File No: STD/1323

June 2009

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

ADK STAB PEP-36

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) (the Act) and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by the Department of Health and Ageing, and conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of the Environment, Water, Heritage and the Arts.

For the purposes of subsection 78(1) of the Act, this Full Public Report may be inspected at our NICNAS office by appointment only at 334-336 Illawarra Road, Marrickville NSW 2204.

This Full Public Report is also available for viewing and downloading from the NICNAS website or available on request, free of charge, by contacting NICNAS. For requests and enquiries please contact the NICNAS Administration Coordinator at:

Street Address:	334 - 336 Illawarra Road MARRICKVILLE NSW 2204, AUSTRALIA.
Postal Address:	GPO Box 58, SYDNEY NSW 2001, AUSTRALIA.
TEL:	+ 61 2 8577 8800
FAX	+ 61 2 8577 8888
Website:	www.nicnas.gov.au

Director
NICNAS

TABLE OF CONTENTS

FULL PUBLIC REPORT 3
1. APPLICANT AND NOTIFICATION DETAILS 3
2. IDENTITY OF CHEMICAL 3
3. COMPOSITION 4
4. PHYSICAL AND CHEMICAL PROPERTIES 4
5. INTRODUCTION AND USE INFORMATION 5
6. HUMAN HEALTH IMPLICATIONS 5
6.1 Exposure assessment 5
6.1.1 Occupational exposure 5
6.1.2. Public exposure 6
6.2. Human health effects assessment 6
6.3. Human health risk characterisation 8
6.3.1. Occupational health and safety 8
6.3.2. Public health 8
7. ENVIRONMENTAL IMPLICATIONS 8
7.1. Environmental Exposure & Fate Assessment 8
7.1.1 Environmental Exposure 8
7.1.2 Environmental fate 9
7.1.3 Predicted Environmental Concentration (PEC) 9
7.2. Environmental effects assessment 9
7.2.1 Predicted No-Effect Concentration 9
7.3. Environmental risk assessment 10
8. CONCLUSIONS AND REGULATORY OBLIGATIONS 10
Hazard classification 10
Human health risk assessment 10
Environmental risk assessment 10
Recommendations 10
Regulatory Obligations 11
APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES 12
APPENDIX B: TOXICOLOGICAL INVESTIGATIONS 15
B.1. Irritation – eye 15
B.2. Skin sensitisation 15
B.3. Repeat dose toxicity 16
B.4. Repeat dose toxicity 17
B.5. Repeat dose toxicity 18
B.6. Repeat dose toxicity - Neurotoxicity 20
B.7. Genotoxicity – bacteria 22
B.8. Genotoxicity – bacteria 22
B.9. Genotoxicity – in vitro 23
APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS 25
C.1. Environmental Fate 25
C.1.1. Ready biodegradability 25
C.1.2. Bioaccumulation 25
C.2. Ecotoxicological Investigations 25
C.2.1. Acute toxicity to fish 25
C.2.2. Acute toxicity to aquatic invertebrates 26
C.2.3. Algal growth inhibition test 27
C.2.4. Inhibition of microbial activity 28
BIBLIOGRAPHY 29

FULL PUBLIC REPORT

ADK STAB PEP-36

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
MARUBENI AUSTRALIA LTD (ABN 53 000 329 699)
Level 19, 367 Collins Street
MELBOURNE VIC 3000

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:
Test facilities details

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: Hydrolysis, Adsorption/Desporption, Dissociation Constant, Flash Point, Stability, Acute Inhalation Toxicity, Induction of Germ Cell Damage, Bioaccumulation, Chronic Toxicity to Invertebrates.

NOTIFICATION IN OTHER COUNTRIES
EU (1993)
USA (1992)
Japan (1987)
Korea

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
ADK STAB PEP-36

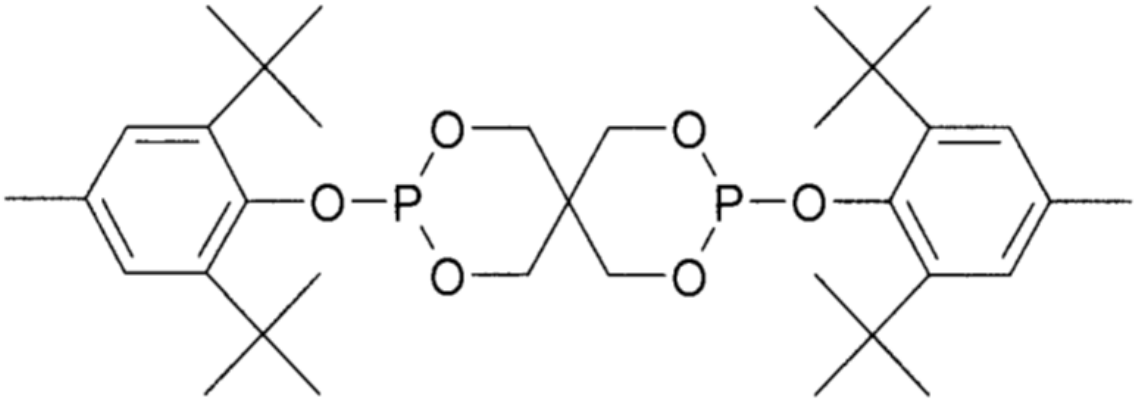
CAS NUMBER
80693-00-1

CHEMICAL NAME
2,4,8,10-Tetraoxa-3,9-diphosphaspiro(5,5)undecane, 3,9-bis(2,6-bis(1,1-dimethylethyl)-4-methylphenoxy)-

OTHER NAME(S)
Phosphorous acid, cyclic neopentanetetrayl bis(2,6-di-tert-butyl-4-methylphenyl) ester
Mark PEP 36
3,9-Bis(2,6-di-tert-butyl-4-methylphenoxy)-2,4,8,10-tetraoxa-3,9-diphosphaspiro[5.5]undecane
3,9-Bis[2,6-bis(1,1-dimethylethyl)-4-methylphenoxy]-2,4,8,10-tetraoxa-3,9-diphosphaspiro[5.5]undecane
Bis(2,6-di-tert-butyl-4-methylphenyl)pentaerythritol diphosphite
Di(2,6-di-tert-butyl-4-methylphenyl)pentaerythritol diphosphite
Pentaerythritol bis[(2,6-di-tert-butyl-4-methylphenyl)phosphite]

MOLECULAR FORMULA
$C_{35}H_{54}O_6P_2$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
633 Da.

ANALYTICAL DATA
Reference NMR, IR, GPC, UV spectra were provided.

3. COMPOSITION

DEGREE OF PURITY > 99%

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (> 1% by weight)

Chemical Name Phenol, 2,6-bis(1,1-dimethylethyl)-4-methyl-
CAS No. 128-37-0 *Weight %* < 1%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20°C AND 101.3 kPa: White powder

Property	Value	Data Source/Justification
Melting Point/Freezing Point	231.7 - 233.2°C	Measured
Boiling Point	Decomposed at > 325°C without boiling	Measured
Density	1,188 kg/m^3 at 20°C	Measured
Vapour Pressure	1.1x10^{-7} kPa at 25°C	Measured
Water Solubility	< 0.01 mg/L at 20°C	Measured
Hydrolysis as a Function of pH	Not determined	Precluded by low water solubility
Partition Coefficient (n-octanol/water)	log Pow > 6	Measured
Adsorption/Desorption	log K_{oc} > 4.5 at 30°C	Measured
Dissociation Constant	Not determined	Precluded by low water solubility
Particle Size	Respirable fraction (<10 μm): 18.3% MMAD* = 59.2 μm	Measured
Surface Tension	73.9 nM/m at 20°C	Measured
Flammability	Not highly flammable	Measured
Autoignition Temperature	Not observed	Measured
Explosive Properties	Not highly explosive	Measured

* MMAD = Mass Median Aerodynamic Diameter.

DISCUSSION OF PROPERTIES
The notified chemical is a high performance phosphite. This class of chemical is known to be very hygroscopic, and to readily undergo hydrolysis, with the release of the substituted phenol, but stability can be improved by changing the form and/or inclusion of additives (Callierotti *et al*, 2001). In light of these performance characteristics, the notified chemical would be expected to undergo ready hydrolysis if released to the environment, but the rate of hydrolysis would be limited by the low water solubility. Steric hindrance by the bulky t-butyl substituents may also protect against hydrolysis, as suggested by the apparent stability of the notified chemical in algal culture medium. For full details of tests on physical and chemical properties, please refer to Appendix A.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL OVER NEXT 5 YEARS
The notified chemical will be imported as a neat powder (> 99%) or a component of polymers (≤ 0.4%).

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	10	10	10	15	15

PORT OF ENTRY
Sydney, Melbourne

TRANSPORTATION AND PACKAGING
The notified chemical will be imported by sea in plastic-lined paper bags or cardboard boxes, before being transported from the dockside by road directly to the notifier's warehouse where it is dispatched to polymer manufacture sites.

USE
The notified chemical will be used as an antioxidant in polymeric resins to make electrical appliances and components of automotive parts.

OPERATION DESCRIPTION
The notified chemical as imported in powder form at > 99% will be manually weighed and added to a mixing vessel where it will be mixed with plastic powder, fillers and other additives and fed automatically into a closed, preheated extruder to produce plastic pellets. The plastic pellets will be weighed and packed into bags for sale to customers.

Plastic pellets containing the notified chemical at ≤ 0.4% will be fed into the hopper of an injection moulding machine. The pellets will be heated and injected as a liquid under pressure, to form plastic articles for use in electrical appliances and automotive parts.

6. HUMAN HEALTH IMPLICATIONS

6.1 Exposure assessment

6.1.1 Occupational exposure

NUMBER AND CATEGORY OF WORKERS

Category of Worker	*Number*	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport	1-2	< 8	5-7
Warehouse	2-3	1	10-20
Plastic pellet formulation	5-10	2-4	60-100
Quality assurance testing	1-2	1	60-100
Cleaning of mixer, hopper and floor	1-2	1	60-100
Maintenance of extruder	1-2	1	12
Finished article moulding	5-10	2-4	60-100
Maintenance of moulding equipment	1-2	1	12

EXPOSURE DETAILS
The main potential for exposure to the notified chemical (> 99%) via the inhalation, dermal and ocular routes will occur during manual weighing and addition to a mixing vessel for formulation into plastic pellets. The notifier states that inhalation exposure will be minimised by the use of local exhaust ventilation in areas where the notified chemical will be handled as well as the use of a ventilated booth for weighing. In addition, personal protective equipment (PPE) such as a particle filter mask, safety glasses, head covering, gloves and overalls are expected to be used during handling to further minimise exposure.

Exposure to the notified chemical could also occur to a lesser degree during cleaning, maintenance and quality assurance testing. However, PPE such as safety glasses, gloves and overalls will be used by workers involved in these activities to minimise dermal and ocular exposure.

Exposure is not anticipated during mixing of the notified chemical into plastic pellets as this will take place in a closed system fitted with exhaust ventilation. Neither is exposure expected during handling or extrusion of plastic pellets containing the notified chemical at ≤ 0.4%. To further reduce the potential for exposure, exhaust ventilation is expected to be in use during the operation of injection moulding machinery and workers are expected to wear gloves and eye protection during handling of plastic pellets.

6.1.2. Public exposure
The notified chemical is intended for industrial use only, and will not be available to the public. Therefore, direct exposure to the notified chemical or the plastic pellets is not expected. The public may come into contact with finished articles containing the notified chemical however it is expected to be bound within the plastic in an inert matrix and no potential for exposure from finished articles is anticipated.

6.2. Human health effects assessment

The results from toxicological investigations conducted on the notified chemical are summarised in the table below. Details on some of these studies can be found in Appendix B.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	oral LD50 > 5000 mg/kg bw low toxicity
Rat, acute dermal toxicity	LD50 > 2000 mg/kg bw low toxicity
Rabbit, skin irritation	non-irritating
Rabbit, eye irritation	mildly irritating
Guinea pig, skin sensitisation – adjuvant test	no evidence of sensitisation
Rat, repeat dose oral toxicity – 28 days.	NOEL ≥ 3222 mg/kg bw/day
Beagle, repeat dose oral toxicity – 90 days.	NOEL = 2000 mg/kg bw/day
Rat, repeat dose oral toxicity – 90 days.	NOEL ≥ 2675 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – *in vitro* chromosome aberration	non genotoxic
Hen, repeat dose oral delayed neurotoxicity – 28 days	NOAEL = 1000 mg/kg bw/day

Toxicokinetics, metabolism and distribution
Absorption of the notified chemical across biological membranes is likely to be limited; while its molecular weight is favourable, its low water solubility and high $\log P_{ow}$ are not (EC, 2003). Absorption from the gastrointestinal tract may be aided by micellar solubilisation of fat-soluble components. However, no evidence of absorption following oral exposure was evident in the findings of repeat dose oral toxicity studies conducted in rats and dogs. Given its lipophilicity and low molecular weight, the notified chemical may be absorbed across the lungs following inhalation of solids or vapours.

Acute toxicity
The notified chemical was found to be of low acute oral toxicity in 5 male and 5 female rats according to the method described by the US EPA Toxic Substances Control Act Test Guidelines, 40 CFR Party 798, Subpart B, 1985 (Test Facility C, 1987). There were no mortalities reported at doses up to 5000 mg/kg bw. Adverse findings reported in the study included discolouration of the kidneys and abnormal contents in the intestines in 3 males and 4 females. These findings were not considered adverse and the oral LD50 was determined to be > 5000 mg/kg bw.

The notified chemical was found to be of low toxicity in a rat acute dermal toxicity study according to OECD TG 402 (Test Facility H, 1991a). No mortality occurred during the study and no clinical abnormalities were reported. The acute dermal LD50 was determined to be > 2000 mg/kg bw.

Irritation and Sensitisation
The notified chemical was found to be non-irritating to rabbit skin in a test conducted according to the US Environmental Protection Agency (EPA) Toxic Substances Control Act 40 CFR sec. 798.4470 (Test Facility C, 1988a).

The notified chemical was found to be mildly irritating to the eyes of rabbits in a test conducted according to the US EPA Toxic Substances Control Act 40 CFR sec. 798.4500 (see Appendix B for details). After instillation of the notified chemical in powder form, conjunctival redness was observed in all animals after 1 hour and persisted in 2 animals after 24 hours. Chemosis was observed in 2 animals 1 hour after treatment and was observed in 1 animal 48 hours after treatment. Discharge was observed in 1 animal 1 hour after treatment and in addition, excessive blinking and rubbing of the eye was observed immediately after treatment in 3 animals. Based on these effects, the notified chemical is considered to be mildly irritating to the eyes.

No evidence for sensitisation potential of the notified chemical was found in a Skin Sensitisation – Guinea Pig Maximisation Test according to OECD TG 406 (see Appendix B for details) when 25% was used as the induction concentration.

Repeated Dose Toxicity
The notified chemical was tested in 3 repeat dose oral toxicity studies; 2 in rats (28-day test and 90-day test) and 1 in beagles (90-day test). Discolouration of organs and faeces was observed in beagles treated with the notified chemical but no effects of toxicological significance were observed in any of the treated animals. The NOEL was estimated as ≥ 3222 mg/kg bw/day (28-day test in rats), 2000 mg/kg bw/day (90-day test in beagles) and ≥ 2675 mg/kg bw/day (90-day test in rats) based on the lack of adverse findings in the high-dose groups (see Appendix B for further details).

Genotoxicity
The notified chemical was found not to significantly increase the number of revertant colonies in the presence or absence of metabolic activation when tested in 2 separate studies conducted according to OECD TG 471 (see Appendix B for further details).

The notified chemical was found not to be cytotoxic nor induce an increase in the frequency of structural or numerical chromosome aberrations in chinese hamster V79 cells under the conditions of the study conducted according to OECD TG 473 (see Appendix B for further details).

The results of these tests indicate that the notified chemical is unlikely to be a genotoxin or mutagen.

Delayed neurotoxicity
The notified chemical was administered to hens for 28 days via oral gavage at 1000 mg/kg bw/day. No significant inhibition of average plasma cholinesterase activity or reduction in neuropathy target esterase levels was observed on day 6 of treatment or 24 hours following the final treatment in comparison to values obtained from the control group. No abnormal clinical signs were observed and histopathological examination of neural tissues did not reveal any significant differences compared to neural tissues of control animals. It was therefore concluded that the NOAEL for neurotoxicity in hens under the conditions of the test was 1000 mg/kg bw/day (see Appendix B for further details).

Health hazard classification

Based on the available data the notified chemical is not classified as hazardous under the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

6.3. Human health risk characterisation

6.3.1. Occupational health and safety

Formulation into plastic pellets

The main potential for exposure to the notified chemical (> 99%) is expected to be via inhalation during manual weighing and addition to a mixing vessel for formulation into plastic pellets. No inhalation toxicity studies were conducted on the notified chemical. However, considering 18.3% of the notified chemical consists of insoluble particles in the respirable range (< 10 μm), there is potential for accumulation in the lungs leading to injury following repeated inhalation. However, the notifier states that inhalation exposure will be minimised by the use of local exhaust ventilation in areas where the notified chemical will be handled as well as the use of a ventilated booth for weighing. In addition, personal protective equipment (PPE) such as a particle filter mask to further minimise inhalation exposure.

Workers may also encounter dermal and accidental ocular exposure to the notified chemical (> 99%) during formulation into plastic pellets. The notified chemical was found to be mildly irritating to the eyes when tested in rabbits. However, the effects seen were not severe and had resolved within 72 hours of application. The anticipated use of safety glasses when handling the notified chemical in powder form during formulation into plastic pellets is expected to minimise any potential for exposure and therefore it is not expected to cause eye irritation. Due to the expected low dermal absorption of the notified chemical and its low acute and repeat dose oral toxicity, systemic toxicity is not expected following repeated dermal exposure. In addition, protective gloves are expected to be worn by workers handling the notified chemical which will further reduce the potential for dermal exposure.

The notified chemical is not considered to pose an unreasonable risk to workers during formulation into plastic pellets.

Extrusion into plastic articles

Exposure to the notified chemical is not expected during handling of plastic pellets as it will be bound within an inert matrix within the pellet. Exposure is not anticipated during extrusion as this will take place within a closed vessel. Once extruded into the finished article the notified chemical will be bound within an inert matrix and will not be bioavailable. Therefore the risk to workers from extrusion into the finished article is not expected to be unreasonable.

6.3.2. Public health

Members of the public will only be exposed to plastic articles in which the notified chemical will be bound within an inert matrix and not bioavailable. Therefore, the risk is not considered unacceptable, given that release from the plastic article is not anticipated.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1 Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will not be manufactured in Australia. Release to the environment during shipping, transport and warehousing will only occur through accidental spills or leaks of the polyethylene bag container. This is expected to be minor due to the packaging of the material, and its physical form as a powder or polymer component, which will be easily cleaned up if spilt.

RELEASE OF CHEMICAL FROM USE

There will be some residual powder left in the empty import bags. This is estimated to be less than 0.1% of the annual import volume (i.e. up to 15 kg annually). Empty bags and any residuals will be disposed of by thermal decomposition or landfill.

During the extrusion process to incorporate the notified chemical into plastic pellets and the production of the final plastic article, waste will be generated by spillage, off-cuts, out-of-specification material and equipment cleaning. This waste accounts for up to 3% of the imported notified chemical (i.e. up to 450 kg annually) and will be collected and disposed of by thermal decomposition or landfill.

The process equipment will not be washed between batches. In each batch the first lot of product is discarded. Any spilt material will be collected and placed into sealable containers ready for disposal.

In the end product the notified chemical is incorporated in an inert matrix and will not be released to the environment.

RELEASE OF CHEMICAL FROM DISPOSAL
All the solid wastes generated containing the notified chemical will either be disposed of to landfill or by thermal decomposition. In landfill the notified chemical will not be mobile and will slowly undergo abiotic and biotic degradation. Thermal decomposition will destroy the notified chemical.

7.1.2 Environmental fate

The notified chemical is not readily biodegradable, but can be expected to undergo hydrolysis if released to the environment, although hydrolysis could be slow because of steric hindrance. Hydrolysis would release the phenol (commonly known as BHT or butylated hydroxytoluene). The SIDS dossier for this chemical (http://www.inchem.org/documents/sids/sids/128370.pdf) reports it to be relatively unstable under environmental conditions, though not readily biodegradable. Degradation pathways include modification of the aromatic methyl substituent. The notified chemical can be expected to degrade through similar pathways.

The environmental fate of the notified chemical will be strongly linked to the plastic in which it is incorporated. Discarded plastic articles will slowly degrade through biotic and abiotic processes, and the notified chemical can be expected to degrade similarly. The notifier indicates that leaching or blooming from the plastic is unlikely. The notified chemical would be expected to sorb strongly to soil if so released, and to degrade. Bioaccumulation is considered unlikely, because of the very low water solubility and low release to aquatic ecosystems. However, some potential for bioaccumulation must be assumed, as the SIDS dossier for BHT reports a wide range of bioconcentration factors, from which a moderate to high bioaccumulation potential is assumed in aquatic species.

7.1.3 Predicted Environmental Concentration (PEC)

It is neither necessary nor meaningful to estimate a PEC for the aquatic compartment as the notified chemical is not expected to be released to water when it is used as proposed as a plastic additive.

7.2. Environmental effects assessment

The results from ecotoxicological investigations conducted on the notified chemical are summarised in the table below. Details of these studies can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	EC50 > 0.01 mg/L	Not toxic to limit of water solubility
Daphnia Toxicity	EC50 > 0.01 mg/L	Not toxic to limit of water solubility
Algal Toxicity	EC50 > 0.01 mg/L	Not toxic to limit of water solubility
Inhibition of Bacterial Respiration	EC50 > 1000 mg/L	Not inhibitory to bacterial respiration

Aquatic toxicity testing was complicated by the very low water solubility of the test substance. Harmful effects were seen in fish and daphnids exposed to suspensions of the notified chemical, but these appeared to be due to undissolved particles as the filtered solutions did not affect survival of fish or mobility of daphnids. It is unclear whether fish and daphnids were exposed to the notified chemical or its degradation products in these filtered solutions. The notified chemical appeared to be relatively stable when dispersed in algal culture medium, but instability was noted when THF was used as auxiliary solvent.

7.2.1 Predicted No-Effect Concentration

The PNEC cannot be calculated as the concentrations of the notified chemical that would cause toxicity to fish, daphnids or algae cannot be determined. No harmful effects are expected at concentrations up to the solubility limit.

7.3. Environmental risk assessment

Very little of the notified chemical is expected to enter aquatic environments given its very low water solubility and incorporation into plastics. The chemical is not harmful to fish, daphnids and algae up to the limits of its water solubility, and is therefore not expected to pose a risk to aquatic life when it is used as proposed.

8. CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification

Based on the available data the notified chemical is not classified as hazardous under the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)].

Human health risk assessment

Under the conditions of the occupational settings described, the notified chemical is not considered to pose an unacceptable risk to the health of workers.

When used in the proposed manner, the notified chemical is not considered to pose an unacceptable risk to public health.

Environmental risk assessment

On the basis of the very low water solubility and the reported use pattern, the notified chemical is not considered to pose a risk to the environment.

Recommendations

CONTROL MEASURES

Occupational Health and Safety

- Employers should implement the following engineering controls to minimise occupational exposure to the notified chemical as introduced in ADK STAB PEP-36:
  - Use ventilated booths during weighing
  - Use local exhaust ventilation during handling

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced in ADK STAB PEP-36:
  - Face mask or respirator suitable for respirable airborne particulates

  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 *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)] workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Disposal

- The notified chemical should be disposed of to landfill.

Emergency procedures

- Spills or accidental release of the notified chemical should be handled by containment, collection and subsequent safe disposal.

Regulatory Obligations

Secondary Notification
This risk assessment is based on the information available at the time of notification. The Director may call for the reassessment of the chemical under secondary notification provisions based on changes in certain circumstances. Under Section 64 of the *Industrial Chemicals (Notification and Assessment) Act (1989)* the notifier, as well as any other importer or manufacturer of the notified chemical, have post-assessment regulatory obligations to notify NICNAS when any of these circumstances change. These obligations apply even when the notified chemical is listed on the Australian Inventory of Chemical Substances (AICS).

Therefore, the Director of NICNAS must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from an additive in polymeric resins, or is likely to change significantly;
- the amount of chemical being introduced has increased from 15 tonnes, or is likely to increase, significantly;
- the chemical has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

The Director will then decide whether a reassessment (i.e. a secondary notification assessment) is required.

Material Safety Data Sheet
The MSDS of the notified chemical provided by the notifier was reviewed by NICNAS. The accuracy of the information on the MSDS remains the responsibility of the applicant.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point/Freezing Point 231.7-233.2ºC

Method	OECD TG 102 Melting Point/Melting Range. EC Directive 84/449/EEC A.1 Melting/Freezing Temperature.
Remarks	Liquid bath
Test Facility	Test Facility B (1992a)

Boiling Point > 325ºC at 101.3 kPa

Method	OECD TG 103 Boiling Point. EC Directive 92/69/EEC A.2 Boiling Temperature.
Remarks	Siwoloboff method. Test samples were observed to darken above 325ºC, indicating decomposition.
Test Facility	Test Facility D (2008)

Density 1,188 kg/m^3 at 20ºC

Method	OECD TG 109 Density of Liquids and Solids. EC Directive 84/449/EEC A.3 Relative Density.
Remarks	Pycnometer method
Test Facility	Test Facility B (1992b)

Vapour Pressure $1.1x10^{-7}$ kPa at 25ºC

Method	OECD TG 104 Vapour Pressure. EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks	Vapour pressure balance
Test Facility	Test Facility D (2008)

Water Solubility < 0.01 mg/L at 25ºC

Method	OECD TG 105 Water Solubility. EC Directive 92/69/EEC A.6 Water Solubility.
Remarks	Column Elution Method
Test Facility	Test Facility D (2008)

Hydrolysis as a Function of pH

Remarks	The hydrolysis test could not be conducted because of the very low water solubility of the test substance. The notified chemical is expected to be susceptible to hydrolysis at the P-O bond, with hydrolytic cleavage of the phenol. Observations in the algal bioassay suggest relative stability in aqueous dispersion, but instability with THF as auxiliary solvent.

Partition Coefficient (n-octanol/water) log Pow > 6 at 25ºC

Method	OECD TGP/94.75 Partition Coefficient – HPLC Method.
Remarks	HPLC Method. The notified chemical eluted from the column after the reference substance DDT.
Test Facility	Test Facility D (2008)

Adsorption/Desorption – screening test log K_{oc} > 4.5 at 30°C

Method	HPLC-screening method for the determination of the adsorption-coefficient on soil.
Remarks	The notified chemical eluted from the column after the reference substance cyfluthrin.
Test Facility	Test Facility E (1997a)

Dissociation Constant

Remarks The dissociation constant could not be measured because of the very low water solubility of the test substance.

Particle Size

Method OECD TG 110 Particle Size Distribution/Fibre Length and Diameter Distributions.

Range (μm)	*Mass (%)*
10	18.30
5	8.60
2.5	3.87
1.25	1.62
0.625	0.95

Remarks Cascade impactor. The notified chemical was determined to have a mass median aerodynamic diameter (MMAD) of 59.5 μm and a geometric standard deviation (GSD) of 6.33.
Test Facility Test Facility E (1997a)

Flammability Not highly flammable

Method EC Directive 84/449/EEC A.10 Flammability (Solids).
Test Facility Test Facility B (1992c)

Auto-ignition Temperature Not observed under the conditions of the test

Method EC Directive 84/449/EEC A.16 Relative Self-Ignition Temperature for Solids.
Remarks Upon melting at 231ºC some of the notified chemical leaked through the pores of the sample tube. As a result after melting the thermocouple was no longer in contact with the test substance.
Test Facility Test Facility B (1992d)

Explosive Properties Not highly explosive

Method EC Directive 84/449/EEC A.14 Explosive Properties. The notified chemical was exposed to thermal and mechanical stress. No positive reaction was observed. The notified chemical decomposed when exposed to mechanical stress by friction.
Test Facility Test Facility B (1992e)

Fat (or n-octanol) Solubility 225 mg/100 g standard fat at 37°C

Method OECD TG 116 Fat Solubility of Solid and Liquid Substances.
Remarks Analytical Method:
Test Facility Test Facility C (1992b)

Surface Tension 73.9 mN/m at 20ºC

Method OECD TG 115 Surface Tension of Aqueous Solutions.
EC Directive 84/449/EEC A.5 Surface Tension.
Remarks Concentration: Solubility limit. The notified chemical is not surface active.
Test Facility Test Facility B (1992f)

Oxidizing Properties Not oxidising

Method EC Directive 92/69/EEC A.17 Oxidizing Properties (Solids).
Test Facility Test Facility D (2008)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Irritation – eye

TEST SUBSTANCE: Notified chemical (> 99%)

METHOD: US EPA Toxic Control Substances Act CFR sec. 798.4500.
- Species/Strain: Rabbit/New Zealand White
- Number of Animals: 6
- Observation Period: 72 hours
- Remarks - Method: None.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Conjunctiva: redness	0.11	1	< 48 hours	0
Conjunctiva: chemosis	0.06	1	< 72 hours	0
Conjunctiva: discharge	0	1	< 48 hours	0
Corneal opacity	0	0	-	0
Iridial inflammation	0	0	-	0

*Calculated on the basis of the scores at 24, 48, and 72 hours for ALL animals.

- Remarks - Results: Conjunctival redness was observed in all animals after 1 hour and persisted in 2 animals until 24 hours after treatment. Chemosis was observed in 2 animals 1 hour after treatment and was observed in 1 animal 48 hours after treatment. Discharge was observed in 1 animal 1 hour after treatment and in addition, excessive blinking and rubbing of the eye was observed immediately after treatment in 3 animals.

CONCLUSION: The notified chemical is slightly irritating to the eye.

TEST FACILITY: Test Facility A (1988b)

B.2. Skin sensitisation

TEST SUBSTANCE: Notified chemical (> 99%)

METHOD: OECD TG 406 Skin Sensitisation – Guinea Pig Maximisation Test
EC Directive 84/449/EEC B.6 Skin Sensitisation – Guinea Pig Maximisation Test.
- Species/Strain: Guinea pig/Himalayan albino
- PRELIMINARY STUDY: Maximum Non-irritating Concentration:
  intradermal: < 1%
  topical: 25%
- MAIN STUDY
  - Number of Animals: Test Group: 20 Control Group: 10
  - INDUCTION PHASE: Induction Concentration:
    intradermal: 5%
    topical: 25%
  - Signs of Irritation: Following intradermal injections with 5% of the notified chemical in ethanol, very slight erythema was observed in 14/19 animals at 24 hours, persisting in 4 animals at 48 hours. In addition, very slight oedema was observed in 8/19 animals at 24 hours after intradermal injection, persisting in 5 animals at 48 hours. Very slight erythema was also observed in 6/10 control animals treated with Freund's Complete Adjuvant and Ethanol (50:50).
- CHALLENGE PHASE
  - 1st challenge: topical: 25%

Remarks - Method

10% sodium dodecyl sulfate (SDS) was applied to the injection sites 24 hours prior to topical induction as no irritation was observed in the preliminary irritation test.
The vehicle used for dilution of the test substance was ethanol for intradermal injections and vaselinum album for epidermal application. No rationale was given for why the highest concentration tested in the preliminary irritation test was only 25%.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after 1st challenge*	
		24 h	*48 h*
Test Group	25%	0	0
Control Group	0%	0	0

Remarks - Results

One animal from the control group died spontaneously on day 22 of the test. One animal from the test group was killed for ethical reasons on day 8 of the test. No evidence of irritation or sensitisation was observed following the 1st challenge consisting of 25% of the notified chemical in vaselinum album. A positive control test using formaldehyde at 20% for induction and 15% for challenge confirmed the sensitivity of the strain to contact allergens.

CONCLUSION

There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.

TEST FACILITY

Test Facility C (1992e)

B.3. Repeat dose toxicity

TEST SUBSTANCE

Notified chemical (> 99%)

METHOD

Analogous to OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents.

Species/Strain: Rat: Sprague-Dawley Crl:CD®
Route of Administration: Oral – diet
Exposure Information: Total exposure days: 28 days
Dose regimen: 7 days per week
Post-exposure observation period: Not included in study

Remarks - Method

The method was analogous to OECD TG 407 except that behavioural assessments were not included in the study.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
0%	5 per sex	Control (0)	0
0.05%	5 per sex	31-55 (M), 36-60 (F)	0
0.15%	5 per sex	88-167 (M), 110-176 (F)	0
0.5%	5 per sex	316-570 (M), 379-587 (F)	0
1.5%	5 per sex	885-1603 (M), 1142-1776 (F)	0
5.0%	5 per sex	3222-5542 (M), 3917-6275 (F)	0

Mortality and Time to Death

No unscheduled deaths were reported.

Food consumption and efficiency
Statistically significant increases in mean food consumption for males treated with 5.0% notified chemical were observed from weeks 2 to 4 of the study and in week 4 only for males treated with 0.5% notified chemical. Statistically significant increases in mean food consumption for females treated with 5.0% notified chemical were observed from weeks 1 to 3 of the study. However, these were not considered to be adverse findings because the increased consumption was considered to be attributable to the lower nutritive value of the diets of the higher-dose groups.

Statistically significant increases in mean food efficiency for males and females treated with 0.15% and 0.5% notified chemical were observed in week 1 and statistically significant decreases in mean food efficiency for males treated with 0.05%, 0.5% and 5.0% notified chemical were observed in week 2. These were not considered to be treatment related given their isolated incidence.

Water consumption
Statistically significant decreases in mean water consumption values for females treated with 0.5% and 5.0% notified chemical were observed in week 2. These findings were isolated and not considered treatment related.

Haematology
No statistically significant differences in haematology values were observed.

Urinalysis
No statistically significant differences in parameters measured in urinalysis were observed.

Clinical Chemistry
A statistically significant decrease in blood urea nitrogen levels was observed in females treated with 0.15%, 0.5% and 1.5% of the notified chemical. However, the decreases were not evident in the highest-dose group and were therefore not dose-dependent and not regarded as treatment-related.
A statistically significant decrease in total bilirubin levels was observed in females treated with 0.15%, 0.5% and 5.0% of the notified chemical. However, these were not considered treatment-related as the lower dose groups showed greater decreases than the highest dose group.

Effects in Organs
No statistically significant variations in organ weights were observed at necropsy. No microscopic changes of toxicological significance were observed at histopathological examination.

Remarks – Results
The variations observed in food and water consumption and clinical chemistry parameters were not considered to be of toxicological significance. This was supported by the lack of variation in organ weights at necropsy or adverse macroscopic or microscopic findings.

CONCLUSION
The No Observed Effect Level (NOEL) was established as 3222-5542 mg/kg bw/day in males and 3917-6275 in females in this study, based on the absence of adverse effects in animals at the highest dose level.

TEST FACILITY	Test Facility F (1989a)

B.4. Repeat dose toxicity

TEST SUBSTANCE	Notified chemical (> 99%)
METHOD	Analagous to OECD TG 409 Repeated Dose 90-Day Oral Toxicity Study in Non-Rodents.
Species/Strain	Dog: Beagle
Route of Administration	Oral – Capsule
Exposure Information	Total exposure days: 90 days Dose regimen: 7 days per week Post-exposure observation period: Not included in the study.
Vehicle	Capsule (gelatin)
Remarks - Method	The method used was analogous to OECD TG 409 with the following deviations:

Measurements of haematology, clinical chemistry and urinalysis parameters were taken before and after the test but not during.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	4 per sex	0	0
low dose	4 per sex	20	0
mid dose	4 per sex	200	0
high dose	4 per sex	2000	0

Mortality and Time to Death
No unscheduled deaths were reported.

Clinical Observations
Abnormal stool colour or consistency was observed in animals in the high dose group of both sexes. The notified chemical was also often found either in the stool or vomit of those animals, occurring more frequently within the first 2 weeks. The amount of notified chemical administered in each capsule is thought to be the reason for these findings rather than its inherent toxicity.

Haematology
Mean corpuscular haemoglobin levels were elevated to statistical significance in males of the high dose group. In the absence of any other related findings, this was not considered to be of toxicological significance.

Clinical Chemistry
Statistically significant decreases in mean potassium levels were observed in mid- and high-dose males and all treated females. However, there were no other associated differences in serum electrolytes, urinary function or microscopic changes and therefore the decreases were considered unrelated to treatment.

Effects in Organs
The effects noted at necropsy upon macroscopic examination were limited to discolouration of digestive organs, lungs, lymph nodes and the liver in a small number of animals. The discolourations were not dose-dependant and not considered to be of toxicological significance. Microscopic examination revealed moderate lymphoid cell infiltrate in the stomach of 1 female in the control group and 2 females in the high-dose group, moderate acute haemorrhagic inflammation of the ileum in 1 female in the high-dose group, moderate subacute arteritis of the urinary bladder in 1 female of the control group, and moderate hyperplasia of the uterus in 1 female of the control group. These effects were not dose dependent and not considered related to treatment. All other effects observed were slight or minimal and were not dose dependant and therefore, not considered related to treatment.

Remarks – Results
There were no toxicologically relevant changes in any of the following parameters following treatment with the notified chemical: clinical signs, body weights, organ weights, food consumption, clinical laboratory investigations (haematology and clinical biochemistry), macroscopic and microscopic examination.

CONCLUSION
The No Observed Effect Level (NOEL) was established as 2000 mg/kg bw/day in this study, based on the absence of treatment related effects observed at the highest dose level.

TEST FACILITY Test Facility G (1997)

B.5. Repeat dose toxicity

TEST SUBSTANCE Notified chemical (> 99%)

METHOD Analogous to OECD TG 408 Repeated Dose 90-Day Oral Toxicity Study in Rodents.

Species/Strain	Rat: Sprague-Dawley Crl:CD®
Route of Administration	Oral – diet
Exposure Information	Total exposure days: 90 days Dose regimen: 7 days per week
Remarks - Method	The method used was analogous to OECD TG 408 with the following deviations: The temperature range for housing the animals was (17.8 – 26.7ºC) which varies from the range recommended in the guidelines (22 ± 3ºC). The humidity range for housing the animals was (40-83%) which varied from the recommended range in the guidelines (30-70%). Assessments of neurological and behavioural responses to stimuli were omitted from the study. No recovery groups were included in the study.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
Control (0%)	20 per sex	0	0
low dose (0.05%)	20 per sex	25 – 52 (M), 31 – 57 (F)	0
mid dose (0.5%)	20 per sex	247 – 505 (M), 328 – 543 (F)	0
high dose (5.0%)	20 per sex	2675 – 5397 (M), 3390 – 5847 (F)	0

Mortality and Time to Death
No unscheduled deaths were reported.

Food consumption
Statistically significant increases in food consumption were observed in high-dose males in weeks 9 and 13 of the study. These increases may be a compensation due to the high level of non-nutritive test material in the feed at the high dose. Other statistically significant variations (increases in food consumption in males in the high-dose group in weeks 1, 4, 6, 8-13; in the mid-dose group in weeks 9, 10; and in the low-dose group in weeks 1, 5, 10) as well as in females in the high-dose group in weeks 2, 8; and in the low-dose group in weeks 5, were observed sporadically but were considered unrelated to treatment.

Water consumption
Statistically significant increases in water consumption were observed in mid-dose males in weeks 6 and 7 but were not considered treatment related.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
No statistically significant variations in measurements between treated and control animals were observed in urinalysis, clinical chemistry or haematological analysis.

Effects in Organs
No statistically significant variations in absolute or relative organ weights were observed between treated and control animals at necropsy.
At post mortem examination, tan/red foci in the lungs of several animals were observed with a higher frequency occurring in treated males compared to control males. However no evidence of pulmonary pathology was observed at the microscopic level.

Histopathological examination revealed effects in the kidneys of male rats in both treated and control groups which included: mononuclear cell infiltrates, foci of regenerative tubular epithelium and interstitial fibrosis.

A number of spontaneous lesions and incidental findings were observed at essentially comparable incidence in control and treated animals. These include:

- Peribronchial, peribronchiolar and perivascular mononuclear cells, foci of interstitial pneumonitis, focal haemorrhage and arterial mineralisation were observed in the lungs of several rats. However, these were not dose-dependent. Focal haemorrhage in the lung and thymus was observed in a few rats from both treated and control groups.
- Examination of the liver revealed mononuclear cell infiltrates in numerous animals of both sexes in both

treated and control animals.
- Nonsuppurative myocarditis was observed in a few rats of both sexes.
- Plasmacytosis and lymphoid hyperplasia were observed occasionally in lymph nodes of a few rats of both sexes in treated and control groups.
- Subchronic inflammation and pigment deposition was observed in the pancreas of a few rats, mainly males.
- Pigment deposition in the spleen of females of both treated (mainly high-dose) and control groups.
- Nonsuppurative prostatitis was observed in a few males in both control and high-dose groups.
- Diffuse tubularatrophy of the testes was observed in 1 teste of 1 male in the control group and in both testes in 1 male from the high-dose group.

These findings occurred sporadically with no evidence of dose-response and were therefore considered to be unrelated to treatment.

Remarks – Results
There were no toxicologically relevant changes in any of the following parameters following treatment with the notified chemical: clinical signs, body weights, organ weights, food consumption, clinical laboratory investigations (haematology and clinical biochemistry), macroscopic and microscopic examination.

CONCLUSION
The No Observed Effect Level (NOEL) was established as 2675 mg/kg bw/day (males), and 3390 mg/kg bw/day (females) in this study, based on the absence of effects observed at the highest dose level.

TEST FACILITY Test Facility F (1989b)

B.6. Repeat dose toxicity - Neurotoxicity

TEST SUBSTANCE Notified chemical (> 99%)

METHOD OECD TG 419 Delayed Neurotoxicity of Organophosphorous Substances: 28-Day Repeated Dose Study

Species/Strain	Hen
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28 days Dose regimen: 7 days per week
Vehicle	Corn oil
Remarks - Method	Tri-ortho-tolyl phosphate (TOTP) was used as the positive control at 30 mg/kg bw/day until day 13 of the test and then at 100 mg/kg bw/day for the remainder of the test. The dose was increased because the hens did not show any changes in behaviour or other neurotoxic effects when receiving 30 mg/kg bw/day. The test group received the notified chemical at 1000 mg/kg bw/day. Palmgreen's silver stain for demonstration of axons was not performed.

RESULTS

Group	*Number of Animals*	*Dose mg/kg bw/day*	*Mortality*
Vehicle Control	18	0	0
Test	18	1000	1
Positive Control (Tri-ortho-tolyl phosphate)	18	30/100	7

Mortality and Time to Death
One animal treated with the notified chemical died spontaneously during the study. The death was considered to be due to an intubation error. In the positive control group, 5 animals died spontaneously and 2 animals were killed *in extremis.*

Food consumption and body weights

No significant variations in food consumption or body weights were observed between control animals and animals treated with the notified chemical. However, reduced food consumption and body weights (11%) were observed at the end of treatment in the animals of the positive control group.

Clinical Observations

No clinical signs were noted in the group treated with the notified chemical or the vehicle control group. Emaciation, ataxia and dyspnea were observed in animals of the positive control group, starting in week 4 (with the exception of 2 hens with observed changes in behaviour in week 3) and extended up to the end of the 14-day recovery period.

No abnormal symptoms were observed in the vehicle or test groups during forced motor activity observations. All animals of the positive control group displayed abnormal symptoms during forced motor activity observations, beginning at Day 20. Signs displayed include: sedation, ataxia, ventral recumbency, head drop and dyspnea.

Laboratory Findings – Esterase activity

Slight inhibition (12%) of average plasma cholinesterase activity was observed in hens treated with the notified chemical on day 6. At day 29, (24 hours after the last dosing), inhibition of 9% was observed in hens treated with the notified chemical. However, there was no inhibition observed in treated hens in that group on day 30, (48 hours after treatment) or at the end of the recovery period on day 42. Inhibition on days 6 and 29 was not statistically significant compared to the values obtained for animals of the vehicle control group.

In the positive control group, 56% inhibition of average plasma cholinesterase activity was observed on day 6. Inhibition of 28% was observed on day 29 and 8% on day 30. Inhibition was statistically significant ($p < 0.01$) in all measurements for the positive control group compared to the vehicle control group. On day 42, activity levels in the 1 surviving hen from the positive control group was 50% higher than controls. However, this was not considered to be of statistical significance.

No reduction in neuropathy target esterase (NTE) activity was observed in the treated animals when compared to animals in the vehicle control group.

In the positive control group, a statistically significant ($p < 0.01$) reduction of NTE activity was observed in the brain (89%) and spinal cord (76%) compared to activity in the vehicle control group on day 29.

Histopathology of neural tissues

Histopathological examination of neural tissue was undertaken 48 hours and 14 days after the final treatment. Single fibre degenerations were observed in hens from the vehicle control, treated and positive control groups in the cervical, lumbar and thoracic segments of the spinal cord as well as the sciatic and tibial nerves. The severity and incidence of neural tissue damage in hens treated with the notified chemical was comparable to that observed in vehicle control hens. Neural damage was more prolific and more severe (rated as moderate) in hens treated with the positive control than in hens of the vehicle control group.

Other effects noted in hens in the vehicle control, treatment and positive control groups included mononuclear or mixed inflammatory cell foci in various tissues, and cell gliosis in the spinal cord, telencephalon or medulla oblongata. The incidence and severity were sporadic and were not considered related to treatment with the notified chemical or the positive control.

Remarks – Results

Animals treated with the notified chemical at 1000 mg/kg bw/day did not display significant reductions in average plasma cholinesterase activity or neuropathy target esterase activity compared to the vehicle control group. Histopathological examination showed that the neural tissue of treated animals was similar to vehicle control animals.

Animals treated with the positive control displayed significant reductions in average plasma cholinesterase activity and neuropathy target esterase activity when compared to the vehicle control group. Histopathological examination also revealed that the incidence and severity of damage to neural tissues was increased in animals of the positive control group compared to the vehicle control group demonstrating the sensitivity of the test in hens.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as 1000 mg/kg bw/day in this study, based on the lack of adverse findings at this dose level.

TEST FACILITY Test Facility C (1997)

B.7. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical (> 99%)

METHOD OECD TG 471 Bacterial Reverse Mutation Test.
EC Directive 92/69/EC B.14 Mutagenicity – Reverse Mutation Test using Bacteria.
Plate incorporation procedure and pre-incubation procedure

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100, TA102.
Metabolic Activation System	S9 mix from rat liver induced with Aroclor 1254
Concentration Range in Main Test	a) With metabolic activation: 33 - 5000 µg/plate b) Without metabolic activation: 33 - 5000 µg/plate
Vehicle	Dimethyl sulfoxide
Remarks - Method	Two tests were conducted in triplicate with concurrent negative and positive controls. The first test was conducted using the plate incorporation procedure and the second the pre-incubation procedure. The cultures were incubated for 10 hours at 37ºC with stirring in a water bath in the pre-incubation procedure.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Plate incorporation Test	*Cytotoxicity in Pre-incubation Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 333.33	> 5000	> 5000	Negative
Test 2	-	> 5000	> 5000	Negative
Present				
Test 1	≥ 333.33	> 5000	> 5000	Negative
Test 2	-	> 5000	> 5000	Negative

Remarks - Results	No substantial increases in the number of revertant colonies were seen in any strain either in the presence or absence of metabolic activation. The negative controls were within normal limits and the positive controls (Sodium azide, 4-nitro-o pheylene diamine, methyl methane sulfonate (-S9); 2-aminoanthracene (+S9)) demonstrated the sensitivity of the assay and the metabolising activity of the liver preparations.

CONCLUSION The notified chemical was not mutagenic to bacteria under the conditions of the test.

TEST FACILITY Test Facility H (1995)

B.8. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical (> 99%)

METHOD Method analogous to OECD TG 471 Bacterial Reverse Mutation Test.
Pre-incubation procedure

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100. *E. coli*: WP2uvrA.
Metabolic Activation System	S9 mix from rat liver induced with 5,6-Benzoflavone and phenobarbital
Concentration Range in	a) With metabolic activation: 78 - 5000 µg/plate

Main Test	b) Without metabolic activation: 78 - 5000 µg/plate
Vehicle	Dimethyl sulfoxide
Remarks - Method	The bacteria were incubated with the notified chemical for 14 hours at 37°C using a rotary shaker at 120 ppm.

RESULTS

Remarks - Results	There was no visible reduction in background lawn growth or evidence of cytotoxicity in any of the tests conducted with or without metabolic activation. No substantial increases in the number of revertant colonies were seen in any strain either in the presence or absence of metabolic activation. The negative controls were within normal limits and the positive controls (Sodium azide, 2-(2-furyl)-3-(5-nitro-2-furyl)-acrylamide (-S9); 2-Aminoanthracene (+S9)) demonstrated the sensitivity of the assay and the metabolising activity of the liver preparations.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Test Facility I (1987)

B.9. Genotoxicity – in vitro

TEST SUBSTANCE	Notified chemical (> 99%)
METHOD	OECD TG 473 In vitro Mammalian Chromosome Aberration Test.
Cell Type/Cell Line	Chinese Hamster V79 cells
Metabolic Activation System	S9 mix from rat liver induced with Aroclor 1254
Vehicle	Dimethyl sulfoxide : Dichloromethane (9:1)
Remarks - Method	25 metaphases per concentration were scored for cells treated with positive controls. This is lower than the recommended 200 metaphases.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	2.0, 30.0, 50.0	4 hrs	18 hrs
Test 1	50.0	4 hrs	28 hrs
Test 2	4.0, 40.0, 50.0	4 hrs	18 hrs
Test 2	50.0	4 hrs	28 hrs
Present			
Test 1	2.0, 30.0, 50.0	4 hrs	18 hrs
Test 1	50.0	4 hrs	28 hrs
Test 2	4.0, 40.0, 50.0	4 hrs	18 hrs
Test 2	50.0	4 hrs	28 hrs

RESULTS

Remarks - Results	No significant increase in the frequency of mutant cells or polyploidy was observed with or without metabolic activation in treated cell cultures. No significant reduction in the mitotic index was observed at any concentration with our without metabolic activation. The negative controls were within normal limits and the positive controls (Ethyl methanesulfonate (-S9); Cyclophosphamide (+S9)) demonstrated the sensitivity of the assay and the metabolising activity of the liver preparations.

CONCLUSION	The notified chemical was not clastogenic to Chinese Hamster V79 cells treated in vitro under the conditions of the test.
TEST FACILITY	Test Facility H (1992)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical.
METHOD	OECD TG 301 B Ready Biodegradability: CO_2 Evolution Test.
Inoculum	Activated sludge from municipal sewage treatment plant in the Netherlands.
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Evolution of CO_2 (precipitated as barium carbonate).
Remarks - Method	The notified chemical was tested at nominal concentrations of 10 and 20 mg/L.

RESULTS

Test substance		*Sodium acetate*	
Day	*% Degradation*	*Day*	*% Degradation*
2	1	2	11
12	2	12	47
28	19	21/28	76

Remarks - Results	The results tabulated above were obtained at 10 mg/L notified chemical. Only minimal degradation (2%) was recorded at 20 mg/L.
CONCLUSION	Not readily biodegradable.
TEST FACILITY	Test Facility B (1992g)

C.1.2. Bioaccumulation

Bioaccumulation was not tested, but is considered unlikely because of the very low water solubility and low release to aquatic ecosystems. However, some potential for bioaccumulation must be assumed, as the SIDS dossier for BHT reports a wide range of bioconcentration factors, from which a moderate to high bioaccumulation potential is assumed in aquatic species.

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 203 Fish, Acute Toxicity Test - static. EC Directive 84/449/EEC C.1 Acute Toxicity for Fish - static.
Species	Rainbow trout
Exposure Period	96 hours
Auxiliary Solvent	None
Analytical Monitoring	None
Remarks – Method	Fish were exposed to a suspension (nominally 1000 mg/L) and dilutions (1:2, 1:4, 1:8 and 1:16) of the water accommodated fraction (WAF) obtained by filtration (4.4 μm).

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*				
Nominal	*Actual*		*2 h*	*24 h*	*48 h*	*72 h*	*96 h*
1000		10	2	7	10	10	10
WAF		10	0	0	0	0	0
WAF (1:2 dilution)		10	0	0	0	0	0
WAF (1:4 dilution)		10	0	0	0	0	0
WAF (1:8 dilution)		10	0	0	0	0	0
WAF (1:16 dilution)		10	0	0	0	0	0

LC50	> 0.01 mg/L at 96 hours
NOEC	0.01 mg/L at 96 hours.
Remarks – Results	The effects of the unfiltered suspension are probably due to undissolved particles.

CONCLUSION Not toxic up to the limit of water solubility.

TEST FACILITY Test Facility C (1992c)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Notified chemical

METHOD OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test - static.
EC Directive 84/449/EEC C.2 Acute Toxicity for Daphnia - static.

Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Analytical Monitoring	Attempts were made to determine the test substance in solution by ultraviolet spectrometry, but only limited details are provided as these attempts were unsuccessful. A solution of the test substance in acetonitrile showed a broad spectrometrical maximum at about 200-230 nm, whereas the supersaturated test solution, after 0.45 µm filtration, showed a maximum at about 200 nm, which shifted to about 190 nm when the aqueous solution was diluted with an equal volume of acetonitrile. The ultraviolet spectrum in chloroform showed absorbance maxima at 242 and 279 nm. While these observations are difficult to interpret, they suggest that the test substance may have undergone some degradation in the test media.
Remarks – Method	Daphnids were exposed to a suspension (nominally 1000 mg/L) and dilutions (1:1, 1:4, 1:8 and 1:16) of the WAF obtained by filtration (4.4 µm)

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
1000		20	4	13
WAF		20	0	0
WAF (1:1 dilution)		20	1	1
WAF (1:4 dilution)		20	1	3
WAF (1:8 dilution)		20	0	3
WAF (1:16 dilution)		20	0	0

LC50	> 0.01 mg/L at 48 hours
NOEC	0.01 mg/L
Remarks - Results	Some daphnids (10-30% in individual replicates) were immobilised in

dilutions of the WAF (1:1, 1:4 and 1:8) but all remained mobile in the 1:16 dilution. These effects were inconsistent between replicates and do not appear to be dose related.

CONCLUSION Not toxic up to the limit of water solubility.

TEST FACILITY Test Facility C (1992d)

C.2.3. Algal growth inhibition test

TEST SUBSTANCE Notified chemical

METHOD OECD TG 201 Alga, Growth Inhibition Test.
EC Directive 92/69/EEC C.3 Algal Inhibition Test.

Species	*Scenedesmus subspicatus*
Exposure Period	72 hours
Concentration Range	Nominal: 0.1 mg/L Actual: 0.072 mg/L
Auxiliary Solvent	DMF
Analytical Monitoring	HPLC after extraction with dichloromethane.
Remarks - Method	A limit test only was conducted at a nominal test concentration of 0.1 mg/L. The test medium was described as an aqueous dispersion. The analytical data showed declining concentrations in pre-study test samples stored for 72 hours, to 87% in light conditions and 90% in the dark when the test bottles were rinsed with extraction solvent, and to 74% in light conditions without rinsing. The auxiliary solvent was changed from THF to DMF because of apparent instability with the former. Measured concentrations in the algal culture media declined from an initial 98% to 51% after 72 hours. The decline was attributed to the relatively unstable nature of the test substance and its adsorption to algal cells.

RESULTS

Biomass		*Growth*	
EC50 *mg/L at 72 h*	*NOEC* *mg/L*	*EC50* *mg/L at 72 h*	*NOEC* *... mg/L*
> 0.01	0.01	> 0.01	0.01

Remarks - Results The results above are expressed as the solubility limit. While analytical data suggest a higher exposure concentration, the data are considered unreliable as the test medium was described as a dispersion, and extracted with solvent to determine the content of notified chemical.

CONCLUSION Not toxic up to the limit of water solubility.

TEST FACILITY Test Facility E (1997b)

C.2.4. Inhibition of microbial activity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test. EC Directive 87/302/EEC C.11 Biodegradation: Activated Sludge Respiration Inhibition Test
Inoculum	Activated sewage sludge (Derbyshire, UK)
Exposure Period	3 hours
Concentration Range	Nominal: 100 and 1000 mg/L
Remarks – Method	3,5-Dichlorophenol was used as reference substance.
RESULTS	
IC50	> 1000 mg/L
NOEC	1000 mg/L
Remarks – Results	The IC50 for the reference substance was 8 mg/L.
CONCLUSION	Not inhibitory to the respiration of sewage sludge microorganisms.
TEST FACILITY	Test Facility E (1997c)

BIBLIOGRAPHY

Callierotti C, Lee RE, Kuvshinnikova OI, Keck-Antoine K & Johnson B (2001) Additive Forms to Drive Continuous Improvement in Polymer Stabilisation. Proceedings, Society of Plastic Engineering Polyolefins RETEC, February 2001, Houston Texas (http://www.e1.greatlakes.com/content/polyolefinretec2001.pdf, accessed 2 April 2009).

EC (2003) EC (2003) Technical Guidance Document on Risk Assessment, Part II. Institute for Health and Consumer Protection, European Chemicals Bureau, Joint Research Centre, European Commission.

FORS (Federal Office of Road Safety) (1998) Australian Code for the Transport of Dangerous Goods by Road and Rail (ADG code), 6th Edition, Canberra, Australian Government Publishing Service

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

NOHSC (2004) Approved Criteria for Classifying Hazardous Substances, 3rd edition [NOHSC:1008(2004)]. National Occupational Health and Safety Commission, Canberra, AusInfo.

OECD SIDS (2002) SIDS Initial Assessment Report for SIAM 14, Paris, France. Organisation for Economic Co-operation and Development, Bonn-Bad Godesberg, Germany, 26-28 March, 2002.

Test Facility A (1987) Acute Oral Toxicity Study in Rats PEP-36 Final Report. Project No. 2476-100. 19 August 1987 (Unpublished report provided by notifier).

Test Facility A (1988a) Primary Dermal Irritation Study in Rabbits with PEP-36, Phosphorous acid, cyclic neopentanetetrayl bis (2,6-di-tert-butyl-4-methylphyenyl) ester. Project No. 2476-102. 20 July 1988 (Unpublished report provided by notifier).

Test Facility A (1988b) Primary Eye Irritation Study in Rabbits with PEP-36, Phosphorous acid, cyclic neopentanetetrayl bis (2,6-di-tert-butyl-4-methylphyenyl) ester. Project No. 2476-103. 22 July 1988 (Unpublished report provided by notifier).

Test Facility B (1991a) Determination of the UV-VIS Absorption Spectra of ADK STAB PEP-36. Project No. 063078. 20 November 1991 (Unpublished report provided by notifier).

Test Facility B (1991b) Determination of the ^{1}H NMR Spectrum of ADK STAB PEP-36. Project No. 063067. 30 November 1991 (Unpublished report provided by notifier).

Test Facility B (1992a) Determination of the Melting Point/Melting Range of ADK STAB PEP-36. Project No. 063089. 22 January 1992 (Unpublished report provided by notifier).

Test Facility B (1992b) Determination of the Density of ADK STAB PEP-36. Project No. 063091. 27 January 1991 (Unpublished report provided by notifier).

Test Facility B (1992c) Determination of the Flammability of ADK STAB PEP-36. Project No. 063113. 22 January 1992 (Unpublished report provided by notifier).

Test Facility B (1992d) Determination of the Auto-Flammability of ADK STAB PEP-36. Project No. 063135. 24 January 1992 (Unpublished report provided by notifier).

Test Facility B (1992e) Determination of the Explosive Properties of ADK STAB PEP-36. Project No. 063124. 27 January 1992. (Unpublished report provided by notifier).

Test Facility B (1992f) Determination of the Surface Tension of ADK STAB PEP-36. Project No. 063102. 22 January 1992. (Unpublished report provided by notifier).

Test Facility B (1992g) Ready Biodegradability: Modified Sturm test with ADK STAB PEP-36. Project No. 066509. 29 January 1992 (unpublished report provided by notifier).

Test Facility C (1991a) Acute Dermal Toxicity Study with ADK STAB PEP-36 in Rats. Project No. 309238. 5 November 1991 (Unpublished report provided by notifier).

Test Facility C (1992a) Determination of the IR Absorption Spectrum of ADK STAB PEP-36. Project No. 309093. 3 March 1992 (Unpublished report provided by notifier).

Test Facility C (1992b) Solubility Determination of ADK STAB PEP-36 in Fat. Project No. 309172. 9 March 1992 (unpublished report provided by notifier).

Test Facility C (1992c) ADK STAB PEP-36: 96-hour Acute Toxicity Study in the Rainbow Trout. Project No. 309262. 27 October 1992 (unpublished report provided by notifier).

Test Facility C (1992d) 48-hour Acute Toxicity Study of ADK STAB PEP-36: to *Daphnia magna* (OECD-Immobilization Test). Project No. 309273. 27 October 1992 (unpublished report provided by notifier).

Test Facility C (1992e) Contact Hypersensitivity to ADK STAB PEP-36 in Albino Guinea Pigs Maximization-Test. Project No. 309240. 30 January 1992 (Unpublished report provided by notifier).

Test Facility C (1997) Delayed Neurotoxicity Study Following 28-Day Oral Application (Repeated Dose Study) with ADK STAB PEP-36 in Laying Hens. Project No. 635657. 5 May 1997 (Unpublished report provided by notifier).

Test Facility D (2008) ADK STAB PEP-36: Determination of General Physico-chemical Properties. Study No. ADK0283. 17 October 2008 (unpublished report provided by notifier).

Test Facility E (1997a) ADK STAB PEP-36: Determination of General Physico-chemical Properties. Project No. 1083/001. 23 May 1997 (unpublished report provided by notifier).

Test Facility E (1997b) ADK STAB PEP-36: Algal Inhibition Test. Project No. 1083/002. 30 October 1997 (unpublished report provided by notifier).

Test Facility E (1997c) ADK STAB PEP-36: Assessment of the Inhibitory Effect on the Respiration of Activated Sewage Sludge. Project No. 1083/003. 11 August 1997 (unpublished report provided by notifier).

Test Facility F (1989a) A Four-Week Dietary Study in Rats With MARK PEP-36 Pathology Report. Project No. 87-3216. 3 July 1989 (Unpublished report provided by notifier).

Test Facility F (1989b) A Subchronic Dietary Study in Rats With MARK PEP-36. Project No. 87-3217. 20 February 1989 (Unpublished report provided by notifier).

Test Facility G (1997) A Subchronic (3-month) Toxicity Study of ADK STAB PEP-36 in the Dog Via Capsule Administration. Study No. 95-3254. 22 January 1997 (Unpublished report provided by notifier).

Test Facility H (1992) Chromosome Aberration Assay in Chinese Hamster V79 Cells *in Vitro* with ADK STAB PEP-36 Report. Project No. 254700. 16 June 1992 (Unpublished report provided by notifier).

Test Facility H (1995) Salmonella Typhimurium Reverse Mutation Assay with ADK STAB PEP-36 Report. Project No. 496101. 10 May 1995 (Unpublished report provided by notifier).

Test Facility I (1987) Mutagenicity test of 2,9-bis(2,6-di-tert-butyl-4-methylphenoxy)-2,4,8,10-tetraoxa-3,9-diphosphaspiro[5,5]undecane by using microorganisms. Study No. 5120. 31 March 1987.

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.