential for significant occupational exposure to the notified chemical in the transport and storage of Doverphos S-9228. There may be exposure during the incorporation of the notified chemical into polymer pellets. After the notified chemical has been incorporated into the polymer pellets, it will be present at low concentrations (0.05 – 0.15 %) and will be encapsulated in the polymer matrix. Little exposure is therefore expected during production of articles from the pellets containing the notified chemical.

During the production of the polymer pellets containing the notified chemical, the main exposure route for the notified chemical will be dermal, if compacted pellets of the notified chemical are used, and dermal or inhalation, if the notified chemical is handled in powder form. The notifier indicates that workers will wear protective clothing and gloves while handling the compacted pellets, and that a dust mask will also be used if the notified chemical is handled in powder form. Given the low toxicity of the notified chemical, these measure should be sufficient to minimise the risk to workers handling Doverphos S-9228.

Public Health
The notified chemical is not available for sale to the public and will be used as an ingredient in plastics manufacture. Members of the public may make dermal contact with plastic articles containing the notified chemical and may eat or drink foodstuffs that may have been in contact with plastic articles containing the notified chemical. The risk to public health from the notified chemical is likely to be low because the notified chemical is present at low concentrations and is likely to be largely contained within the plastic matrix.

13. RECOMMENDATIONS

To minimise occupational exposure to Doverphos S-9228 the following guidelines and precautions should be observed:

- Safety goggles, chemical resistant industrial clothing and footwear and impermeable gloves should be used while handling the notified chemical; where engineering controls and work practices do not reduce particulate exposure to safe levels, respiratory protection should also be used;

- 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, 1999), 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, 1994a); for respirators, in AS/NZS 1715 (Standards Australia/ Standards New Zealand, 1994b) and AS/NZS 1716 (Standards Australia/ Standards New Zealand, 1994c) and other internationally acceptable standards.

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. Secondary notification will also be required if any longer term repeat dose toxicity studies become available. No other specific conditions are prescribed.

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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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