Australian Government
Department of Health and Aged Care
Australian Industrial Chemicals Introduction Scheme

Benzene, 1,1'-oxybis-, tetrapropylene derivs., sulfonated, sodium salts

Assessment statement (CA09920)

18 December 2024

Table of contents

AICIS assessment (CA09920)

Chemical in this assessment

CAS name	CAS number
Benzene, 1,1'-oxybis-, tetrapropylene derivs., sulfonated, sodium salts	119345-04-9

Reason for the assessment

An application for an assessment certificate under section 31 of the *Industrial Chemicals Act 2019* (the Act).

Certificate application type

AICIS received the application in a Health and Environment Focus type.

Defined scope of assessment

The chemical has been assessed:

- as imported into Australia for a combined volume at up to 39 tonnes/year
- as imported as a liquid formulation containing the assessed chemical at less than 50% concentration for local reformulation
- for end use in coating and cleaning products at less than 1% concentration by consumers and less than 3% concentration by professional workers.

Summary of assessment

Summary of introduction, use and end use

The assessed chemical will not be manufactured in Australia. It will be imported into Australia at less than 50% concentration in plastic drums or intermediate bulk containers (IBC) for further local reformulation into finished end use coating and cleaning products containing the assessed chemical at less than 3% concentration. Reformulation activity will not take place at the applicant's Australian facilities.

For end use in coating products, the plastic drums and IBC containers containing the assessed chemical at less than 50% concentration as imported will be sold to coating manufacturers for formulation of emulsion polymers or resins. Coating manufacturers will further sell the emulsion polymers or resins containing the assessed chemical to paint manufacturers with the package of 1,000 L or ISO tanks. The final paint containing the assessed chemical at less than 3% concentration and at less than 1% concentration, respectively, will be made available to professional workers and to consumers within 20 L to 1,000 L plastic containers.

For end use in cleaning products, the assessed chemical at less than 50% concentration will be sold to the cleaning products formulators with the package as imported. The final cleaning products containing the assessed chemical at less than 1% concentration for consumers and

at less than 3% concentration for professional workers will be made available in varying container sizes from 0.5 L plastic bottles to 205 L drums. For professional Clean in Place end use, cleaning products containing the assessed chemical will be diluted with water 20-24 times.

Human health

Summary of health hazards

The submitted toxicological data on the assessed chemical and analogue chemicals (see **Supporting information**) indicate that the assessed chemical is:

- of low acute oral toxicity (LD50 > 2,000 mg/kg bw in rats)
- of low acute dermal toxicity (LD50 > 2,000 mg/kg bw in rabbits)
- considered to cause serious eye damage
- not a skin sensitiser
- not considered to be genotoxic
- not considered to be carcinogenic

Two repeat dose toxicity studies on the assessed chemical indicated No Observable Adverse Effect Level (NOAEL) as 128 and 150 mg/kg bw/day in dogs and rats, respectively, based on reduced body weight gain at higher doses.

In an extended one-generation reproductive toxicity study in rats, a NOAEL of 1,000 ppm, equivalent to dose levels ranging from 62 to 91 mg/kg bw/day, was established for the assessed chemical, based on lower mean numbers of implantation sites and longer gestation period observed at higher doses. In the same study, a NOAEL of 1,000 ppm, equivalent to dose levels ranging from 62 to 91 mg/kg bw/day, was also established for developmental toxicity, based on pup survival (lower mean number of pups born and live litter sizes) at higher doses.

In a developmental toxicity study in rabbits, a NOAEL of 1,500 ppm (56 mg/kg bw/day) was established for the assessed chemical for both maternal and developmental toxicity, based on lower mean body weight gain corresponding with reduced mean food consumption and on the lower foetal body weights observed at the higher doses.

Therefore, based on the effects observed in the reproductive and developmental toxicity studies at a dose level greater than 56 mg/kg bw/day, the assessed chemical warrants hazard classification as Reproductive toxicity - Category 2.

The skin irritation study provided on the assessed chemical used only one rabbit, but with 3-5 repeated applications. Slight skin irritation was observed after repeated exposure, indicating the assessed chemical is not corrosive. However, skin irritation of the assessed chemical cannot be ruled out. It is noted that this study is not suitable to consider classification of the assessed chemical using the GHS criteria. Even if the assessed chemical is classified as a Category 2 skin irritant, the end use concentration of the assessed chemical is below the GHS cut-off concentration for Category 2 skin irritation.

No acute and repeat dose inhalation toxicity data were provided for the assessed chemical.

Hazard classifications relevant for worker health and safety

Based on the data provided by the applicant (see above), the assessed chemical satisfies the criteria for classification according to the *Globally Harmonized System of Classification and*

Labelling of Chemicals (GHS) (UNECE 2017) for hazard classes relevant for worker health and safety as adopted for industrial chemicals in Australia.

Health hazards	Hazard category	Hazard statement
Serious eye damage/eye irritation	Eye Irrit. 1	H318: Causes serious eye damage
Reproductive toxicity	Repro. Tox. 2	H361fd: Suspected of damaging fertility. Suspected of damaging the unborn child

Summary of health risk

Public

Potential exposure of the public to the assessed chemical at less than 1% concentration may occur through the use of coating and cleaning products. Coating products containing the assessed chemical will be applied by do-it-yourself (DIY) users as architectural coatings using brush and roller. The toilet cleaning products containing the assessed chemical will be applied using a wash or squeeze bottle or as a liquid cleaner to soak on the inside surface for a while and then flushing the toilet or using a toilet brush for cleaning before flushing.

The principal route of exposure through the use of coating and cleaning products will be dermal, while ocular and inhalation exposures are also possible. However, considering the infrequent use, low use concentration of the assessed chemical (< 1%) and the low vapour pressure, exposure to the general public is expected to be minimal.

This assessment does not identify any risks to public health that would require specific risk management measures.

Workers

Potential exposure of workers to the assessed chemical at up to 50% concentration may occur during formulation operations and at less than 3% concentration during professional end use applications of coatings and cleaning products (see **Supporting information** section). Coating products will be applied by roller, brush, dipping, or spray. Cleaning products will be diluted with water 20-24 times and used for industrial Clean in Place operations or as a liquid stream/liquid cleaner. The principal route of exposure for coating and cleaning products will be dermal, while ocular and inhalation exposures are also possible.

Given the risks of critical health effects of the assessed chemical (eye damage, reproductive toxicity), control measures to minimise exposure are needed to manage the risk to workers (see **Means for managing risk** section). Control measures to minimise inhalation exposure may be also needed if aerosols or mists are formed during reformulation and during spray application of coating products containing the assessed chemical.

Environment

Summary of environmental hazard characteristics

According to the *Australian Environmental Criteria for Persistent, Bioaccumulative and/or Toxic Chemicals* (DCCEEW, 2022) and based on the available data, the assessed chemical is:

- Persistent (P)
- Not Bioaccumulative (not B)
- Not Toxic (not T)

Environmental hazard classification

The assessed chemical satisfies the criteria for classification according to the GHS (UNECE, 2017) as Acute Category 2 (H401) and Chronic Category 2 (H411) based on the toxicity data for fish, invertebrates and algae. Considerations were also made for the biodegradation of the assessed chemical.

Environmental Hazard	Hazard Category	Hazard Statement
Hazardous to the aquatic environment (acute / short-term)	Aquatic Acute 2	H401: Toxic to aquatic life
Hazardous to the aquatic environment (long-term)	Aquatic Chronic 2	H411: Toxic to aquatic life with long lasting effects

Summary of environmental risk

The assessed chemical will be introduced in liquid form at a concentration less than 50% and will be reformulated into end use cleaning and coating products. These uses may result in the release of the assessed chemical to sewers, surface waters and soils. In these compartments, the assessed chemical is expected to partition to phase boundaries.

Although the assessed chemical is persistent according to the Australian Environmental Criteria for Persistent, Bioaccumulative and/or Toxic Chemicals (DCCEEW, 2022), it does not meet all three PBT criteria. It is unlikely to have unpredictable long-term effects, and its risk may be estimated by the risk quotient method (RQ = PEC ÷ PNEC). Based on calculated RQ values < 1 for the river and ocean compartments, the environmental risk from the introduction of the assessed chemical can be managed.

Means for managing risk

Workers

Recommendation to Safe Work Australia

- It is recommended that Safe Work Australia (SWA) update the *Hazardous Chemical Information System* (HCIS) to include classifications relevant to work health and safety (see **Hazard classifications relevant for worker health and safety**).

Information relating to safe introduction and use

The information in this statement, including recommended hazard classifications, should be used by a person conducting a business or undertaking at a workplace (such as an employer) to determine the appropriate controls under the relevant jurisdiction Work Health and Safety laws.

The following control measures could be implemented to manage the risk arising from exposure to the assessed chemical during reformulation and end use application:

- Use of engineering controls such as
  - Enclosed and automated systems where possible
  - Adequate workplace ventilation to avoid accumulation of dusts, mists or aerosols
- Use of safe work practices to
  - Avoid contact with skin and eyes
  - Avoid inhalation of mists or aerosols
- Use of personal protective equipment (PPE)
  - Impervious gloves
  - Protective clothing
  - Safety glasses/goggles or face mask
  - Respiratory protection

- Spray applications should be carried out in accordance with the Safe Work Australia *Code of Practice for Spray Painting and Powder Coating* (SWA 2020) or relevant State or Territory Code of Practice.

- The storage of the assessed chemical should be in accordance with the Safe Work Australia *Code of Practice for Managing Risks of Hazardous Chemicals in the Workplace* (SWA 2023) or relevant State or Territory Code of Practice.

- A copy of the Safety Data Sheet (SDS) should be easily accessible to workers.

Conclusions

The Executive Director is satisfied that the risks to human health or the environment associated with the introduction and use of the industrial chemical can be managed.

Note:

1. Obligations to report additional information about hazards under s 100 of the *Industrial Chemicals Act 2019* apply.
2. You should be aware of your obligations under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Supporting information

Chemical identity

CAS number	119345-04-9
CAS name	Benzene, 1,1′-oxybis-, tetrapropylene derivs., sulfonated, sodium salts
Molecular formula	Unspecified

Additional chemical identity information

The assessed chemical is an unknown or variable composition, complex reaction product or biological material (UVCB) and has a purity of approximately 96%.

Relevant physical and chemical properties

Physical form	White powder
Density	972 kg/m^3 at 20 °C
Vapour pressure	< 1.33 x 10^{-8} Pa at 20 °C
Water solubility	> 1,000 g/L at 20°C, 8.3 pH
Ionisable in the environment	Yes
p*K*$_a$	pK_{a1} ≥ -0.68 to ≤ -0.53 at 25°C
	pK_{a2} ≥ -0.91 to ≤ -0.24 at 25°C
log K_{ow}	≤ -2.68 at 20°C
log K_{oc}	4.54 – 4.81 *

*Tested on a suitable analogue

Human exposure

Workers

Reformulation

The assessed chemical in liquid form at less than 50% concentration is incorporated into final coatings products via two main steps: production of emulsion polymers or resins and further reformulation of emulsion polymers or resins into the final coating products in liquid form.

During formulations of emulsion polymers or resins, the assessed chemical at less than 50% concentration will be pumped into the closed emulsion polymerisation reactor along with other ingredients such as monomers and additives. The finished emulsion polymer or resin containing the assessed chemical at less than 3% concentration will then be filled into 1,000 L or ISO tanks via closed pipes and transfer lines.

At the specialised coating product formulation facilities, emulsion polymers or resins containing the assessed chemical at less than 3% concentration will be pumped into closed mixing vessels through automated processes and combined with fillers, extenders, pigments, and other components to create the final coating formulations. The completed coating products containing less than 3% of the assessed chemical will then be packaged into 20 L to 1,000 L plastic containers using closed pipes and transfer lines. These production processes are expected to be conducted under local exhaust ventilation. According to the applicant, worker exposure is expected to be minimised through the use of PPE such as long-sleeved clothing and/or coveralls, impermeable gloves, eye protection, and safety shoes.

During reformulation activities, dermal and ocular exposure of workers to the assessed chemicals at less than 50% or at less than 3% concentration may occur during the connection and disconnection of lines blending, quality control analysis, and cleaning of equipment and the product filling process. According to the applicant, exposure of workers during reformulation activities will be minimised through the use of PPE such as long-sleeved clothing and/or coveralls, impermeable gloves, eye protection, and safety shoes, and through the use of local exhaust ventilation.

Cleaning products, as per the applicant, are generally formulated in a closed mixing vessel. The assessed chemical at less than 50% concentration will be either automatically pumped into the closed mixing vessel from a plastic drum or IBC container, or it may be manually added through a manifold and metering system from a drum or storage vessel via pump. The final product containing the assessed chemical at less than 3% concentration is then automatically packed into containers varying from 0.5 L plastic bottles to 205 L drums either by gravity feed from the mixing vessel or by pneumatic filling. According to the applicant, worker exposure is expected to be minimised through the use of PPE including splash-proof goggles, chemically resistant gloves, boots, aprons, or other protective clothing, as well as appropriate respirators when required. In addition, adequate ventilation will also be implemented to prevent worker exposure.

Given the low vapour pressure of the assessed chemical, minimal inhalation is expected, if no mists/aerosols are formed.

Professional End Use

Finished coating products containing the assessed chemical at less than 3% concentration are typically applied to substrates by experienced personnel and professional workers under controlled conditions. For industrial paint and lacquer coating applications, the coatings are primarily applied using brushes and rollers. While spraying and dipping are also possible methods for applying coating products, these methods are not commonly used particularly considering that the main application is in the construction industry. Workers may experience dermal, ocular and inhalation exposure to the assessed chemical at a concentration of less than 3% during the application of coatings. According to the applicant, these workers are expected to wear PPE, including long-sleeved clothing, boots, chemical-resistant gloves, and goggles. Once applied to the substrate, the assessed chemical is expected to be encapsulated within the dried polymeric layer of the coating, thereby will not be available for further exposure to workers or professional painters.

The cleaning products containing the assessed chemical at less than 3% concentration, in most cases, need to be diluted 20-24 times with water prior to industrial Clean in Place application, depending on the type of surface to be cleaned, the soil loading, and the type and method of application. Once diluted, the cleaning product containing the assessed chemical will be automatically pumped into all closed pipes or containers and vats through the closed CIP cleaning system to clean all blending facilities or equipment. Workers may experience dermal, ocular and inhalation exposure to the assessed chemical at a concentration of less than 3% during the reformulation of cleaning products. According to the applicant, workers in industrial plants will also wear splash-proof goggles, chemically resistant gloves, boots, aprons, or other protective clothing, as well as appropriate respirators when necessary.

A small proportion of the assessed chemical (less than 10% of annual importation volumes) will be available for use in institutional and household toilet cleaning formulations, specifically as a thickened bleach toilet cleaner product. Professional workers will generally apply the cleaning product containing the assessed chemical at less than 3% concentration either as a liquid stream (such as a wash or squeeze bottle) or as a liquid cleaner to soak on the surface for a while and then flushing the toilet or using a toilet brush for cleaning before flushing.

Health hazard information

Toxicokinetics

The metabolism of the assessed chemical was investigated *in vitro*, in a non-guideline study conducted with liver microsomes collected from laboratory rats and human donors using the radiolabelled assessed chemical. Metabolic processing of the radiolabelled assessed chemical was notably more pronounced in human liver microsomes (~40% parent recovered) than in rat liver microsomes (~60% parent recovered). This enhanced metabolic conversion corresponded with the formation of aliphatic chain dihydroxylated metabolites, detected exclusively in human microsomes (~5% of initial substrate concentration), while monohydroxylated metabolites were detected in both human (~38% of initial substrate concentration) and rat (~14% of initial substrate concentration) liver microsomes.

Acute toxicity

Oral

In a non-guideline acute oral toxicity study, 3 female Fischer 344 rats were administered the assessed chemical as a single dose of 2,000 mg/kg bw via oral gavage. The animals were

observed for 14 days after administration. All animals survived until the end of the 14-day study period. Clinical signs indicative of systemic toxicity consisted of faecal and urine soiling, salivation, chromorhinorrhea, decreased activity, and thin appearance. The clinical signs were first observed two hours post dose and persisted through test day four. All animals gained weight over the two weeks observation period. The acute oral median lethal dose (LD50) of the assessed chemical was determined to be greater than 2,000 mg/kg bw.

Dermal

In a non-guideline acute dermal toxicity study, the assessed chemical was applied as a single dose of 2,000 mg/kg bw to the clipped trunks of 2 male New Zealand White rabbits under an impervious occlusive bandage for 24 hours. The animals were observed for 14 days after application. All animals survived until the end of the 14-day study period. All animals showed the expected body weight gains over the study period. The acute dermal median lethal dose (LD50) of the assessed chemical was determined to be greater than 2,000 mg/kg bw.

Corrosion/Irritation

Skin irritation

In a non-guideline study, the neat, assessed chemical was tested for skin irritation using 1 male New Zealand White rabbit. The neat chemical was applied to the ear (0.1 mL), and to intact skin (0.5 mL) and abraded skin (0.5 mL) on the abdomen in one male New Zealand White rabbit. A single 24-hour, occluded application of the undiluted test substance to the skin of the ear produced no irritation.

Five consecutive single daily, occluded applications of the undiluted test substance for 24 hours to the intact abdomen site produced very slight erythema after the last application. Three consecutive single daily, occluded application of the undiluted test substance for 24 hours to the abraded abdomen site produced very slight erythema on test day two through to test day five. The study was terminated 72 hours after the final dose. No clinical signs indicative of systemic toxicity were observed. The information provided is not adequate to consider classifying the chemical using the GHS criteria. However, the limited information indicates that the assessed chemical is not corrosive to the skin. Under the conditions of this study, the assessed chemical could be slightly irritating to the skin.

Eye irritation

The assessed chemical was tested for eye irritation using 3 male albino New Zealand rabbits (OECD TG 405). A single application of the undiluted test substance (0.1 mL) to one eye of each rabbit produced effects on cornea, iris, and conjunctivae. The corneal injury was seen as opacity (maximum grade 1 or 2) and epithelial damage (maximum 90% of the corneal area). As a result of the corneal injury, pannus (neovascularisation of the cornea) was apparent at days 7 or 14 after instillation in two animals. The corneal changes have resolved within 14 or 21 days in two animals but persisted in one animal until termination. Irritation of the conjunctivae (redness, chemosis and discharge) which had completely resolved within 14 or 21 days in two animals but also persisted in one animal until termination. The mean conjunctival redness/chemosis/irritation scores at 24, 48 and 72 hours were 2.7/3.0/2.0, 2.7/2.7/1.67 and 2.3/1.67/1.44, respectively. The corneal injury had resolved within 14 or 21 days in two animals but persisted in one animal until termination. Iridial irritation (grade 1) was observed, which had completely resolved within 24 hours or 7 days. Considering the severity of the eye changes observed in the study, the assessed chemical is classified as a Category 1 eye irritant (H318: Causes severe eye damage) according to GHS criteria.

Sensitisation

Skin sensitisation

One *in chemico* assay on analogue chemical 1, two in vivo studies on analogue chemical 2, and a Human Repeat Insult Patch Test study on the assessed chemical at 15% were provided.

A direct peptide reactivity assay (DPRA) was provided on an analogue chemical at 45.2%. DPRA is an *in chemico* method and aims to address the first key event (KE) (molecular initiation) of the Adverse Outcome Pathway (AOP) for skin sensitisation (OECD TG 442C). Based on the peptide depletion results from the analogue chemical incubated with cysteine and lysine peptides, the mean percentage depletion values of cysteine and lysine peptide resulting from the test material were 0.0% and 8.3%, respectively. Therefore, under the conditions of this study, the analogue chemical at 45.2% concentration was negative in the DPRA, indicating no protein binding activity.

The skin sensitisation potential of an analogue chemical was assessed using the guinea pig maximisation test (GPMT) in 10 female Dunkin Hartley albino guinea pigs (OECD TG 405). An intradermal induction was applied at 0.5% and 1% concentration in Freund's complete adjuvant. A topical induction was performed at 50% concentration of the analogue chemical. Two weeks after the epidermal application, all animals were challenged with epidermal application of 20% and 50% concentration of the test substance. A second challenge was performed one week later with epidermal application of 5% and 10% concentration of the test substance. No positive skin reactions were reported during the challenge phases. Under the conditions of this study, the analogue chemical was not considered to be skin sensitising.

The skin sensitisation potential of an analogue chemical was assessed using the Buehler test in female albino Dunkin-Hartley guinea pigs (OECD TG 406). Twenty animals were treated with 75% concentration of an analogue chemical in distilled water under occlusion at the same site for 6 hours once a week for a total of 3 exposures (days 0, 7, and 14). The animals were challenged with 75% concentration of the test substance in distilled water under occlusion for 6 hours on day 28. Adverse reactions were not noted following induction with the test substance. Similarly, challenge with the test material did not result in allergic skin reactions in any of the treated animals. Under the conditions of this study, the test substance was reported to be non-sensitising.

Based on the negative skin sensitisation results of the analogue chemicals, the assessed chemical is not considered to be a skin sensitiser.

The skin sensitisation potential of the assessed chemical was tested in a human repeat insult patch test (HRIPT) study in 50 subjects (25 male and 25 female), conducted according to the method of Shelanski and Shelanski (Shelanski, 1953). The assessed chemical, as a 15% aqueous solution, was applied 5 times a week for 3 weeks to the subjects. Two to three weeks after induction, a challenge application was made to each person at the same site. According to the test method, a skin sensitisation potential is noted if the response during the challenge phase is greater than the response observed during the induction phase. None of the 50 subjects displayed a response in challenge phase greater than observed during the induction phase. The study concludes that, under the conditions of the HRIPT study, the assessed chemical at 15% concentration is not likely to produce skin sensitisation.

Repeat dose toxicity

Oral

In a non-guideline repeat dose oral toxicity study, the assessed chemical was administered to Beagle dogs (n = 4/sex/dose, except the highest dose with 2 males and 4 females) via diet for two years at 34, 65, 128, and 319 mg/kg bw/day. No clinical signs of toxicity, mean body weight gain changes, haematology parameters, and mortalities were observed in animals treated with the assessed chemical at up to 128 mg/kg bw/day. Reduced mean body weights gains were noted in the 319 mg/kg bw/day group in both sexes (mean body weight gain decreased by 29.9% in males and 25.7% in females compared to control animals of the same sex). The liver function tests with bromsulfophthalein dye retention (at 12 months) and of transaminase activity (at 12 and 24 months), showed no change when compared to the control group. No increase in absolute kidney weights, haematological parameters, serum urea nitrogen determinations, and gross and microscopic examination of the tissues was observed in the 319 mg/kg bw/day group. Under the conditions of this study, the no-observed-adverse-effect level (NOAEL) was established as 128 mg/kg bw/day.

In a non-guideline repeat dose oral toxicity study, the assessed chemical was administered to rats (strain not specified) (n = 30/sex/group) via diet over a two-year period at concentrations of 15, 50, 150, and 500 mg/kg bw/day. No clinical signs of toxicity, difference in food consumption, mortality or changes in haematology/coagulation parameters, organ weights, and gross and microscopic examination of the tissues were observed throughout the treatment period at all tested concentrations of the assessed chemical. At 24 months, the average body weight of females in the 500 mg/kg bw/day group was significantly lower than in the control group of the same sex (194 g average body weight for the 500 mg/kg bw/day group; 240 g for the control group). The male rats in this group showed a slighter, statistically insignificant growth retardation (351 g average body weight for the 500 mg/kg bw/day group; 364 g for the control group). Under the conditions of this study, the NOAEL in female rats was established as 150 mg/kg bw/day.

Genotoxicity

The assessed chemical was found to be non-mutagenic in a bacterial reverse mutation assay using *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and *Escherichia coli* strain WP2*uvr*A (pKM101), with or without metabolic activation (S9-mix) (OECD TG 471). No significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains at any tested concentration (initial assay: 1.53, 5.1, 15.3, 51, 153, 510, 1,530 and 5,100 µg/plate; confirmatory assay: 159.375, 318.75, 637.5, 1,275, 2,550 and 5,100 µg/plate), with or without metabolic activation (S9-mix).

The assessed chemical was found to be non-mutagenic in a mammalian gene mutation assay in the hypoxanthine-guanine phosphoribosyl transferase (Hprt) locus in Chinese hamster ovary (CHO) cells, with or without metabolic activation (S9-mix) (OECD TG 476). No significant increase in mutation frequencies was observed at concentrations from 75 to 300 µg/mL in the absence of S9-mix and concentrations from 400 to 900 µg/mL in the presence of S9-mix.

The assessed chemical was also found to be non-mutagenic in a Mammalian Chromosomal Aberration test using rat lymphocytes, with or without metabolic activation (S9) (OECD TG 473). No statistically significant increases in the proportion of polyploid or endoreduplicated metaphase cells were observed after 4 hours exposure period at any tested concentration, with (6.1, 164.2, and 492.7 µg/mL) or without (54.7, 164.2, and 1478.2 µg/mL) metabolic

activation (S9). The assessed chemical also showed no mutagenic properties after 24 hours exposure at any tested dose (54.7, 164.2, and 492.7 µg/mL), without metabolic activation.

Carcinogenicity

Carcinogenicity of the assessed chemical was tested as part of a non-guideline repeat dose toxicity study in Beagle dogs (see above). The assessed chemical was administered to Beagle dogs (n = 4/sex/dose) via diet for two years at 34, 65, 128, and 319 mg/kg bw/day. No significant lesions or tumour growth was observed in the tissues from dogs at the highest treatment group (319 mg/kg bw/day). Based on the results from the highest treatment group, the tissues of the groups administered 128 mg/kg bw/day and below were not assessed.

The carcinogenicity of the assessed chemical was also assessed as part of a non-guideline repeat dose toxicity study in rats (see above). Rats (n = 30/sex/group) were fed diets containing the assessed chemical over a two-year period at concentrations of 15, 50, 150, and 500 mg/kg bw/day. Records of mortality and incidence of tumorous growths showed no relationship to the inclusion of the assessed chemical in the diet of rats.

Overall, under the conditions of the studies the assessed chemical is not considered to be carcinogenic.

Reproductive and development toxicity

In an extended one-generation reproductive toxicity study (OECD TG 443), the assessed chemical was administered to Crl:CD(SD) rats (n = 25/sex/group except n = 30/sex/6,000 ppm group) via their diet at dose levels of 0, 1,000 ppm, 2,400 ppm and 6,000 ppm. The assessed chemical was administered to F_0 male rats continuously in their diet for a minimum of 70 days prior to mating and continuing through the day before euthanised (minimum of 17 weeks). F_0 female rats were administered the assessed chemical continuously in the diet for a minimum of 70 consecutive days prior to mating and continuing throughout mating, gestation, and lactation until euthanised. The offspring selected for the F_1 generation were administered the assessed chemical following weaning until euthanasia (postweaning day 91) and following the reproductive assessment. The females selected for the F_2 generation were administered the test diet following weaning through post-natal day (PND) 42. For F_0 and F_1 females and F_1 and F_2 pups, the concentration of the assessed chemical was reduced by 50% during the lactation and postweaning (day 21-35) periods, respectively, to accommodate the higher caloric demands due to milk production and rapid pup growth rates.

For the F_0 generation, there were no treatment-related effects on survival clinical observations, thyroid hormone, clinical pathology parameters, organ weights, gross observations, or histopathology findings noted in males and females.

In the 6,000 ppm male group, a treatment-related statistically significant lower mean body weight gain without corresponding effects on food consumption was noted (up to 8.3% lower than controls). Due to the magnitude of change in body weight and absence of effects on survival at this concentration, effects on body weights were not considered adverse.

For females in the 2,400 and 6,000 ppm groups, treatment-related lower mean body weight gains, without corresponding lower mean food consumption, were also noted (up to 6.8% and 11.7% lower than controls, respectively), on Gestation Day (GD) 20. However, in females in the 2,400 and 6,000 ppm groups, the body weight effects were attributed to the lower mean numbers of implantation sites (pre-implantation loss) and consequently fewer mean numbers of pups born noted in these groups.

No test substance-related effects were observed on F_0 sperm parameters (mean epididymal sperm numbers and sperm production rate, sperm motility, or sperm morphology) in males at any dietary concentration.

A statistically significantly lower mean numbers of implantation sites and pups born was observed at 2,400 and 6,000 ppm compared to the control group. Similar effects were reported at these concentrations in the F_1 generation. Mean numbers of post-implantation loss in these groups, however, were comparable to the control group. Therefore, the lower mean numbers of pups born in the 2,400 and 6,000 ppm groups were due to the lower mean numbers of implantation sites (pre-implantation loss), and not post-implantation loss. This conclusion is further supported by the similar gestation indices in the 2,400 and 6,000 ppm F_0 groups (96.4% to 100.0%) compared to the control group (100.0%).

There were no treatment-related effects on survival in the F_1 generation, and there were no treatment-related clinical observations at any concentration. No treatment-related effects on organ weights or histopathology in the F_1 generation were observed.

The mean numbers of pups born (9.9 and 7.2 pups/litter) and live litter sizes on postnatal day (PND) 0 (9.8 and 7.1 pups/litter) at 2,400 and 6,000 ppm, respectively, were lower than the control group (14.3 and 14.2 pups/litter, respectively). In addition, lower mean postnatal survival was reported in the 6,000 ppm group during PND 0–1 (90.4% per litter), and consequently during birth to PND 4 (88.3% per litter) compared to the control group values (99.6% and 98.0% per litter, respectively). Although the difference in postnatal survival during PND 0–1 was primarily attributed to two dams – each delivered one pup only and with subsequent total litter loss on PND 1, the above differences were considered test substance-related and adverse by the study author. No treatment-related effects of the assessed chemical in these groups on mean postnatal survival were reported during PND 4–21.

There were no test substance-related effects on mean male and female F_1 pup body weights, mean body weight gains, mean anogenital distance, F_1 oestrous cyclicity, pre-coital intervals, reproductive performance (male and female mating and fertility, male copulation, and female conception indices), and the process of parturition at any dietary concentration.

A treatment-related and adverse longer mean gestation length was observed at 6,000 ppm (22.7 days) compared to the control group (22.0 days).

In the 6,000 ppm group, only 10 gravid females delivered live pups, while the other six females in this group failed to deliver live pups. To a lesser extent, 2 of 17 gravid females in the 2,400 ppm group also failed to deliver live pups. This higher post-implantation loss in the 2,400 ppm and 6,000 ppm groups was considered test substance-related. This was further supported by the differences in gestation indices in the 2,400 and 6,000 ppm groups (88.2% and 62.5%, respectively) compared to the control group (100.0%).

An adverse clinical eye finding (missing left eye) was observed for two pups from two litters in the 6,000 ppm group on PND 21. Macroscopic examination also revealed a test substance related and adverse eye findings (missing eye/optic nerves) in two F_1 males at 6,000 ppm group on PND 21, which corresponded with the clinical observation data.

During the F_2 generation, there were no treatment-related effects on survival of females in the F_2 generation. Mean F_2 female body weights, body weight gains, food consumption, food efficiency, and age at first occurrence of oestrus were unaffected by the treatment. There were no test substance-related effects on mean body weight and body weight gain in F_2 pups during the preweaning period or on anogenital distance (absolute and relative to cube root of pup body weight) when evaluated on PND 1 at any dietary concentration.

The mean numbers of pups born (9.9 and 6.7 pups/litter) and live litter sizes on PND 0 (9.7 and 6.6 pups/litter) at 2,400 and 6,000 ppm, respectively, were lower than the control group (12.9 and 12.7 pups/litter, respectively).

Test substance-related and adverse clinical eye findings (partial or complete closure, enophthalmus) were noted for nine pups from four litters in the 6,000 ppm group on PND 21. Macroscopic examination also revealed adverse eye findings (small eyes, missing eyes, enophthalmus, missing optic nerves, and/or dilated ventricles of the brain) in five F_2 males at 6,000 ppm on PND 21 which corresponded with the clinical observation data.

Following weekly clinical examination, adverse eye findings (complete closure, enophthalmus) were reported for five F_2 females in the 6,000 ppm group during PND 28 to PND 42. At the scheduled F_2 female necropsy on PND 42, four females at 6,000 ppm had missing eyes, missing optic nerves, and/or dilated ventricles of the brain. The other F_2 female with ocular-related clinical observations did not have corresponding necropsy findings.

There were no test substance-related macroscopic findings in F_2 pups that were found dead or culled. No internal findings that could be attributed to test substance exposure were observed in the 1,000 and 2,400 ppm groups. There were no test substance-related effects on mean absolute or relative organ weights for F_2 females at any dietary concentration.

Based on lower mean numbers of implantation sites (pre-implantation loss) for F_0 females at concentrations of 2,400 and 6,000 ppm, as well as a longer gestation period at 6,000 ppm, a NOAEL of 1,000 ppm, equivalent to dose levels ranging from 62 to 91 mg/kg bw/day, was established by the study authors for F_0 female reproductive toxicity.

Based on pup survival (lower mean number of pups born and live litter sizes) in F_1 litters at 2,400 and 6,000 ppm, a dietary concentration of 1,000 ppm, equivalent to dose levels ranging from 62 to 91 mg/kg/day for F_0 females was established as the NOAEL for F_1 neonatal toxicity.

In a developmental toxicity study (OECD TG 414), the assessed chemical was administered to time-mated female New Zealand White rabbits (n = 24/group) via their diet continuously at dose levels of 0, 500, 1,500 and 4,000 ppm (equivalent to 0, 18, 56, and 118 mg/kg bw/day) during Gestation Days (GD) 7–29.

Four females in the 4,000 ppm group were euthanised on GD 18 or 19 due to reduced food consumption (≤ 41 g/day) for 4 consecutive days. All other females survived to the scheduled necropsy on GD 29.

A lower (17%) mean body weight gain with corresponding reduced mean food consumption (25%) were observed only in the 4,000 ppm group. Although the difference was not statistically significant, it was of a magnitude that the study authors considered it as adverse.

No treatment-related changes in adjusted body weight changes, food utilisation, and gravid uterine weights were noted in any of the treatment groups.

No treatment-related macroscopic findings were observed at any dose level at the scheduled necropsy. Mean foetal body weights were significantly lower (13.2%) as compared to the control group in the highest treatment group (4,000 ppm). Intrauterine survival and foetal morphology at 500, 1,500, and 4,000 ppm and intrauterine growth at 500 and 1,500 ppm were unaffected by the treatment.

Based on lower mean body weight gain with corresponding reduced mean food consumption at the highest tested dose (4,000 ppm), the NOAEL for maternal toxicity was determined to be

1,500 ppm (56 mg/kg bw/day). Based on the lower foetal body weights at the highest tested dose (4,000 ppm), the NOAEL for developmental toxicity was also determined to be 1,500 ppm (56 mg/kg bw/day).

In a developmental toxicity study (OECD TG 414), the assessed chemical was administered to time-mated female Crl:CD(SD) rats (25/group) via their diet continuously at dose levels of 0, 850, 2,500 and 7,500 ppm (equivalent to 0, 57, 170, and 443 mg/kg bw/day) once daily during Gestation Days (GD) 6–20.

There were no mortalities or treatment-related changes in clinical signs, or organ weights. Furthermore, macroscopic and microscopic examination did not reveal any findings that were related to treatment with the assessed chemical at up to the highest tested dose (7,500 ppm).

Lower mean absolute body weight (11.4%, statistically significant) as compared to the control group was noted only at the highest test dose (7,500 ppm) at the end of the study on gestation day (GD) 21. Furthermore, a lower mean gravid uterine weight (13.3%), adjusted body weight (10.2%), and adjusted body weight gain (32.7%), as compared to control group, were also noted only at the highest test dose (7,500 ppm). These effects were considered test substance-related and adverse.

Statistically significantly lower mean food consumption (18.2%) was noted during the entire exposure period (GD 6-21). Statistically significantly lower mean foetal body weights (11.9%) were noted in the highest dose level (7,500 ppm). However, intrauterine survival and mean anogenital distances were not affected in any treatment group.

Based on reduced maternal body weights, body weight gains, food consumption, and foetal body weights reported at the highest dose (7,500 ppm), a NOAEL of 2,500 ppm (173 mg/kg bw/day) was established for maternal and prenatal developmental toxicity.

Therefore, based on the effects observed in the reproductive and developmental toxicity studies at a dose level greater than 56 mg/kg bw/day, the assessed chemical is classified as Category 2 reproductive toxicant (H361fd: Suspected of damaging fertility. Suspected of damaging the unborn child) according to GHS criteria.

Environmental exposure

The assessed chemical will be imported into Australia to be reformulated into end-use products to be used in a variety of applications including coatings as well as in cleaning products such as industrial Clean in Place and domestic toilet cleaning products.

Reformulation and repackaging will occur in both closed and open processes. Significant released of the assessed chemical to the environment are not expected during, transport, storage or reformulation. Any liquid waste containing the assessed chemical will be recycled or directed to wastewater, while solid waste will be disposed of as industrial trade waste.

The assessed chemical will be included in a wide range of products, resulting in a variety of exposure scenarios.

Consumer and professional end use of the assessed chemical in industrial Clean in Place and domestic toilet cleaning products as cleaning agents is expected to result in the release of the assessed chemical “down the drain” and into the sewers. Consequently, the assessed chemical will be treated at sewage treatment plants (STPs) before release to surface waters.

Use of the assessed chemical in coating products will not result in direct release of the assessed chemical into the environment. Conservatively, for these uses, it is assumed that up to 5% of the annual import volume of the assessed chemical may be disposed of to sewers, down drains, or to the ground from spills, waste disposal and washing of application equipment.

Environmental fate

Partitioning

The assessed chemical is readily soluble in water (water solubility > 1,000 g/L at 20°C), immobile in soil (log K_{oc} = 4.54 – 4.81) and is surface active (surface tension = 37.3 mN/m at 20°C). Therefore, it is expected to partition to the phase boundary when released to the environment.

Due to its very slight volatility (vapour pressure = 1.33 x 10^{-8} Pa) the assessed chemical is not expected to partition to air.

Degradation

Based on its measured degradation in water, the assessed chemical is categorised as persistent.

A supplied OECD TG 309 test on simulated mineralisation of the assessed chemical in water, showed a total recovery of 92.1 – 97.8%, in 28 days, indicating little mineralisation of the assessed chemical and a half-life greater than 60 days. Therefore, the assessed chemical is persistent in water.

This is supported by a ready biodegradation screening test conducted using a modified OECD TG 302B Zahn-Wellens test, showing a 58% primary biodegradation (based on loss of parent chemical) and 21% mineralisation in 28 days (based on loss of dissolved organic carbon (DOC)) for the assessed chemical.

Supplied experimental data from an OECD TG 307 test evaluating the mineralisation of the assessed chemical, in four soil samples, showed calculated half-lives ranging between 8.47 days to 70.4 days. These half-life values are below the domestic threshold of 180 days for persistence in soil, therefore, the assessed chemical is not considered persistent in soil.

Bioaccumulation

The assessed chemical does not have the potential to bioaccumulate based on its measured bioconcentration factor (BCF) values.

A supplied BCF study conducted using OECD TG 305 test demonstrated BCF values of 2.3 – 3.3 L/kg that are below the domestic threshold for bioaccumulation. Hence the assessed chemical is categorised as not bioaccumulative.

Predicted environmental concentration (PEC)

A combined predicted environmental concentration (PEC) for Australian waters was calculated assuming 5% of the 36,000 kg used in coatings is released to sewers and 100% of the 3,000 kg used in cleaning agents will be directly released to sewers resulting in 12.3% of the total introduction volume being released to sewers.

The total volumes of the assessed chemical used in coatings and cleaning products released to sewers are expected to be 1,800 kg and 3,000 kg respectively:

The calculation of the PEC is detailed in the table below:

Total Annual Import Volume	39,000	kg/year
Proportion expected to be released to sewer	12.3 %	
Annual quantity of chemical released to sewer	4,797	kg/year
Days per year where release occurs	365	days/year
Daily chemical release	13.14	kg/day
Water use	200.0	L/person/day
Population of Australia	25.423	Million
Removal within STP	0 %	Mitigation
Daily effluent production	5,085	ML/day
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River	2.58	µg/L
PEC - Ocean	0.26	µg/L

The extent to which the assessed chemical is removed from the effluent in sewers is based on its physicochemical properties, modelled by SimpleTreat 3.0 (Struijs, 1996), and is estimated to be 0%. Therefore, 5% of the introduction volume used in coatings and 100% of the introduction volume used in cleaning agents are estimated to be released to the aquatic environment.

The cumulative PEC of the assessed chemical that will be released to river and ocean waters from the assessed chemical's end uses are calculated to be 2.58 µg/L and 0.26 µg/L respectively.

Environmental effects

Effects on aquatic Life

Acute toxicity

The following measured median lethal concentration (LC50) and nominal median effective concentration (EC50) values for model organisms for the assessed chemical and its suitable analogues were supplied by the applicant:

Taxon	Endpoint	Method
Fish	96 h LC50 = 1.28 mg/L	*Pimephales promelas* (flathead minnow) OECD TG 203 Semi-static conditions Nominal concentration
Invertebrate	48 h EC50 = 1.64 mg/L* (adjusted for 100% active ingredient)	*Daphnia magna* (water flea) Immobility OECD TG 202 Static conditions Nominal concentration
Algae	72 h ErC50 = 15,939 mg/L*	*Scenedesmus capricomutum* (Green algae) Growth rate OECD TG 201 Static conditions Mean measured concentration

* Conducted on a suitable analogue

Chronic toxicity

The following nominal No observed effect concentrations (NOEC) and nominal 10th-percentile effective concentration (EC10) values for model organisms for the assessed chemical and its suitable analogues were supplied by the applicant.

Taxon	Endpoint	Method
Fish	33 d NOEC = 0.15 mg/L	*Pimephales promelas* (flathead minnow) Mortality OECD TG 203 Flow through conditions Nominal concentration
Invertebrates	21 d EC10 = 1.74 mg/L	*Scenedesmus capricomutum* (Green algae) Growth rate inhibition OECD TG 201 Static conditions Nominal concentration
Algae	72 hr NOErC = 297.5 mg/L*	*Scenedesmus capricomutum* (Green algae) Growth rate OECD TG 201 Static conditions Mean measured concentration

* Conducted on a suitable analogue

Effects on terrestrial Life

The following measured no effect concentration (NOEC) values for model organisms were supplied for the assessed chemical:

Taxon	Endpoint	Method
Earthworms	28 d NOEC = 1,000 mg/kg soil dry wt	*Eisenia fetida* (earthworm) Body weight OECD TG 222 Static conditions Nominal concentration
	56 d NOEC = 566 mg/kg soil dry wt	*Eisenia fetida* (earthworm) Reproduction OECD TG 222 Static conditions Nominal concentration

Predicted no-effect concentration (PNEC)

A predicted no-effect concentration (PNEC) of 15 µg/L was calculated for the assessed chemical in the aquatic environment. This value was derived using the most conservative endpoint value for fish (0.15 mg/L). An assessment factor of 10 was applied to this endpoint as acute and chronic toxicity data were provided for all three trophic levels (EPHC, 2009).

Categorisation of environmental hazard

The categorisation of the environmental hazards of the assessed chemical according to the *Australian Environmental Criteria for Persistent, Bioaccumulative and/or Toxic Chemicals* (DCCEEW, 2022) is presented below:

Persistence

Persistent (P). Based on measured degradation study in water, the assessed chemical is categorised as Persistent.

Bioaccumulation

Not Bioaccumulative (Not B). Based on a measured bioconcentration factor (BCF) below 2,000 mg/kg in fish, the assessed chemical is categorised as Not Bioaccumulative.

Toxicity

Not Toxic (Not T). Based on available acute aquatic ecotoxicity values above 1 mg/L and chronic aquatic ecotoxicity values above 0.1 mg/L for all three trophic levels, the assessed chemical is categorised as Not Toxic.

Environmental risk characterisation

Although the assessed chemical is persistent, it does not meet all three PBT criteria. It is hence unlikely to have unpredictable long-term effects (EPHC 2009). An estimate of risk may therefore be determined using the risk quotient method.

Based on the PEC and PNEC values determined above, Risk Quotients (RQ = PEC ÷ PNEC) have been calculated for release of the assessed chemical to water, soil and sediment:

Compartment	PEC	PNEC	RQ
River	2.58 µg/L	15 µg/L	0.172
Ocean	0.26 µg/L	15 µg/L	0.017

For the river and ocean compartments, an RQ less than 1 indicates that introduction of the assessed chemical, in line with the defined scope of assessment, is not expected to pose a risk to the environment. As such, the risk from the assessed chemical can be managed, based on consideration of the environmental hazard characteristics and estimated releases.

References

DCCEEW (2022) Australian Environmental Criteria for Persistent, Bioaccumulative and/or Toxic Chemicals, DCCEEW, accessed 23 Sept 2024.

EPHC (Environment Protection and Heritage Council) (2009), Environmental Risk Assessment Guidance Manual for industrial chemicals, Prepared by: Chris Lee-Steere Australian Environment Agency Pty Ltd, February 2009. ISBN 978-1-921173-41-7.

Shelanski HA and Shelanski MV (1953), A new technique of human patch test, *Proceedings of Scientific Section*, Number 19, May 1953.

Struijs J (1996), SimpleTreat 3.0: a model to predict the distribution and elimination of chemicals by sewage treatment plants, National Institute of Public Health and the Environment.

UNECE (United Nations Economic Commission for Europe) (2017). Globally Harmonized System of Classification and Labelling of Chemicals (GHS), Seventh Revised Edition. Accessed 5 November 2024.

SWA (Safe Work Australia) (2020), Code of Practice: Spray Painting and Powder Coating, Safe Work Australia, Accessed 6 November 2024.

SWA (Safe Work Australia) (2023), Code of Practice: Managing Risks of Hazardous Chemicals in the Workplace, Safe Work Australia, Accessed 6 November 2024.