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May 2006

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Component of Preventol OF 45

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Director
NICNAS

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1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
LANXESS Pty Ltd (ABN 58 071 919 116)
Unit 1, 31 Hill Rd
Homebush Bay NSW 2127

NOTIFICATION CATEGORY
Standard: Chemical other than polymer (more than 1 tonne per year).

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: Data items and details claimed exempt from publication:

- Other Names
- Molecular Weight
- Spectral Data
- Non Hazardous Impurities
- Composition
- Additives
- Import Volume
- Recipient
- Specific use

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: particle size, acute inhalation toxicity, skin sensitisation, repeat dose toxicity. Analogue data were provided for the latter three endpoints. Data for particle size were not required as the chemical is never isolated as a pure substance but is always used in aqueous solution.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None.

NOTIFICATION IN OTHER COUNTRIES
The notified chemical is listed in EINECS, TSCA, in DSL/Canada, under METI/Japan (METI No. 1-1676), in the Philippines and Korea.

2. IDENTITY OF CHEMICAL

CHEMICAL NAME
[1,1'-biphenyl]-2-ol, potassium salt

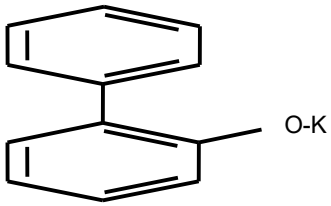
MARKETING NAME(S)
Aqueous solutions of the notified chemical:

Preventol OF 45
Preventol OF

CAS NUMBER
13707-65-8

MOLECULAR FORMULA
$C_{12}H_9KO$

STRUCTURAL FORMULA



SPECTRAL DATA

METHOD Infrared spectroscopy
Remarks A reference spectrum was provided.

METHODS OF DETECTION AND DETERMINATION

METHOD Infrared and Mass spectra
Remarks Reference spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
> 60%

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (> 1% by weight)
Contains > 20% water in bound form.

ADDITIVES/ADJUVANTS
A minor additive at < 1% is contained in the notified chemical.

Preventol OF 45 as imported contains 53 – 58% notified chemical in an aqueous solution containing 0.5 – 1% potassium hydroxide.

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured in Australia and will be imported as a component in Preventol OF 45 at 53 – 58% in 1100 L bulk plastic containers.

MAXIMUM INTRODUCTION VOLUME OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	30 - 100	30 - 100	30 - 100	30 - 100	30 - 100

USE
The notified chemical functions as a preservative in the manufacture of water based products used in paper manufacture.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, transport and storage

PORT OF ENTRY
The notified chemical will be imported through Melbourne by wharf

IDENTITY OF MANUFACTURER/RECIPIENTS
The notified chemical is not manufactured in Australia but will be stored in a licensed dangerous good store at the recipient's premises.

TRANSPORTATION AND PACKAGING
The notified chemical will be imported in 1100 Litre bulk containers made of plastic with steel supports in FCL shipments totalling 18 bulk containers. The FCL shipment will be transported directly from the wharf to the recipient by road.

5.2. Operation Description

The notified chemical will be imported into Australia at < 60% concentration and transported by road in 1100 L bulk plastic containers to the formulation site where it will be stored and formulated into calcium carbonate slurries.

Formulation of calcium carbonate slurry
During formulation of calcium carbonate slurries, an operator will open the 1100 L bulk plastic container, connect pumping equipment to the container and dose the required amount of the notified chemical into a mixing vessel mixing tank containing calcium carbonate-water slurry. Other ingredients will also be added and the mixture is blended in a closed mixing vessel. The mixing operation is automated. The final concentration of the notified chemical in the slurry will be < 0.5%. Prior to packaging, sampling and quality testing of the slurry is carried out in the laboratory. The slurry will then be transferred by pump into a bulk storage tank and 1100 L bulk containers. This process is highly automated, and will be carried out under local exhaust and general ventilation. The concentration of the notified chemical in the products will be a maximum of 0.5%.

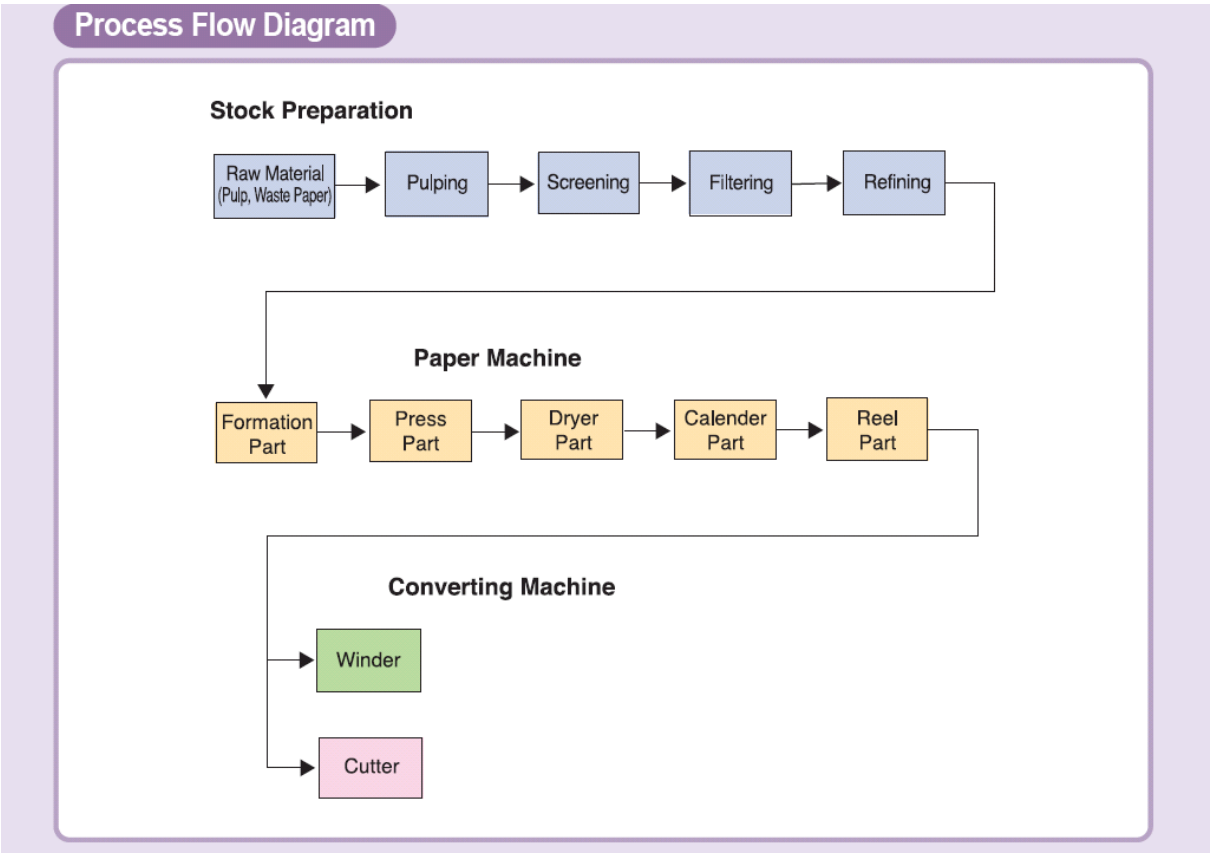
The bulk storage tanks and 1100 L bulk containers will be transported and distributed to the paper manufacturing industry by road.

Manufacturer of paper
Stock Preparation Section
In this section, raw feed materials of kraft or virgin pulp are mixed with waste paper and chemicals are added to make the base material for papermaking. This section includes slurry (containing the notified chemical), screen, deflaker, and refiner parts.

Papermaking Section
The headbox in the papermaking section ejects the refined solution onto the wire to create a thin slurry layer. This layered slurry is dehydrated by the press and dried by drier. Its weight and thickness are adjusted by the calendar machine. Finally, this paper is rolled in preparation for moving to the next step.

Coating Section
The coating machine uses a blade or road bar type coater to coat the paper with a pigment, largely CaCO3, to enhance the surface condition for printing. After the coated paper is dried by the heat dryer, it is to sent to a super calendar or soft calendar for surface polishing. Coatings are applied here for printing paper or expensive industrial paper.

Rewinding, Cutting & Packing Section
After being coated, the paper is rolled and cut according to the user's requirements. Finally, the cut or rolled paper is packed for delivery to the retailers, officers wholesale suppliers etc..



5.3. Occupational Exposure

Number and Category of Workers

Category of Worker	*Number*	*Exposure Duration*	*Exposure Frequency*
Transport & Storage	2	4 hours/day	2 days/year
During formulation			
Operator	2	4 hours/day	26 days/year
Quality Control	1	2 hours/day	2 days/year
Fitter	1	8 hours/day	1 day/year
During paper manufacture			
Operators	4	8 hours/day	250 days/year
Quality control	2	2 hours/day	250 days/year
Fitter	2	2 hours/day	250 days/year
End-use			
Office workers	> 10000	6 hours/day	250 days/year

Exposure Details

Transport and storage

Exposure of workers involved in the importation, storage and transport of the notified chemical is not expected except in the unlikely event of an accidental spill. Gloves, coveralls and goggles are available if required.

During formulation

Dermal and ocular exposure to the notified chemical (< 60%) may occur during opening of the drums, dosing the required amount of the notified chemical into a mixing vessel and connecting and disconnecting transfer and filling lines. Following formulation any exposure will be to slurry containing < 0.5% of the notified chemical. Dermal and ocular exposure to the finished product may occur during packaging of finished products.

The mixing vessels are enclosed and the filling machines are automated and fitted with local exhaust ventilation. To prevent exposure workers wear overalls, face mask, safety glasses and/or safety shoes

and impervious gloves.

Limited dermal exposure to small quantities may occur during sampling and testing or during machine maintenance. To minimise exposure workers will wear laboratory coats, safety glasses and impervious gloves.

During maintenance on pump and dosing equipment, the workers will wear safety glasses, coveralls and gloves when conducting maintenance.

During paper manufacture
Dermal exposure from drips and spills to the notified chemical in the slurry may occur when connecting the pump to bulk storage tanks and or 1100 L bulk storage containers to pump the slurry into stock preparation tank. Dermal exposure may also occur during maintenance and cleaning of the paper making machine. Exposure will be limited as the slurry is added to the mixing tank via a dedicated automated pump. The paper manufacturing plant is enclosed and local exhaust ventilation fitted above the mixing tank on the papermaking machine. To prevent exposure, workers wear overalls, face mask, safety glasses and/or safety shoes and impervious gloves.

End-use
Office workers will make dermal contact with the dried form of the notified chemical when handling paper items, the exposure from the notified chemical is likely to be low because it is unlikely to be bioavailable and present at very low concentrations.

5.4. Release

RELEASE OF CHEMICAL AT SITE
The notified chemical is used in slurry products for the paper industry. There is expected to be minimal release during the reformulation of the notified chemical into the slurry products. The mixing is conducted in an enclosed automated system with the 1100 L containers and the equipment during cleaning being rinsed with water with the rinseate being returned to the manufacturing process. The areas are bunded to minimise release of the chemical from spills.

RELEASE OF CHEMICAL FROM USE
The reformulated product containing less than 0.5% w/w will then be used in the paper making industry probably throughout Australia. The chemical slurry containing the notified chemical is mixed with paper pulp. The paper matrix is oven dried and the chemical is intimately bound with the paper product. Release of the chemical is only likely to occur during cleaning of equipment. The rinseate will be treated in the effluent treatment plant before release to the sewer. A portion will remain bound to the sludge with the remainder entering the sewer. The sludge will be dried and disposed by incineration. The bulk slurry containers are refilled with slurry without rinsing and are therefore not expected to be a source of exposure of the chemical to the environment.

The notified chemical is intimately bound with the paper product and will share the same fate as that product. It is expected that there will be virtually no release of the chemical during the useful life of the paper product.

5.5. Disposal

The vast majority of the chemical will be released to the environment at the end of the paper product's useful life. A large proportion will be landfilled with some undergoing in-situ degradation and the remainder being leached from the paper product. During recycling of paper a portion will partition to the sludge with the remainder entering the sewer. A small portion of the paper product may also be disposed by incineration.

5.6. Public exposure

The notified chemical is not available for sale to the public. The potential for public exposure to the notified chemical during transport, reformulation and manufacture of paper is likely to be negligible. Although members of the public will make dermal contact with dried form of the notified chemical, however, when handling treated paper, public exposure is expected to be low.

6. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20ºC and 101.3 kPa White crystals

Melting Point 51.4ºC

METHOD EC Directive 92/69 A.1 Melting Point
Remarks Method: Differential Thermal Analysis.
TEST FACILITY Bayer (2002a)

Boiling Point Not determined

METHOD EC Directive 92/69/EEC A.2 Boiling Temperature.
Remarks Boiling point not detected up to the exothermal reaction of the test substance.
TEST FACILITY Bayer AG (2002a)

Density 1350 kg/m^3 at 20ºC

METHOD EC Directive 92/69/EEC A.3 Relative Density.
Remarks Relative Density by Displacement.
TEST FACILITY Bayer AG (2002a)

Vapour Pressure 2.41 kPa at 20°C
3.14 kPa at 25ºC
5.19 kPa at 35°C

METHOD EC Directive 92/69/EEC A.4 Static Method Vapour Pressure.
Remarks Four measurements of vapour pressure were taken at 22.1°C, 27.9°C, 32.0°C and 36.9°C. The results were interpolated for 20°C, 25°C and 35°C. The relatively high vapour pressure reflects the presence of bound water.
TEST FACILITY Bayer AG (2003)

Water Solubility 687 g/L at 20ºC

METHOD Water Solubility test corresponds to
EC Directive 92/69/EEC A.6 Water Solubility.
Remarks Flask Method with no variations from protocol for Preventol OF (dry product) containing the notified chemical. The pH of the solutions was 15.5 - 15.6. Detection of notified chemical was by HPLC/UV. Determination of Preventol OF constituents was made by identification by FTIR, notified chemical content determination by potentiometric titration with hydrochloric acid and water content determined by Karl Fischer. Confirmation of potassium content was made by ICP-OES. Corrections made for measured content of notified chemical.
TEST FACILITY Bayer AG (2002b)

Hydrolysis as a Function of pH Considered hydrolytically stable.

METHOD OECD TG 111 Hydrolysis as a Function of pH.
EC Directive 92/69/EEC C.7 Degradation: Abiotic Degradation: Hydrolysis as a Function of pH. Preliminary tests were performed at pH 4, 7 and 9 at 50°C.

pH	*T (°C)*	$t_{½}$
4	50	> 5 days
7	50	> 5 days
9	50	> 5 days

Remarks Less than 10% hydrolysed in 5 days.

TEST FACILITY Bayer AG (1990a)

Partition Coefficient (n-octanol/water) Log Pow at 2.4 at 25°C
Log Pow at 2.4 at 25°C at pH 5
Log Pow at 2.4 at 25°C at pH 7
Log Pow at 2.4 at 25°C at pH 9

METHOD OECD TG 117 Partition Coefficient (n-octanol/water), HPLC Method.
EC Directive 92/69/EEC A.8 Partition Coefficient.
Remarks Test results for water, pH buffers 5, 7, 9; Test substance dissociates, but as pKa is 11.4 it will remain in its un-dissociated form in the environmental pH range.
TEST FACILITY Bayer AG (2001a)

Adsorption/Desorption – screening test log K_{oc} = 2.5 at 25°C.

METHOD OECD TG 121 Adsorption – Desorption, HPLC Method.
Remarks Buffer pH 6, eluted towards the end of six reference standards.
TEST FACILITY Bayer AG (2001b)

Dissociation Constant pKa = 11.4

METHOD OECD TG 112 Dissociation Constants in Water. No deviations reported.
Remarks Will not dissociate in the environmental pH range of 4 - 9
TEST FACILITY Bayer AG (2001a)

Particle Size Not determined

METHOD OECD TG 110 Particle Size Distribution/Fibre Length and Diameter Distributions.
Remarks Test data not available

Flash Point Not determined.

Remarks The notified chemical will be imported as an aqueous solution and is not expected to be flammable. As a solid the notified chemical has a melting point of 130°C.

Flammability Limits Not highly flammable.

METHOD EC Directive 92/69/EEC A.12 Flammability (Contact with Water).
Remarks Test substance does not liberate gases in hazardous amounts upon contact with water as defined in EC Guideline A 12.
TEST FACILITY BAYER Industry Services (2003)

Autoignition Temperature Does not self ignite.

METHOD EC Directive 92/69/EEC A.16 Relative Self-Ignition Temperature for Solids.
Remarks Test substance does not undergo spontaneous combustion in the sense of EC Guideline A 16 up to the melting point.
TEST FACILITY BAYER Industry Services (2003)

Explosive Properties Not expected to be explosive.

Reactivity

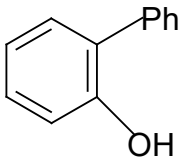
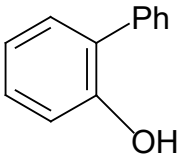
Remarks Expected to be stable under normal environmental conditions.

7. TOXICOLOGICAL INVESTIGATIONS

No data were available for the notified chemical for the following end-points:

- Acute inhalation toxicity
- Skin sensitisation
- Repeat dose toxicity

To fill the data gaps above the following analogues were used:

Notified chemical	*Analogue A*	*Analogue B*
	2-phenylphenol CAS No. 90-43-7	2-phenylphenol sodium salt CAS No.132-27-4
		
# K		# Na

Information for the analogues were extracted from O-Phenylphenol and its Sodium and Potassium Salts: A Toxicological Assessment. Critical Reviews in Toxicology, Volume 32, Number 6:551-626, 2000. A range of studies on absorption, metabolism and excretion of analogues A and B show strong similarities and their toxicological profile is also similar. Therefore the notified chemical should also have similar properties. Analogues were used for data on acute inhalation toxicity, skin sensitisation and repeat dose toxicity.

Endpoint and Result	*Assessment Conclusion*
Rat, acute oral for Preventol OF (36.7% of the notified chemical)	Low toxicity, LD50 2573 mg/kg bw (male); 2118 mg/kg bw (female). Moderate toxicity for the notified chemical.
Rat, acute dermal Preventol OF (36.9% of the notified chemical)	Low toxicity, LD50 > 2000 mg/kg bw. Low to moderate toxicity for the notified chemical.
Rat, acute inhalation toxicity based on analogue A:	
1–h-inhalation	LC50 > 949 mg OPP/m^3
4-h-inhalation	LC50 > 36 mg/m^3
Rabbit, skin irritation	Corrosive
Rabbit, eye irritation	Corrosive
Guinea pig, skin sensitisation based on analogue OPP and sodium o-phenylphenol (SOPP)	
Maximisation Test:	Non-sensitiser
Buehler Method:	Non-sensitiser
Rat, Oral repeat dose toxicity - 28 days based on OPP (Analogue – parent compound of the notified chemical)	NOAEL was established as > 300 mg/kg bw/day
Genotoxicity - bacterial reverse mutation	Non mutagenic
Genotoxicity – in vitro Mammalian Cell – Gene Mutation Test.	Non mutagenic
Genotoxicity – in vivo - Comet Assay	Non mutagenic

7.1. Acute toxicity – oral

TEST SUBSTANCE	A 37% solution of the notified chemical.
METHOD	EC Directive 84/449/EEC – Acute Oral Toxicity
Species/Strain	Rat – Wistar WISW (SPF Cpb)
Vehicle	None, test substance administered as supplied
Remarks – Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality%*
Male	5	200	0
	5	1000	0
	5	2000	20
	5	2500	40
	5	3150	80
Female	5	200	0
	5	1000	0
	5	2000	40
	5	2500	80
	5	3150	80

LD50	2573 mg/kg rat, male (952 mg/kg notified chemical) 2118 mg/kg rat, female (784 mg/kg notified chemical)
Signs of Toxicity	After dosages 1000-2000 mg/kg hypersalivation, gasping breathing, respiratory sounds, bloody snout, nasal discharge, increased diuresis, ruffled up skin, sedation as well as bad general condition were determined as poisoning symptoms.
Effects in Organs	Liquid or gas accumulations in stomach and/or intestines were observed during evaluation in gross pathology of the dead animals. The stomach was in some cases filled with a brownish mass. The gastric mucous membrane and/or the intestinal mucosa was mostly discoloured reddish black.
CONCLUSION	The test substance containing 37% notified chemical is of low toxicity via the oral route.
TEST FACILITY	Bayer AG (1988a)

7.2. Acute toxicity – dermal

TEST SUBSTANCE	A preparation contained 36.9% solution of notified chemical.
METHOD	EC Directive 84/449/EEC – Acute Oral Toxicity
Species/Strain	Rat – Wistar WISW (SPF Cpb)
Vehicle	None, test substance administered as supplied
Type of dressing	Occlusive.
Remarks – Method	None.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
Male	5	2000	0
Female	5	2000	0

LD50	> 2000 mg/kg bw
Signs of Toxicity - Local	Black discoloration of the skin was discovered on application site. The

	discoloured area hardened and peeled off from the 8th day of study. The affected area was about 1 cm in diameter. The skin changes persisted until the end of the study.
Signs of Toxicity - Systemic	Growth of male rats not affected whilst slight decrease in body weight was recorded for females.
Effects in Organs	No gross pathological changes were observed .
Remarks – Results	None

CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	Bayer AG (1991)

7.3. Acute toxicity – inhalation

Method	*Results*	*Reference*
In the 1-hour inhalation experiment groups of 20 male Wistar rats were exposed nose-only to aerosol concentrations of 228, 447 and 949 mg OPP/m^3 dissolved in a mixture of ethanol and polyethylene glycol 400. Postexposure observation period was 7 days.	All animals survived with no signs of intoxication.	Cited in Bomhard *et al.* (2002)
In the 4-h-inhalation study groups of five male and five female F344 rats were exposed to maximum attainable dust concentrations of OPP, that is, 36 mg/m3 after pre-grinding with a jet mill.	No effects were seen within the 2-week observation period.	Cited in Bomhard *et al.* (2002)
OPP was dynamically evaporated (200 L air passed through 500 g) at room temperature (approximately 20ºC) in the inhalation hazard test. Five male and five female rats were exposed once over 7 h. The follow-up period was 14 days.	All animals survived the exposure period. Male rats displayed a conjunctival reaction lasting for about 10 min after exposure. No other intoxication, irritation or organ damage was observed.	Cited in Bomhard *et al.* (2002)

7.4. Irritation – skin

TEST SUBSTANCE	A preparation contained 36% solution of 2-phenyl phenol K (Preventol OF)
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion.
Species/Strain	Rabbit
Number of Animals	1
Vehicle	Not available
Observation Period	Not available

Type of Dressing	Not available.
Remarks – Method	Due to the pH value and under observing the (German) Animal protection Act no further investigation was undertaken.
RESULTS	The notified chemical is corrosive to skin.
Remarks – Results	Only a single animal was used due to the pH of the test solution. Only a statement of the result was provided.
CONCLUSION	The notified chemical is corrosive to skin.
TEST FACILITY	Bayer AG (1988b)

7.5. Irritation – eye

TEST SUBSTANCE	A preparation contained 36% solution of 2-phenyl phenol K (Preventol OF)
METHOD	OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain	Rabbit
Number of Animals	1
Observation Period	Not available
Remarks – Method	Due to the pH value and under observing the (German) Animal protection Act no further investigation was necessary.
RESULTS	The notified chemical is corrosive to eyes
Remarks – Results	
CONCLUSION	The notified chemical is corrosive to the eye.
TEST FACILITY	Bayer AG (1988b)

7.6. (a) Skin sensitisation

TEST SUBSTANCE	*o*-Phenylphenol (OPP) and Sodium *o*-Phenylphenol (SOPP) Analogues of the notified chemical
METHOD	Maximisation Test
Species/Strain	Female Guinea pigs
MAIN STUDY	
induction phase	Induction Concentration:
	intradermal injection 0.5% and 5% OPP (in propylene glycol) or SOPP (in water).
	topical application 25% OPP or SOPP in yellow petrolatum were used
CHALLENGE PHASE	
1st challenge	topical application: 5% formulations of both OPP and SOPP in yellow petrolatum 3 weeks after induction
Remarks – Results	According to results obtained, both substances were not classified as sensitisers.
CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the two analogues under the conditions of the test.
TEST FACILITY	Data cited in Cited in Bomhard *et al.* (2002)

7.6. (b) Skin sensitisation

TEST SUBSTANCE	*o*-Phenylphenol (OPP) and Sodium *o*-Phenylphenol (SOPP) Analogue of the notified chemical
METHOD	Buehler Method
Species/Strain	10 male Guinea pigs
PRELIMINARY STUDY	Maximum Non-irritating Concentration: intradermal: topical:
MAIN STUDY	
Number of Animals	Test Group: Control Group:
induction phase	Ten male guinea pigs per treatment group were administered 0.4 g of neat OPP or 0.4 g SOPP moistened with 0.2 ml distilled water under occlusive conditions 6 h to the left side clipped free of hair once weekly during a 3-week induction period.
Signs of Irritation	
CHALLENGE PHASE	
1st challenge	Two weeks after the last induction application the animals were challenged by application of 0.4 g neat OPP or 0.4 ml of a 7.5% SOPP suspension in distilled water (0.4 g OPP was not considered irritating based on a skin irritation screening, the 7.5% SOPP suspension was the highest non-irriatative concentration).
RESULTS	Under these conditions, OPP did not cause dermal sensitisation in male guinea pigs.
CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.
TEST FACILITY	Data cited in Cited in Bomhard *et al.* (2002)

7.7. Repeat dose toxicity

TEST SUBSTANCE	Ortho-Phenylphenol (OPP) (analogue – parent compound of the notified chemical)
METHOD	Studies were carried out in accordance with the Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Human and Domestic Animals (NTIS Report PB83-153916, 1982) and series 83-1 Chronic Test Guideline specified by the Environmental Protection Agency (EPA) in their Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Human and Domestic Animals (EPA, 1984).
Species/Strain	Beagle dogs
Route of Administration	Oral – diet.
Exposure Information	Total exposure days: 28 days
Vehicle	Peanut oil
Remarks – Method	Two male and 2 female dogs per sex per group were given 0, 100, 200, 300 mg OPP/kg/day in a peanut oil vehicle via gastric intubation, 5 days/week for a 4 week period. High dose group dogs were initially given 400 mg OPP/kg/day, however following repeated emesis by these dogs after dosing, this dosage was lowered to 300 mg OPP/kg /day for the duration of the dosing period.

RESULTS

Mortality and Time to Death

None.

Clinical Observations

Dose related emesis was noted in all dogs during the in-life phase. The only response to OPP treatment was repeated emesis by both sexes given 200 mg OPP/kg of 300 mg OPP/kg in a peanut oil solution. Emetic activity was observed to occur more frequently and to involve greater volumes in the high dose group than in dogs administered lower dosages. The frequency with which this occurred was dose-related, and the emesis was noted over the entire dosing period. The emesis was categorized as a local transitory response of the mucosal lining of the upper alimentary tract rather than being initiated via the central nervous system.

Body weights in both sexes of dogs given OPP were not significantly different than controls. Feed consumption for male or female dogs was not affected by treatment ingestion of OPP.

Ophthalmologic observations were normal and were consistent upon histologic examinations of the eyes.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Haematology

Males given 300 mg OPP/kg/day had a 34% decreased mean platelet value and a 35% increased mean white blood cell value, as compared to control values. Segmented neutrophils were also increased relative to controls. In addition, the mean white blood cells of males given 100 mg OPP/kg and females given 200 mg OPP/kg were increased by 39% and decreased by 26%, respectively, as compared to the control values. The platelet and white blood cell values were well within the historical range. There were no significant lesions noted upon histopathologic examination of tissues that appeared to correlate with these hematologic findings.

Male dogs given 300 mg OPP/kg/day had a slightly lower number of RBCs, haemoglobin concentration and hematocrit than the controls (24, 20 and 22% decrease, respectively); however, adequate red blood cell precursors and erythrocytic maturation were noted upon examination of bone marrow smears. Unusually high values were observed for these parameters in one of the 2 control male digs effectively confounding any comparisons. Similar observation or hematologic parameters were note in the female high dose group. Therefore, these observations were not interpreted to be toxicologically significant.

Occult blood was not detected in the faeces or emesis of dogs given OPP indicating the absence of gastrointestinal haemorrhage in these animals.

Urinalysis – No treatment-related effects upon parameters examined were noted for either sex of dog given OPP.

Clinical chemistry

No treatment-related changes in any measured parameter were found. All differences between mean values for treated and control group dogs were attributed to normal variability between animals. The individual AP activity of one male and the calcium levels of another male given 200 mg OPP/kg/day were slightly decreased when compared to their 2 pre-exposure samples and the control values. However, these values were within the historical control ranges. Therefore, these isolated decreased values were not interpreted to be toxicologically significant.

Individual serum AP values of 2 female dogs were higher than mean control values at the 2 prestudy bleeds and higher for another dog at the 4-week sampling. These values were believed to represent normal biological variability since the relatively high values were noted at prestudy intervals.

A few spurious intragroup elevated creatinine phosphokinase (CPK) activities were also recorded during 2 pre-exposure sampling periods for the male dogs and at the 4-week sampling for the females. This elevation in CPK activity was attributed to probable increased muscular activity during the blood sampling process. Any other minor differences in clinical chemistry parameters between treated and control group were attributed to normal variation and did not reflect a treatment-related effect.

Effects in Organs

There were no treatment-related effects seen in the organ weights of any dog.

Gross pathologic observation

The results of the necropsy and histopathologic examinations of the dogs from the 4-week study show relatively few observations made at necropsy with no lesions attributable to OPP treatment. Focal or mutifocal consolidated areas in the lungs were noted in 4 dogs.

Histopathologic observations
There were no histopathologic lesions attributed to OPP treatment.

Remarks – Results
This study indicates there is no adverse toxicologic effects in the multiple parameters used to monitor the response of male and female Beagle dogs given maximum possible oral dosage of 300 mg of OPP/kg in a peanut oil solution via gastric intubation 5 days/week for 4 weeks.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as > 300 mg/kg bw/day in this study, based on results of these oral studies.

TEST FACILITY	The Dow Chemical Company (1990)

7.8. Genotoxicity – bacteria

TEST SUBSTANCE	A preparation contained 36% solution of 2-phenyl phenol K (Preventol OF)
METHOD	Standard for mutagenicity testing using microorganisms (Notification No. 76 (1/09/89) and OECD Guideline for testing of chemicals
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 *E. coli*: WP2 *uvr*A,
Metabolic Activation System	Liver Fraction (S9 mix)
Concentration Range in Main Test	a) With metabolic activation: 50-5000 µg/plate. b) Without metabolic activation: 50-5000 µg/plate.
Vehicle	Water
Physical Form	Liquid – test substance was dissolved in water for injection.
Remarks – Method	No significant protocol deviations

RESULTS

Remarks – Results	The number of revertant colonies in positive controls increased markedly as compared with negative control.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	JBC Inc. Research Laboratory (1989)

7.9. Genotoxicity – in vitro

TEST SUBSTANCE	Preventol o-extra (o-phenylphenol)
METHOD	Mutagenicity study for the detection of induced forward mutations in the CHO-HGPRT Assay *in vitro* in accordance with: EEC Directive 87/302/EEC, Mutagenicity, *In vitro* Mammalian Cell – Gene Mutation Test. OECD Guidelines for Testing of Chemicals, Genetic Toxicology: *In vitro* Mammalian Cell Gene Mutation Assay, Adopted: 4 April 84, No. 475 New and revised Health Effects Test Guidelines October 1984. (US) Environmental Protection Agency Washington DC (PB 84-233295) HG – Gene Mutation – Somatic Cells, October 1984.
Species/Strain	Chinese Hamster/CHO-WB1
Cell Type/Cell Line	Chinese hamster ovary (CHO) cells

Metabolic Activation System	Liver fraction (S9 mix) from rats pretreated with Aroclor 1254
Vehicle	DMSO
Physical Form	Not applicable
Remarks – Method	No deviations from protocol noted.
Remarks – Results	Preventol o-extra, was assayed for mutagenic activity at the HGPRT locus in CHO cells from 6.25 µg/ml to 100 µg/ml without activation and from 12.5 µg/ml to 115 µg/ml with activation. Under both treatment conditions, a wide range of cytotoxic effects was induced. The absolute cloning efficiencies for the vehicle controls varied from 67.7% to 87.3% without activation and from 59.5% to 89.3% with activation demonstrating good cloning conditions for the assays. Cytotoxicity tests showed that the test substance was cytotoxic in a preliminary test with 79% of cells surviving a dose of 62.5 µg/ml without activation but this dropped to 7.4% at 100 µg/ml. With activation the corresponding survival percentages were 49.3 and 42.4%, respectively. In the main test survival percentages without activation at 50 µg/ml were 40.7, 46.6 and 87.6 with higher toxicity above this dose. With activation survival percentages at this dose were at least 100% but there was toxicity at higher doses. The vehicle control mutant frequencies were all in the normal range of background frequencies for the assay. In contrast, the positive controls EMS and DMBA induced a distinct mutagenic effect in mutant frequency, which was significantly increased over the negative controls demonstrating the sensitivity of the test system and the ability to detect known mutagens. Preventol o extra is considered non-mutagenic in the CHO-HGPRT Forward Mutation Assay, due to its lack of dose-related and reproducible increases in mutant frequency, both with and without metabolic activation. However, some positive results were seen but were discounted. Without activation there was in the first trial an increase in mutation frequency at 75 µg/ml but at high cytotoxicity. In the second trial the mutation frequency was elevated in two 25 µg/ml and one 50 µg/ml culture. In a third trial only one of two cultures at 25 µg/ml showed an elevation. With activation in the first trial the mutation frequency of only one culture at 25 µg/ml was increased. In the second assay increases in one of two cultures were seen at 12.5, 25 and 50 µg/ml and at 100 µg/ml. In a third trial no increases were seen.
CONCLUSION	The notified chemical was evaluated as non mutagenic to Chinese Hamster ovary (CHO) cells treated in vitro under the conditions of the test. The elevations seen were not strongly dose related and were sporadic or observed at high cytotoxicity so were discounted as not fulfilling *a priori* test criteria.
TEST FACILITY	Bayer AG (1992)

7.10. Genotoxicity – in vivo

TEST SUBSTANCE	Preventol O extra
METHOD	Comet Assay in vivo was performed according to Singh *et al.* (1988) with minor modifications. The different steps are comparable to the procedure described by Sasaki *et al.* (1997)
Species/Strain	Male CD-1 mice (Crl:CD-1(1CR)BR, SPF)
Route of Administration	Oral – gavage
Vehicle	Olive oil

Remarks – Method None.

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Sacrifice Time Hours*
Negative control	12 male	0	4 animals at 3 hours 4 animals at 8 hours 4 animals at 24 hours
Preventol O extra	12 male	250	4 animals at 3 hours 4 animals at 8 hours 4 animals at 24 hours
Preventol O extra	12 male	2000	4 animals at 3 hours 4 animals at 8 hours 4 animals at 24 hours
Ethylmethanesulfonate (EMS)	12 male	400	4 animals at 3 hours 4 animals at 8 hours 4 animals at 24 hours

RESULTS

Doses Producing Toxicity

After single oral administrations of 250 and 2000 mg/kg Preventol O extra, males treated with 2000 mg/kg showed the following compound-related symptoms until sacrifice: apathy, semi-anaesthetised state, roughened fur, pallor, staggering gait, sternal recumbency, spasm, shivering, languor, wide-legged gait and slitted eyes. Two of 12 treated males died during the test period, due to the acute oral toxicity of 2000 mg/kg Preventol O extra. These findings demonstrate relevant systemic exposure of males to Preventol O extra. No symptoms were recorded for the control groups. No animal died in these groups.

Genotoxic Effects

Hepatocytes and kidney cells of negative controls showed good cell viabilities after all three sacrifice times. No relevant cytotoxic effects could be observed in hepatocytes or kidney cells of mice exposed to Preventol O extra. The same was true for cells of the positive control animals.

Comet Assay

According to assessment criteria Preventol O extra caused no biologically relevant increase in tail length in liver and kidney cells of treated mice for all sacrifice times. This assessment is supported by the tail length distribution of single cells. No biologically relevant difference to the respective negative control could be observed.

Clear increases in tail length were observed in liver and kidneys of EMS-treated mice for all sacrifice times.

Remarks – Results None.

CONCLUSION The notified chemical was not clastogenic in this in vivo Comet assay under the conditions of the test.

TEST FACILITY Bayer AG (2000)

8. ENVIRONMENT

8.1. Environmental fate

8.1.1. Ready biodegradability

TEST SUBSTANCE	Preventol OF 45 containing > 95% notified chemical on dry basis.
METHOD	OECD TG 301 E Ready Biodegradability SOP devised in accordance with appendix V C.3 degradability: Modified OECD Screening Test Commission Directive 84/499/EEC.
Inoculum	Activated Sludge from secondary effluent from a laboratory scale unit receiving predominantly domestic sewage.
Exposure Period	28 Days
Auxiliary Solvent	Nil
Analytical Monitoring	Dissolved Organic Carbon (DOC)
Remarks - Method	The test substance (nominally 20 mg/L DOC) was suspended in a mineral medium, inoculated with activated sludge (0.5 mL/ 900 mL) under aerobic conditions in the dark at 20- 25°C.

RESULTS

Day	*Blank DOC mg/L*	*Test substance DOC*	*% Degradation*
0	2	18	0
7	3	3	100
14	3	3	94
21	2	2	100

Remarks - Results	100% biodegradation was reached after 7 days, therefore the test was completed after 21 days
CONCLUSION	The test substance is readily biodegradable. However this result must be treated with some caution as a reference (control) substance was not tested.
TEST FACILITY	Bayer AG (1991a)

8.1.2. Bioaccumulation

Not determined

The compound is water soluble and readily biodegradable and is therefore unlikely to bioaccumulate.

8.2. Ecotoxicological investigations

8.2.1. Acute toxicity to fish

TEST SUBSTANCE	Preventol OF containing > 95% notified chemical on dry basis.
METHOD	Suggested procedure: Federal Environment Agency, Berlin, May 1984 Ed. - static test.
Species	Zebra Fish (*Brachidanio Rerio)*
Exposure Period	96 Hours
Auxiliary Solvent	Nil
Water Hardness	8.8 °dH ≡ 157 mg $CaCO_3$/L
Analytical Monitoring	HPLC analysis
Remarks – Method	Ten fish were used for each treatment at concentrations of 7.8, 11, 16, 22,

31, 44, 63 mg/L and as a control. Observations for mortality and visible abnormalities were performed at 2, 24, 48 72 and 96 h.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*2 h*	*24 h*	*48 h*	*72 h*	*96 h*
Control	<0.5	10	0	0	0	0	0
7.8	<0.5 - 7.88	10	0	0	0	0	0
11	10.8 - 8.98	10	0	0	0	0	0
16	7.41 - 16.2	10	0	0	1	0	3
22	21.4 - 22.2	10	0	10			
31	30.4 - 30.9	10	0	10			
44	43.1 - 43.8	10	0	10			
63	61.9 - 62.4	10	0	10			

LC50 16 mg/L of Preventol OF at 96 hours ≡ 6.2 mg/L notified chemical.
LOEC 11 mg/L of Preventol OF at 96 hours ≡ 4.3 mg/L notified chemical.

Remarks – Results The concentration of the notified chemical was tested at each time interval during the test. The concentration decreased slightly during the test. The LC50 was determined by probit analysis. At 11 mg/L all fish were lethargic at all times. Water quality measurements (pH, dissolved oxygen and temperature) were within acceptable limits throughout the test.

CONCLUSION The notified chemical is toxic to fish.

TEST FACILITY Bayer AG (1991b)

8.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Preventol OF containing > 95% notified chemical on dry basis.

METHOD Suggested procedure: Federal Environment Agency, Berlin, May 1984 Ed. - static test.

Species *Daphnia magna*
Exposure Period 48 hours

Auxiliary Solvent Nil
Water Hardness 15.5 °dH ≡ 277 mg $CaCO_3$/L
Analytical Monitoring HPLC analysis
Remarks - Method Duplicate analysis of ten daphnids was performed for each treatment at concentrations of 2.0, 2.8, 3.9, 5.5, 7.7, 11, 16, 22 and 31 mg/L and as a control. Reference substance potassium dichromate was used.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
Control	<0.50	20	0	0
2.0	2.12- 2.24	20	0	0
2.8	Not tested	20	0	0
3.9	Not tested	20	0	0
5.5	Not tested	20	2	5
7.8	Not tested	20	2	12
11	Not tested	20	10	19
16	Not tested	20	20	
22	Not tested	20	20	
31	30.9- 31.2	20	20	

	10 mg/L at 24 hours ≡ 3.9 mg/L of notified chemical
LC50	7.0 mg/L at 48 hours ≡ 2.7mg/L of notified chemical
NOEC (or LOEC)	3.0 mg/L at 48 hours ≡ 1.5 mg/L of notified chemical
Remarks - Results	The concentration of the notified chemical was tested at each time interval during the test. The concentration decreased slightly during the test. Water quality measurements (pH, dissolved oxygen and temperature) were within acceptable limits throughout the test. The reference substance was tested at nominal concentrations of 0.5, 1.0, 1.5, 2.0, 3.0, 4.0 and 5.0 mg/L. The EC50 of potassium dichromate at 24 hours was found to be 10 mg/L outside of the range of 0.9 mg/L- 1.9 mg/L stated in the guidelines. Drift from the guideline value is said to have occurred over the years. As the drift is significant, the validity of the result must be viewed with caution.
CONCLUSION	The notified chemical is toxic to daphnia.
TEST FACILITY	Bayer AG (1991c)

8.2.2.1 Chronic toxicity to aquatic invertebrates

TEST SUBSTANCE	Preventol OF containing > 95% notified chemical on dry basis.
METHOD	OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test – semi-static system
Species	*Daphnia magna*
Exposure Period	21 days
Auxiliary Solvent	Nil
Water Hardness	Not specified
Analytical Monitoring	HPLC analysis
Remarks - Method	Ten parallel analyses of a single daphnia were performed for each treatment at concentrations of 0.07, 0.22, 0.7, 2.2 and 7.0 mg/L and as a control. Illumination was approximately 1000 Lux. No deviations form standard test procedure.

RESULTS

Concentration mg/L			*# Immobilised*	*Reproduction*	
Nominal	*Actual*	*Number of D. magna*	*After 21 days*	*Young per parent*	*Percent*
Control	<0.50	10	0	111.3	100
0.07	<0.50 - 0.13	10	0	93.3	83.8
0.22	0.14 - 0.23	10	0	111.2	99.9
0.7	0.63 - 0.73	10	0	91.5	82.2
2.2	1.95 - 2.32	10	0	41.5	37.3
7.0	6.85 - 7.51	10	10	-	-

EC50 (Immobilisation)	3.92 mg/L at 21 days ≡ 1.52 mg/L of notified chemical
EC50 (Reproduction)	1.30 mg/L at 21 days ≡ 0.50 mg/L of notified chemical
NOEC (Reproduction)	0.22 mg/L at 21 days ≡ 0.09 mg/L of notified chemical
LOEC (Reproduction)	0.7 mg/L at 21 days ≡ 0.27 mg/L of notified chemical
Remarks - Results	To allow for subitaneous eggs fifteen parallel tests were performed on the control and twelve on each of the test sample concentrations. These were reduced to ten parallel tests as required. Concentration of test substance was performed at start, 24 hours, 48 hours, after 1st replacement of test medium and 72 hours of exposure. EC 50 was determined by the geometric mean of EC and EC 100. EC50 reproduction was determined by probit analysis. NOEC and LOEC were determined by Dunnett test.
CONCLUSION	The notified chemical is moderately chronically toxic to daphnia.
TEST FACILITY	Bayer AG (1991d)

8.2.3. Algal growth inhibition test

TEST SUBSTANCE	Preventol OF containing > 95% notified chemical on dry basis.
METHOD	DIN Standard 38412 Pt 9 May 1989
Species	*Scenedesmus subspicatus* (CHODAT)
Exposure Period	72 hours
Concentration Range	Nominal: 0 - 100 mg/L Actual: … mg/L
Auxiliary Solvent	Nil
Water Hardness	Not Specified
Analytical Monitoring	HPLC
Remarks - Method	Algal suspensions containing 10^4 cells per mL were used for each treatment at concentrations of 0.10, 0.32, 1.00, 3.16, 10.0, 31.6 and 100 mg/L and as a control. The effect on biomass and growth rate was recorded after 72 hours.

RESULTS

Concentration mg/L at 72 h	*Biomass Integral of biomass*	*Growth Rate day^{-1}*
0	308 000	1.52
0.1	343 000	1.57
0.32	336 000	1.56
1.00	323 000	1.55
3.16	237 000	1.45
10.0	89 600	1.07
31.6	10 200	0.25
100	4 920	0.07

Remarks - Results
EC50 biomass 1.5 mg/L ≡ 0.6 mg/L of notified chemical.
EC50 growth rate 12 mg/L ≡ 4.6 mg/L of notified chemical.
Water quality measurements (pH, dissolved oxygen and temperature) were within acceptable limits throughout the test.

CONCLUSION
The notified chemical is highly toxic to algae.

TEST FACILITY
Bayer AG (1991e)

8.2.4. Inhibition of microbial activity

TEST SUBSTANCE
Preventol OF containing > 95% notified chemical on dry basis.

METHOD
International Standard ISO-1986 (E) SOP 3.005
Inoculum: Activated sludge
Exposure Period: Not Specified
Concentration Range: Nominal: 56- 560 mg/L

Remarks – Method
Inoculums containing 6g/L SS were used for each treatment at concentrations of 56, 100, 180, 320, 560 mg/L and as a control. The respiratory rate was measured. 3, 5-dichlorophenol was used as a reference standard.

Result

Test concentration mg/L	Respiratory Rate mg/L.h	Inhibition %
56	24.0	17.2
100	21.4	26.2
180	14.0	51.7
320	5.1	82.4
560	2.4	91.7

Remarks – Results
EC50 157 mg/L ≡ 57.6 mg/L of notified chemical. No data was supplied for the reference standard result.

CONCLUSION
The notified chemical is moderately toxic to bacteria.

TEST FACILITY
Bayer AG (1991f)

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

The notified chemical is used in paper products. The notifier indicates that a portion of the product will degrade over the lifespan of the useful product whilst the remainder will be intimately bound to the paper product. Release from reformulation and manufacture of the paper products is expected to be minimal. A large portion of the paper products at the end of their useful life will be landfilled with some being incinerated. It is however expected according to the notifier's submission that approximately 50% of the paper product will be recycled. (See http://www.apic.asn.au/recycling/default.htm#How%20much%20waste%20).

The notified chemical is water soluble, is surprisingly volatile given its ionic structure, has only limited affinity for soil or sludge, but is readily bio-degradable. When disposed to landfill the chemical is expected to be leached from the paper product where it will be fairly mobile in the aqueous compartment, with a portion expected to volatilise. The chemical is likely to bio-degrade rapidly and is hence unlikely to be released from landfill.

During incineration the chemical is expected to be combusted to form oxides of carbon and water vapour with the potassium oxide reporting to the ash.

It is expected that up to 50 tonnes of the chemical will enter the paper recycling process. This is likely to occur at recycling centres all around Australia. A worst case scenario would involve assuming that none of the chemical is degraded, volatilised or absorbed to the sludge either in the water treatment plant or sewage plant.

Chemical released. kg	Annual sewage outfall across Australia assuming 20.5 million persons and 200L per person per day. GL	Concentration. µg/L
50000	1496	33.42

Therefore the worst case PEC is 33.42 µg/L

Taking into account the chemical's propensity to volatilise, degrade or absorb sludge a more realistic aquatic concentration can be predicted. Henry's law constant is calculated from the vapour pressure of 2.41 kPa at 20°C and the water solubility of 687 g/L at 20ºC resulting in a value of 0.73. The logarithm of Henry's Law constant (-0.14), the Kow (2.4) values and the chemical's ready biodegradability may be used to estimate the percentage which will remain in the aqueous compartment after waste water treatment. According to the Simple Treat model approximately 12% will remain in the aqueous phase.

Chemical released. kg	Amount of chemical remaining in aqueous phase assuming 88% is lost from volatilisation, absorption or biodegradation. kg	Annual sewage outfall across Australia assuming 20.5 million persons and 200 L per person per day. GL	Concentration. µg/L
50000	6000	1496	4.01

A more realistic PEC at the sewage outfall is therefore 4.01 µg/L.

9.1.2. Environment – effects assessment

The results of the aquatic toxicity tests for the notified chemical are listed below. As daphnia showed the highest toxic effect for the three trophic levels, EC50 (Reproduction) at 0.5 mg/L chronic effects on daphnia based on the notified chemical will be used as the toxicological endpoint.

Organism	Duration	End Point	Toxicity. mg/L
Zebra Fish	96 hours	LC50	6.2
Daphnia (acute)	48 hours	EC50	2.7
Daphnia (chronic)	21 days	EC50 (reproduction)	0.5
Daphnia (chronic)	21 days	EC50 (Immobilisation)	1.52
Algae	72 hours	EC50 biomass	0.6
Algae	72 Hours	EC50 growth rate	4.6
Sludge micro-organisms	Not reported	EC50	57.6

A predicted no effect concentration (PNEC- aquatic ecosystems) of 10 µg/L has been derived by dividing the daphnia chronic end point of 0.5 mg/L by an uncertainty (safety) factor of 50 (as toxicity data are available for three trophic levels and chronic data are available for daphnia.)

9.1.3. Environment – risk characterisation

In a worst case scenario, where the waste water from paper recycling is discharged to sewer after treatment it is assumed that no biodegradation, volatilisation or absorption to sludge occurs. This results in a PEC of 33.42 µg/L at the sewage outfall. This results in an unacceptable risk to river environments. However, as the product is readily biodegradable it is expected that a large portion of the notified chemical will decompose during waste water treatment with some also volatilising and absorbing to the sludge. A more realistic PEC at sewage outfall is calculated as 4.01 µg/L.

		PEC µg/L	PNEC µg/L	RQ (PEC/PNEC)
Worst Case	River	33.42	10	3.34
	Ocean	3.34	10	0.33
Mitigated	River	4.01	10	0.40
	Ocean	0.40	10	0.04

From the more realistic RQ the release of the chemical to the environment is not expected to pose an unacceptable risk.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

The primary site of exposure to the notified chemical will occur via opening of the 1100 L bulk containers, their connection to mixing vessels and the cleaning and maintenance of lines, couplings and pumps. Exposure during these operations appears to be controlled by the use of personal protective equipment and be limited to drips and spills. Therefore, potential exposure is likely to be intermittent and can occur on a maximum of 26 days per year.

Once the notified chemical is part of a formulation it is at a concentration of < 0.5%. Therefore, exposure of workers involved in paper manufacture will be low for this reason and because the system is largely automated.

9.2.2. Public health – exposure assessment

The notified chemical is not available for sale to the public. The potential for public exposure to the notified chemical during transport, reformulation and manufacture of paper is likely to be negligible. Although members of the public will make dermal contact with dried form of the notified chemical when handling treated paper, public exposure is expected to be low.

9.2.3. Human health – effects assessment

The notifier has provided a number of studies and literature reference on the toxicology of the notified chemical, its parent free acid (OPP) and sodium salt of the free acid. The notifier has also provided argument that the biological activity of a solution of salt is independent of it actual salt form (Bayer AG, 1991h).

The notified chemical was demonstrated to be of (probable) low toxicity via the oral and dermal routes in rats although the pure chemical was not used in these studies. The parent compound of the notified chemical was of low toxicity in acute inhalation toxicity studies cited in Bomhard *et*

al. (2002). The notified chemical was corrosive to the skin and eyes of rabbits. Analogues of the notified chemical were not skin sensitisers in guinea pigs and were not genotoxic in short term tests. The NOAEL for the parent compound in a 28-day oral repeat dose study in Beagle dogs was > 300 mg/kg bw/day.

As the notified chemical, its parent compound (OPP) and the analogous sodium salt (SOPP) are used as fungicides and disinfectants with OPP and SOPP in widespread use, an extensive toxicological database exists and has been evaluated by Bomhard *et al.* (2002). Studies on chronic toxicity, reproductive toxicity, teratogenicity and immuntoxicity have not revealed any effects. The incidence of hepatocellular adenomas was elevated in male mice in one 2 year study with OPP. Papillomas and transition cell carcinomas were observed in the urothel of the urinary bladder (at very high doses also of the renal pelvis and the papilla) of rats following repeated oral exposure. Male rats were much more sensitive than female rats. In mice, hamsters, guinea pigs and dogs, urothelial lesions do not develop even at very high doses. The tumorigenic effects in rats and male mice were considered by Bomhard *et al.* (2002) to represent high dose, sex- and/or species specific phenomena, based on nongenotoxic mechanisms of action. They conclude that conventional margin of safety approaches are appropriate when assessing the risk of applications of OPP and its salts.

Based on the available data, the notified chemical is classified as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC 2004) and assigned the risk phrase R34 – Causes burns.

The International Agency for Research on Cancer (IARC) has classified OPP as group 3, not classifiable as to its carcinogenicity to humans and the sodium salt of OPP as group 2B, possibly carcinogenic to humans. However, as noted above, Bomhard *et al.* (2002) have reviewed the extensive literature on the genotoxicity and carcinogenicity of these chemicals and concluded that the tumorigenic effects in rats and male mice represent high dose, sex- and/or species specific phenomena, based on nongenotoxic mechanisms of action. Therefore, classification as a category 3 carcinogen according to the NOHSC criteria would seem to be unwarranted at this time.

9.2.4. Occupational health and safety – risk characterisation

The notified chemical is classified as corrosive. The imported formulation at < 60% is also classified as corrosive. Therefore, there is a risk of burns to transport and storage workers in the event of accidental breach of the containers.

Once the 1100 L bulk containers containing the imported formulation of the notified chemical, are received at the reformulation plant, there is a risk of burns to skin or eyes from drips and spills occurring during transfer of the formulation to the mixing vessel. The mixing process is stated to be automated and enclosed. The notifier has indicated that adequate personal protective equipment will be worn during formulation and maintenance activities. Provided this PPE is adequately used and correctly chosen and maintained, the risk of burns should be adequately mitigated. Once the notified chemical is completely mixed into the final product at < 0.5% there will be a low risk of burns to workers involved in packing off and in the end use of papermaking.

The control measures required to be in place to mitigate the risk of burns should adequately protect against unforeseen or unknown carcinogenicity. It should be noted that the risk of carcinogenicity is considered to low solely on the basis of toxicological data in long term animal studies. Therefore, with the PPE in place as indicated by the notifier together with the fact that formulation takes place on only 26 days per year, the risk of carcinogenicity is further reduced.

9.2.5. Public health – risk characterisation

The only possibility of the public coming into contact with the notified chemical should be in the event of a transport accident where rupture of the containers occur. Therefore, the risk of burns to the public from this scenario can be considered to be low. Once the notified chemical is delivered to sites of reformulation, the risk to the public should be negligible.

Office workers will make dermal contact with the dried form of the notified chemical when handling paper items. The risk to public health from the notified chemical is likely to be low

because the notified chemical is unlikely to be bioavailable and present at very low concentrations.

10. CONCLUSIONS – ASSESSMENT LEVEL OF CONCERN FOR THE ENVIRONMENT AND HUMANS

10.1. Hazard classification

Based on the available data the notified chemical is classified as hazardous under the NOHSC *Approved Criteria for Classifying Hazardous Substances*. The classification and labelling details are:

R34 – Causes burns

and

As a comparison only, the classification of notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations, 2003) is presented below. This system is not mandated in Australia and carries no legal status but is presented for information purposes.

Corrosive to the skin Category 1 and an eye irritant Category 1 (irreversible effects on the eye)

10.2. Environmental risk assessment

On the basis of the PEC/PNEC ratio:

The chemical is not considered to pose a risk to the environment based on its reported use pattern.

10.3. Human health risk assessment

10.3.1. Occupational health and safety

There is Low Concern to occupational health and safety under the conditions of the occupational settings described.

10.3.2. Public health

There is Negligible Concern to public health when used as described.

11. MATERIAL SAFETY DATA SHEET

11.1. Material Safety Data Sheet

The MSDS of a product containing the notified chemical provided by the notifier was in accordance with the NOHSC *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC 2003). It is published here as a matter of public record. The accuracy of the information on the MSDS remains the responsibility of the applicant.

11.2. Label

The label for a product containing the notified chemical provided by the notifier was in accordance with the NOHSC *National Code of Practice for the Labelling of Workplace Substances* (NOHSC 1994). The accuracy of the information on the label remains the responsibility of the applicant.

12. RECOMMENDATIONS

REGULATORY CONTROLS
Hazard Classification and Labelling

- The NOHSC Chemicals Standards Sub-committee should consider the following health hazard classification for the notified chemical:
  - R34: Causes burns

- Use the following risk phrases for products/mixtures containing the notified chemical:
  - ≥ 10%: R34 Causes burns
  - 10% ≥ concentration ≥ 5%: R36, R38 Irritating to skin and eyes

CONTROL MEASURES
Occupational Health and Safety

- Employers should implement the following engineering controls to minimise occupational exposure to the notified chemical as introduced:
  - Controls to minimise spillage during transfer should include dry couplings and lines and pumps designed to be used with corrosive liquids.

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced:
  - Industrial clothing and gloves whose material has been tested to be resistant to corrosive chemicals and chemical safety googles with side shields

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

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

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

Environment

Disposal

- The notified chemical should be disposed of by authorised incineration.

Emergency procedures

- Spills or accidental release of the notified chemical should be handled by physical containment using absorbing material (sand, vermiculite etc) and transferred to labelled closable containers for disposal.

12.1. Secondary notification

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

(1) Under Section 64(2) of the Act:
  - if any of the circumstances listed in the subsection arise.

The Director will then decide whether secondary notification is required.

No additional secondary notification conditions are stipulated.

13. BIBLIOGRAPHY

Bayer AG (1988a) Preventol Trial Product OC 3041 = Preventol OF Investigation of Acute Oral Toxicity on Male and Female Wistar Rat. Study No. 17260. Bayer AG Institute for Toxicology, Germany (unpublished report submitted by notifier).

Bayer AG (1988b) Preventol Trial Product OC 3041. Bayer AG Institute for Toxicology, Germany (unpublished report submitted by notifier).

Bayer AG (1990a) Hydrolysis as a function of pH of Preventol O, Study No. G 89/0056/02 LEV, ZF- D Zentrale Analytik Builiding O 13 D- 5090 Leverkusen Germany (unpublished report submitted by notifier).

Bayer AG (1991a) Preventol OF Acute Dermal Toxicity Study in Male and Female Wistar Rats. Study No. 20817. Bayer AG Institute of Industrial Toxicology, Germany (unpublished report submitted by notifier).

Bayer AG (1991b), Biodegradation of Preventol OF, Study No. 255 A/910, Institut fur Umweltanalyse und Bewetungen Geb. W 15 5090 Leverkusen Germany (unpublished report submitted by notifier).

Bayer AG (1991c) Acute Toxicity Fish of Preventol OF, Study No. 255 A/91 F Institut fur Umweltanalyse und Bewetungen Geb. W 15 5090 Leverkusen Germany (unpublished report submitted by notifier).

Bayer AG (1991d) Acute Daphnia Toxicity of Preventol OF, Study No. 255 A/91 D Institut fur Umweltanalyse und Bewetungen Geb. W 15 5090 Leverkusen Germany (unpublished report submitted by notifier).

Bayer AG (1991e) Chronic Toxicity Daphnia of Preventol OF, Study No. 255 A/91 DL Institut fur Umweltanalyse und Bewetungen Geb. W 15 5090 Leverkusen Germany

Bayer AG (1991f), Growth Inhibition Test (Green Algae) of Preventol OF, Study No. 255A/91 AL Institut fur Umweltanalyse und Bewetungen Geb. W 15 5090 Leverkusen Germany (unpublished report submitted by notifier).

Bayer AG (1991g), Bacterial Toxicity of Preventol OF, Study No. 255 A/91 B Institut fur Umweltanalyse und Bewetungen Geb. W 15 5090 Leverkusen Germany (unpublished report submitted by notifier).

Bayer AG (1991h) The Similarity of the Free Acid and the Salt Form of Phenols. Bayer AG, Leverkusen, Germany (unpublished report submitted by notifier).

Bayer AG (2000) Preventol O extra Comet Assay in vivo in Mouse Liver and Kidney. Report No. PH 30130. Bayer AG PH-PD Toxicology, Wuppertal Germany (unpublished report submitted by notifier).

Bayer AG (2001a) Partition Coefficient (n-octanol/water)/Dissociation Constant of Preventol O, Study No. A 00/0068/03 LEV, ZF- Zentrale Analytik Gebaude Q 18 51368 Leverkusen (unpublished report submitted by notifier).

Bayer AG (2001b) Determination of the Adsorption/Desorption of Preventol O, Study No. A 00/0068/04, ZF-Zentrale Analytik Gebaude Q 18 51368 Leverkusen (unpublished report submitted by notifier).

Bayer AG (2002a) Physicochemical Properties. Study No. A 02/0060/01 LEV. ZF- Zentrale Analytik Gebaude Q 18 51368 Leverkusen (unpublished report submitted by notifier).

Bayer AG (2002b) Water Solubility of Preventol OF, Study No. A 02/0060/03, ZF- Zentrale Analytik Gebaude Q 18 51368 Leverkusen (unpublished report submitted by notifier).

Bayer AG (2003) Vapour Pressure of Preventol OF, Study No. 03/010/01, BTS-PT-RPT-KPM Gebaude B310 51368 Leverkusen (unpublished report submitted by notifier).

Bayer Industry Services (2003) Determination of Safety-Relevant Data of Preventol OF. Study No. 03/00303. Bayer Industry Services, Laboratories for Safety Data and Measurements, Leverkusen, Germany (unpublished report submitted by notifier).

Bomhard E M, Brendler-Schwaab S Y, Freyberger A, Herbold B A, Leser K H and Richter M (2002) *O*-Phenylphenol and its Sodium and Potassium Salts: A Toxicological Assessment. Critical Reviews in Toxicology **32:** 551 – 626.

JBC Inc Research Laboratory (1989) Reverse Mutation Assay using Microorganisms. Test No. 1097. JBC Inc Research Laboratory, Japan (unpublished report submitted by notifier).

NOHSC (1994) National Code of Practice for the Labelling of Workplace Substances [NOHSC:2012(1994)]. National Occupational Health and Safety Commission, Canberra, Australian Government Publishing Service.

NOHSC (2004) Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)]. National Occupational Health and Safety Commission, Canberra, AusInfo.

NOHSC (2003) National Code of Practice for the Preparation of Material Safety Data Sheets, 2nd edn [NOHSC:2011(2003)]. National Occupational Health and Safety Commission, Canberra, Australian Government Publishing Service.

Sasaki Y F, Saga A, Akasaka K, Yoshida E, Nishidate Y Q, Matsusaka Su N and S Tsuda (1997) Mutat Res **395:** 189 – 198.

Singh N P, McCoy R R, Tice R R and E L Schneider (1988) Exp Cell Res **175:** 184 – 191.

The Dow Chemical Company (1990) Ortho-Phenylphenol: Palatability/Probe, Four-Week and One-year Oral Toxicity Study in Beagle Dogs. Report No. K-001024-039. The Dow Chemical Company, USA (unpublished report submitted by notifier).

United Nations (2003) Globally Harmonised System of Classification and Labelling of Chemicals (GHS). United Nations Economic Commission for Europe (UN/ECE), New York and Geneva.